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Introduction

The Business of Commercialization and Innovation

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ABSTRACT

We focus on the processes and strategies utilized by entrepreneurs to commercialize new technologies, thereby creating significant change and value in new, or existing markets, i.e. innovation. A cross-industry approach utilizes available theories and strategies applicable to commercialization and innovation. Our contribution is to leverage these theories, but augment their application by informed use of design thinking, and lean entrepreneurial principles to create and apply an iterative and unified framework for innovation. The coupling of strategy with informed execution is intended to provide the entrepreneur (or innovator) with an early and evolving understanding of unmet customer and user need, and how to address that need thru offerings from market entry through growth. We also utilize the "jobs to be done" framework to identify opportunity to create value for the customer/user, and for the entire ecosystem in multi-sided, networked markets. Section One covers our methodology, surveys the extant theories, and provides a framework that is applicable to commercialization and innovation in any industry. Also, we describe in Section One the innovation culture that is needed to drive and support innovation. We present our extension of the Balanced Scorecard – the Innovation Strategy Dashboard - as an appropriate methodology to measure innovation in any organization. Section Two is dedicated to applications of these principles and models to emerging opportunities in Biopharma, MedTech and Digital Medicine. Section Two includes a general healthcare industry overview highlighting its evolution and current challenges. We also include contributed articles pertinent to the production side of the healthcare industry, e. g. marketing and product positioning for biopharma, and further extend the role of design thinking to service design in healthcare. These are followed by several mini-case studies applicable to biopharma, MedTech, and digital medicine.

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INTRODUCTION AND OVERVIEW

Most companies seek innovation, but few succeed at bringing new products or services to market while sustaining their innovation pipelines over time. Commercialization can be thought of as the processes utilized to bring a new product or service to market, generally crossing from the laboratory to the development stage to the market entry then growth. We view innovation as an *outcome* whose goal is the creation of significant change and value to new or existing markets. In order to cover markets that may not yet exist, we prefer to use a definition of the market as: 1) the job to be done, 2) the job executors, and, 3) the context. In this two-volume publication, we explore how to achieve innovation for companies spanning the various stages from startup, and product/market development, then progressing to market entry, growth, and maturity. We survey a number of theories and strategies that have become popular for achieving and sustaining innovation over the last few decades and discuss how they can be utilized in practice. These include Disruptive Innovation, Blue Ocean Strategy, Design Driven Innovation, Platform Strategy, and the increasingly important approach taken through use of Open Innovation principles. We also review other concepts and approaches that have been used in the entrepreneurial community to achieve positive innovation outcomes. These include: the lean startup methodology for determining product/market fit achieved by validating hypotheses iteratively; the business model canvas for aligning the organization with the market to create, deliver and capture value; and, with various marketing strategies

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utilized to introduce new products and services to the market and then growing market share.

We find that adoption of the extant strategic theories and tools is not sufficient for success without the parallel development and implementation of a corporate culture (and tool set) that embraces customer/user centricity. That is the original contribution of this monograph. Accordingly, we advocate embedding design-thinking methodologies into the organization as the company/product life cycle evolves not only for the development of products and services, but also for evolving the organizational structure and culture itself. An additional benefit to utilizing design-thinking methodologies is to achieve a better understanding of "what customers want and need". The "wants or needs", articulated or not, often include emotional components that influence economic decision-making factors. Design thinking which explicitly incorporates observation, questioning, experimentation, networking, and associative thinking thereby augments and balances more quantitative marketing methodologies that are most often employed.

Metrics to measure outcomes are an essential management tool. To facilitate the development and implementation of appropriate metrics, we synthesize an "Innovation Strategy Dashboard" that builds on the Balanced Scorecard approach, but we also incorporate metrics and outcomes specific to innovation. This set of metrics can be used to measure progress, and for achievement of broader corporate goals and targets. We recognize that it is important to create and empower a culture of innovation by acquiring and developing the resources, processes and values (culture) of the organization appropriate for the form of innovation sought; disruptive, technology-driven, outcomes-driven, etc.

Our work focuses on merging existing innovation theory with market centered approaches to commercialization, which taken together produces a unified and comprehensive framework for innovation. In that regard, we have created a suite of processes, models, and tool sets, coupled with insights into the organizational framework that underlies organizations that are industry leaders engaged in need- seeking/customer-driven innovation.

The monograph is organized into two sections.

Section One – Bridging Theory and Practice for Commercialization and Innovation – a market-centered perspective for cross-industry applications. Here we take an "industry agnostic" view of building an innovation culture that is "markets first" or customer/user centric. The section is authored by Arthur A. Boni with selected contributions on design thinking from Tim Cunningham and Jean Marie Sloat. The theories and concepts described therein are applicable to most industries, particularly our focus on knowledge-based organizations. These may or may not be technology – driven or enabled.

Section Two – Innovation Practices in Biopharma, MedTech, and Digital Health is dedicated to applications exclusively in the healthcare industry with a focus on the "producer-side" of that industry. We include material as applied to biopharma (the converged pharmaceutical and biotech industry), medical devices and diagnostics, and the emerging sector of digital medicine. Mini case studies are provided in this section that examine commercialization strategies taken from specific innovations in these market sectors. We also include perspectives from the design-thinking community for application of this methodology to healthcare technologies and to service design. The articles in Section Two are contributed from the Special Editor, Arthur A. Boni, and from other authors to illustrate the principles and approaches summarized in Section One. These authors include (alphabetically) Matt Beale, Dario Don Cabrera, Tim Cunningham, Nate DeCarolis, Sarah-Marie Foley, Thanigavelan Jambulingham,Craig Shimasaki, Prakash Thakur, and Ned Uber.

CONTENT

Section One – Bridging Theory and Practice for Commercialization and Innovation – a market-centered perspective for cross-industry applications. This section overviews and summarizes the principles that apply to innovation across multiple industries. This section includes and Introduction (written by Arthur A. Boni), followed by 7 Chapters with authorship noted;

1. Market Immersion and Building the Innovation Culture – A Strategic Perspective, *Arthur A. Boni*
2. The Lean (and Agile), Needs-driven Innovation Process and Approach, *Arthur A. Boni*
3. Leveraging Design Thinking to Understand Articulated and Unarticulated Customer and User Need, *Arthur A. Boni, Tim Cunningham and Jean Marie Sloat*
4. Overview of Selected, extant theories for Bringing Innovation to the Market and Building Sustained Competitive Advantage, *Arthur A. Boni*
5. The Design Culture – Characteristics of Designers and Their Thinking. With sidebar on Citrix, *Tim Cunningham and Jean Marie Sloat with Arthur A. Boni*

6. Incorporating Culture and Metrics into an Innovation Dashboard, *Arthur A. Boni, Tim Cunningham and Jean Marie Sloat*
7. Conclusions and Post Scripts, *Arthur A. Boni*

Section Two – Innovation Practices in Biopharma, MedTech, and Digital Medicine. This section applies the principles presented and summarized in Section One to the production side of the healthcare industry and consists of 7 Chapters. We include biopharma (the converged pharma and biotech segments), MedTech, and digital medicine. We also include a focus on areas of convergence of technology, healthcare, and biopharma as the broader industry has begun adoption of a customer-centric business model that incorporates solutions that merge drugs, devices, and digital technology to impact the entire healthcare system. The 7 chapters are summarized below:

1. **Innovation Principles in the Pharma 3.0 Business Model Paradigm: User-Centric Applications to Biopharma, MedTech, Digital Medicine with Cross Sector Convergence**. This section is an overview that summarizes the challenges of innovating in biopharma and MedTech, and the emergence/evolution of digital health, and convergence of technology and MedTech. Contrast differences and similarities (B2B or B2C vs. B2/5P (patient, physician, provider, payer, and partner – the 5Ps) in a science-driven, regulated market; lean thinking applied to Biopharma; and, managing additional risk factors associated with healthcare innovation such as IP, regulatory, reimbursement, privacy and cyber security. *Arthur A. Boni*

2. **The R&D Marketing Interface in Biopharma and MedTech.** This article highlights the importance of building an extended team that incorporates the expertise needed to guide product development, strategy, and marketing during the development process for biopharma and medtech products. We focus on the importance of marketing at the earliest stages of company formation and product development to shape the product life cycle. Marketing focuses on creating an appealing target product profile (TPP) as a means for ensuring commercial success. We describe a methodology and rationale for creating the TPP to achieve better outcomes for products brought to market. *Thanigavelan Jambulingham, Professor, Haub School of Business, Saint Joseph's University.*

3. **Design Thinking at Daedalus**. Developing solutions for biopharma/medtech/digital medicine products and services requires a cross disciplinary team to engage a broad cross section of the healthcare ecosystem. Unlike technology products, the ecosystem is more complex and involves patients, physicians, providers, payers, and partners. Each of these parties must be engaged to understand overall market need, requirements, and constraints. This article focuses on design thinking as part of the overall strategic and marketing resources that can be used to observe, question, and understand the needs of the entire ecosystem. The interdisciplinary commercialization team can thereby reach a common understanding of the outcome of each component of the job to be done from the perspectives of each party, and thereby achieve overall product/market fit for the product design and overall business model components. This chapter outlines the perspective and approach of Daedalus, a full-service, interdisciplinary product development firm with decades of experience working with medtech companies. The article is complementary and supplementary to the materials on design thinking in Part One of this monograph/special edition. It also covers several examples as mini cases that are pertinent to healthcare from projects undertaken by Daedalus, Inc. from their industry portfolio of achievements. *Matt Beale, President of Daedalus, Inc., and Tim Cunningham, Founder and former President of Daedalus Design, and Adjunct Professor at Carnegie Mellon University.*

4. **Service design for delivery of user-centered products and services in healthcare.** In this paper, the essential elements of service design are covered, since service is an important element in the evolving Pharma 3.0 business model where patient centricity is important. Also, we recognize that the evolving healthcare system stresses the importance of interaction throughout the ecosystem. We then go on to provide examples as seen a number of mini-case studies. *Sarah-Marie Foley, Master of Science in Interaction Design, School of Design, Carnegie Mellon University*

5. **Innovation, Commercialization and Business Development Strategies for Three-Dimensional-Bioprinting Technology: A Lean Business Model Perspective.** This chapter focuses on translational medicine in regenerative medicine based on research and commercialization at Carnegie Mellon

University and the University of Pittsburgh. It covers the commercialization and innovation approach for a novel 3D Bioprinting invention originating at CMU with multiple applications including tissue-based drug discovery. *Prakash Thakur (University of Pittsburgh, Hillman Cancer Center), Dario Don Cabrera, Nate DeCarolis, and Arthur A. Boni (all with Tepper School of Business at Carnegie Mellon University).*

6. **Medrad Innovation Journey - from start-up to Industry Standard: Mountain Climbing, Spelunking, Over the Horizon Home Runs, and creating a "DC-3 Effect"**- Medrad was a pioneer and is now a current leader in the medical imaging industry; which, after acquisition is now part of Bayer Radiology. In this case study, we describe the customer and user centric processes employed by the company to identify underserved and unserved market needs, and to commercialize its technology. Also, the company culture is described along with their innovation principles, in most cases before they were popularized in the literature. *Arthur E. "Ned" Uber, III*, Fellow at Bayer in Pittsburgh.

7. **Moleculera Labs Story: Lessons in a Capital Efficient Start-Up** – This case study focuses on Moleculera Labs, an emerging biotechnology R&D company focused on clinical diagnostics and identification of new therapeutic targets. The article covers the commercialization and innovation strategy applicable to an emerging biotech company that has utilized patient centric, capital efficient, and lean principles for development, validation, and go to market strategies. The case study includes key factors that are essential for successful biotechnology companies. These range from management of technology, market, and team/leadership risks to those risks dealing with financing, regulatory, IP, and reimbursement issues. *Craig Shimasaki, President and CEO of Moleculara Labs*

Section One

Bridging Theory and Practice for Commercialization and Innovation – a Market-Centered Perspective for Cross-Industry Applications

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INTRODUCTION

Growth thru innovation is a stated goal of organizations ranging from startups to growth companies and to mature, well-established Fortune 500 companies.[1] Different forms of innovation may be pursued depending on the strategic goals of the organization. Smaller entrepreneurial companies, typically startups or "skunk works operations" are well suited to pursue disruptive innovation, or alternatively to create new "blue ocean" markets by exploiting the uncontested space while not unconstrained by an existing (and perhaps profitable) business model that is not well suited to the new markets – Christensen's Innovators Dilemma.[2] Conversely, incumbents often dominate sustained or incremental innovation for growth of existing markets or customer bases. We highlight below that need- seeking/customer-driven innovation is predominant in the Silicon Valley innovation ecosystem. Given this success, why is a broader segment of the US economy not following this model?

Our central thesis is that in order to pursue needs-driven innovation, the culture of the organization must incorporate a user-centric focus. Further, the resources and processes of the organization should include the user-centricity inherent in the design thinking methodology. We combine the lean startup methodology with design thinking for success in organizations of any size or in any industry. We have developed a framework for an Innovation Strategy Dashboard to guide the inspiration, ideation, and implementation of effective innovation in organizations. We suggest that a balanced scorecard following Kaplan and Norton (outlined later in this article)) can be used to communicate and measure an innovative design thinking strategy throughout the organizational culture. *Balanced scorecards tell you the knowledge, skills, and systems that your organization will need to build and sustain the strategic capabilities and processes to deliver value.* To be successful, clearly understood measures of success and metrics must be established to measure progress.

Innovation is a goal that most companies seek, but which few achieve and sustain. Failure rates are high, prompting Ulwick[1] and others to state that asking customers what they want (using customer-driven thinking) or extrapolating from their own perspective is not the best way to identify new product (or service) categories. Failure rates for new products and services are in the 50% to 90% range depending on the source, and also on the particular form of innovation. Therefore, determining why potential innovation failure rates are

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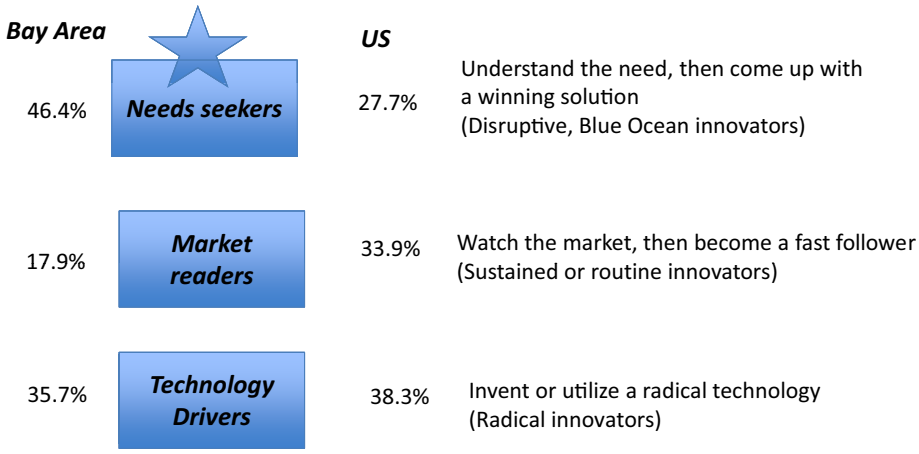

Figure 1: What kind of an innovator do you want to be?

so high is a very relevant question to be posed. Ulwick advocates adopting a needs-first (or outcome driven) approach where the need (along with the importance and level of satisfaction of the job executor) is identified prior to proposing a solution. Many, including the authors would adopt that position. Therefore, a prerequisite for this "needs first" paradigm is for the innovator to be able to define or quantify "the job to be done". Ulwick[1], Christensen,[2] Levitt,[3] and others have advocated the jobs to be done framework recognizing that there are underlying needs, many of which are being addressed in other ways. We take the position that the user-centered, design thinking methodology and associated "tool set" is a necessary element for any organization (or startup) to adopt in order to identify and understand the jobs to be done, thereby increasing the innovation success rate by filling existing need that often is not recognized explicitly.

A recent study titled "The Culture of Innovation – What Makes San Francisco Bay Area Companies Different"[4] found that Bay Area (BA) companies practice "need seeking innovation strategies" more prevalently than the broader US industry base. They found that 46.4% of BA companies utilize a needs-driven (or need seeking) approach vs. 27.7% for the overall company survey, c. f. Figure 1. In their study, they also identified two other categories of companies pursuing innovation – 1) market driven companies, and 2) technology driven companies. Market driven companies are basically "fast followers" who have the resources to enter and compete once the entry markets have been established by the need seeking organizations, that have also reduced the risk of entry into new markets or product categories. On the other hand, technology driven companies pursue radical or disruptive technologies, which take some time to evolve into innovations via the development and validation of suitable business models.

Pisano,[5] in a recent HBR article (June 2015), suggests that in the pursuit of innovation, an organization should choose how much to focus their strategy on technological innovation vs. business model innovation. He has developed a 4-category matrix to describe 4 identifiably different modes of innovation – disruptive, routine, radical, and architectural. He suggested that there are two axes to consider – technology innovation and business model innovation. This approach is similar to that taken by Verganti[6] in his classic text, "Design Driven Innovation". His axes are technology and meaning. In this article, we approach innovation by combining the business strategic approach, with emphasis on a user-centric methodology incorporating design-thinking methods. For illustrative purposes, we have created an innovation model chart as illustrated in Figure 2.

Along the Performance and Technology axis we show:

- Market Pull or Sustained innovation for leveraging the continued evolution of existing technology in the lower left hand corner, &
- Radical or technology push to leverage technology breakthroughs in the upper left-hand quadrant

Along the business model axis (or change in meaning axis) as we show:

- Disruptive innovation (and Blue Ocean innovation), both of which are largely innovations in the business model of the organization.

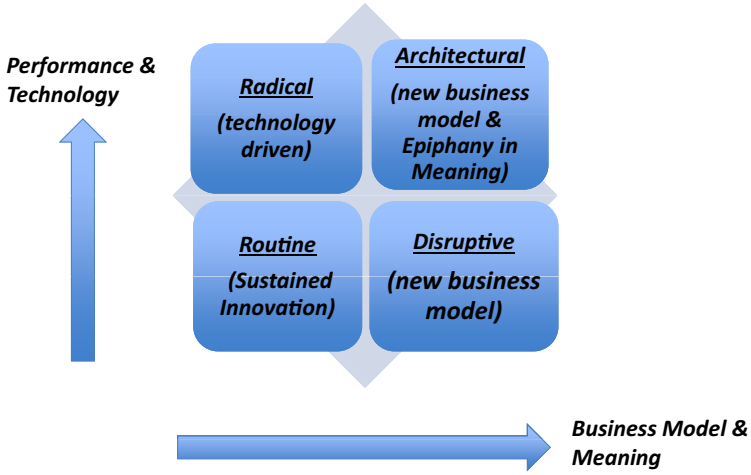

Figure 2: An innovation map (adapted from Verganti and Pisano)

- In the upper right corner, we see where both technological and business model evolution lead to design driven innovation (a change in meaning as termed by Verganti)[6] or architectural innovation as termed by Pisano.[5]

Christensen[2, 7] has pointed out the difficulty of changing the business model of any organization to pursue disruptive innovation (the Innovators Dilemma), leading to the pursuit of sustained innovation as the predominant mode of innovation in larger organizations. Sustained innovation is largely constrained and driven by extensions of existing business models that are possible by the evolution, improvement and diffusion of the underlying technology over time into new market segments. This model is well illustrated by the product life cycle (PLC) concept popularized by Geoffrey Moore[8] in "Crossing the Chasm". Pisano titles this mode of innovation as Routine and it occupies the lower left box of Figure 2. In the design literature, Verganti[6] has used the term "design-driven innovation", which we prefer since one is indeed changing the meaning of the product, service or platform.

Pisano also notes that the root cause of failure to sustain innovation is "that companies fall into the trap of adopting the best practices that are in vogue, or aping the exemplar innovator of entrepreneur of the moment, instead of following a more strategic approach to innovation based on theory". We would add, being design driven is always a good approach to take and provides the necessary customer/user centricity required for success. We take the position that both innovation strategies and corporate cultures must evolve to stay ahead of the competition or to "leap frog" it into new dimensions. The business model must evolve to meet both articulated and non-articulated customer need using design-thinking methods to continuously create, deliver and capture value for existing and new customer market segments.

The CEO provides leadership for organizational change and innovation. However, a framework for communication of the vision, empowering creativity in the organization, and developing metrics for measuring its progress and effectiveness is required. Later in this paper we suggest use of the 8-step framework proposed by Kotter to drive change in organizations.

Building an organization where innovation culture and strategy are aligned and focused around the needs-driven, or outcome driven approach is consistent with the design thinking methodology that is advocated and practiced by the design community. Companies that have adopted this approach to innovation, utilize a design-driven culture that fuels the development of products and services that customers and users adopt and embrace as discussed above. Success is achieved because the job to be done is well understood through the use of customer and user market research tools. This approach also permits the incorporation of both functional and emotional value in the context of experience/service, therefore leading to higher profitability.

It is quite common to read about the power of design thinking in industry today. Design thinking is prevalently recognized as a methodology and set of tools to devise strategies and to manage/lead change, c. f. Harvard Business Review (September 2015),[9] "The Design of Business" (Martin),[10] and "Change by Design" (Brown).[11] The recent publication in the New York Times by Steve Lohr[12] states that "IBM is challenging its stodgy reputation by hiring thousands of designers and turning them loose on conventional thinking".

Our survey summarizes and uses a combination of design thinking and innovation theory to enhance the innovative output of any organization, and to the evolution of the organization to respond to or create change in a world in need of new products and services. We adopt design thinking as a key component, but link that with a set of metrics to measure progress to achieve broader corporate goals and targets. It is not enough to understand the principles of disruptive innovation, open innovation, or other theories. It is important to create and empower a culture of innovation by acquiring and developing the resources, processes and values (culture) of the organization appropriate for the form of innovation sought; disruptive, technology-driven, needs-driven, etc. These focus on opportunity identification and development. The culture is more in the domain of leadership and team processes. Recall that the entrepreneurial process consists of following components: Opportunity, Resources, Team and Leadership.

There is a cohort of successful companies that have gone beyond the current strategic frameworks. They use design thinking not only for products and services, but also for the development and evolution of the organization itself; see Martin,[10] and Brown.[11] For example, Martin has reviewed companies like Apple, Procter & Gamble, Target, Google, & IDEO. As noted earlier, one key observation is that the change is indeed led by the CEO or another C-level officer in the company (reporting to the CEO) who empowers the organization as a whole to participate effectively. In this article, we recognize the impact of active executive level leadership that links strategy with culture and execution, resulting in the potential for a continuous stream of products and services that meet and anticipate customer demand. To expand on the work of Brown and of Martin, we include a mini case as a sidebar highlighting an approach taken by Citrix. We also include later in this article a summary titled The Design Culture - Characteristics of Designers and Their Thinking that summarizes our Top 10 characteristics that we derived from visits with several Silicon Valley/Bay Area organizations that have incorporated design thinking into their innovation cultures, including LinkedIn, Capital One, Intuit and others.

In order to combine design thinking with the metrics commonly used in modern organizations, we adopt a framework combining metrics with organizational culture. We use the term "The Innovation Dashboard" that is built on the Balanced Scorecard approach of Kaplan and Norton.[13] We suggest that the dashboard can be used to manage innovation, linking strategy with execution. Much like the Business Model Canvas promoted by Osterwalder,[14] this Dashboard is designed to "get everyone on the same page" regarding innovation – employees, customers, shareholders and investors, and partners. The Dashboard links vision and strategy with business processes: learning and growth, financial performance, and customers/users. It is described more fully below.

CHAPTER ONE – MARKET IMMERSION AND BUILDING THE INNOVATION CULTURE - A STRATEGIC PERSPECTIVE

Peter Thiel[15], in his recent book titled "Zero to One; Notes on Startups, or How to Build the Future" points out that one should ask the question – "what valuable company is no one else building"? Both uniqueness (differentiation) and the ability to anticipate or drive change come to mind in this regard. In order to answer this question, we have to observe customers, interview potential users, companies, and understand the evolving socio-economic, and technological (SET) factors that are driving, or can be used to drive change and opportunity. Where is opportunity and how can we create unique, differentiable, and lasting solutions that deliver value?

In this context, Scott Cook,[16] founder of Intuit has stated, "observation is the big game changer". He also has stated that identification of the job to be done is the most important concept popularized by Clayton Christensen. In effect, an innovator identifies those important, but not well-served jobs by observing and/or questioning potential users. Christensen[2] also goes on to say that solutions to jobs are "rented" until a better solution comes along to replace the current product or service, and which time that solution is "fired". Often, we find it is useful to frame the job to be done using the following framework: *when___, I want to ___, so I can* ___(see the following reference for more info on this framework: https://jtbd.info/replacing-the-user-story-with-the-job-story-af7cdee10c27. Just fill in the blanks to describe the job relevant to your current situation. Note that there may be multiple jobs as product evolve from a single market segment to broader markets.

Recognize that each job has a functional, emotional, and social component to be satisfied. Some needs can be *articulated* and some needs are *unarticulated* by the user. Later in this article, we point out that the need is not only important, but the lack of satisfaction of getting those important jobs done is also essential to identifying real opportunity that will be adopted by users and customers.

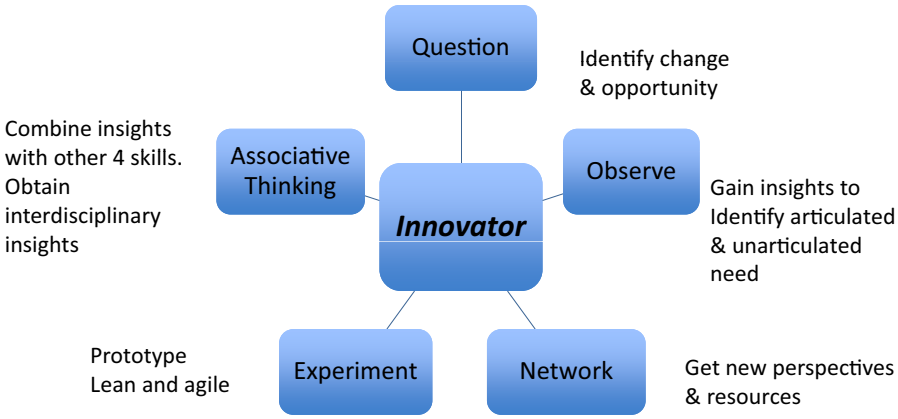

Figure 3a: The behavioral skills of successful innovators [adapted from The Innovators DNA; Dyer, Gregorson, and Christensen (2011)]

In a recent book by Dyer, Gregerson and Christensen[17] titled "The Innovators DNA", the authors provide a very important perspective on building and growing an innovation culture. They have identified **5 skills or traits of innovators**, and observation, noted above is one of them (See Figure 3a):

1. Questioning
2. Observing
3. Experimenting
4. Networking
5. Associative thinking (or, connecting the dots - especially via collaborative, interdisciplinary teams)

Our perspective is that any organization seeking to innovate should look for individuals who possess these skills or traits, and to build these into the organizational culture where they can collaborate. Wagner,[18] in his book "Creating Innovators" observes that innovation prevails where expertise, creative thinking skills, and motivation/fit come together (see Figure 3b). The innovation culture is comprised of: interdisciplinary collaborative teams that possess these skill sets; embracing and supporting team work; encouraging interdisciplinary problem solving; empowerment; and incorporation of intrinsic incentives, c. f. Boni, Weingart and Todorova (2014).[19] We would add that there are several additional important components:

- Having an outward focus while seeking opportunities to create value for the organization continuously
- Ability to incorporate lean and agile processes into the adaptive and iterative learning process

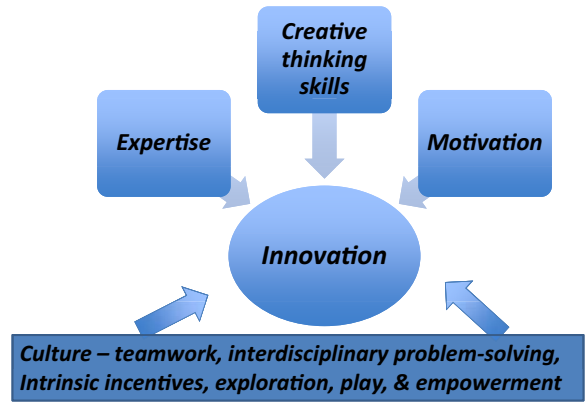

Figure 3b: Creating a culture of innovation skill, will, & fit [Adapted from "Creating Innovators", Wagner (2012)]

- Incorporating the skills or traits of "design thinkers" to complement and supplement the Innovators DNA (outlined above.

In an HBR article,[20] "How GE teaches teams to lead", the authors list a number of dimensions of an effective organization (well beyond the startup stage) as taught in the GE leadership development program at Croton. These include challenge/involvement, freedom, trust and openness, time for ideas, playfulness/humor, conflict (but not too much), idea support, debate, and risk taking.

So, in addition to building a team with the appropriate characteristics and skill sets as listed above, the processes employed would be built on a framework of lean and agile methodologies. Test and pivot until the product-market fit is demonstrated and business model validated.

One further perspective and example on building an innovation culture comes from Google. The summary of

Recent interviews with Silicon Valley investors identifies the following traits for the potential CEO – 1) persistence (tenacity); passion (motivation or drive); 2(integrity, savvy (clarity of thought); 3) ability to communicate and tell a story; 4) confident, but with humility (leave ego at the door); 5) curiosity.

Google's 9 principles is paraphrased from Fast Company (Kathy Chin Leong, 10.20.13)

1. Innovation comes from anywhere in the organization
2. Default to open – be receptive to ideas from the outside
3. Focus on the user – revenues will come
4. Think 10x better, not 10% - have a grand vision and make significant change with products, add significant value
5. Bet on technical insights (from your expertise) – but, have resources to execute as the technology evolves
6. Ship and iterate – get it to market and then improve
7. 20% time – ability for all employees to pursue new ideas and "get paid for it"
8. Fail well – be willing to take a risk and to fail fast (and learn from the experience)
9. Have a mission that matters

We have already suggested, and will also make this point later in the article that to build an innovation culture, the CEO must be personally engaged and leading the change. We would add that requirement to the above list from Google as a 10th principle (and if you examine Google it is observed that the CEO and senior executive team does indeed provide leadership for change – note the structural changes that have occurred with the recent organizational changes and formation of Alphabet.

Change in the face of crisis or challenge in the marketplace or internally is even more difficult to lead. Kotter,[21] in his book, "Leading Change" has proposed one strategy (the sense of urgency) and 4 tactics for leading change. First of all, most organizations can become naturally complacent, so sometimes it is necessary to create a real sense of urgency (that is the key to the strategy). Then the four tactics are to "bring the outside in", behaving with urgency every day, finding opportunities in crisis, and dealing with those who say no to anything dealing with change of the status quo (the "no no's" as they are appropriately named by Kotter).

He then goes on to describe in some detail his famous 8-step process (and as noted by Kotter, these steps need to be followed in order).

1. Establish a sense of urgency
2. Create a guiding coalition
3. Develop and vision and strategy
4. Communicate the change vision
5. Empower broad-based action
6. Generate short-term wins
7. Consolidate gains and produce more change
8. Anchor new approaches in the culture

Once the innovation culture is in place and an outward focus is established, the organization should be able to identify and pursue potential opportunities through business environmental analysis that would include scanning to detect change or to identify where change can be made to occur through company initiatives. In our work, we adopt the definition of market as follows:

Market = Job to be done + executors + context.

The approach taken in "Seeing What's Next" by Christensen[2] suggests employing three, iterative steps of analysis and assessment:

Step One – Looking for Signals of change

- Look for non-market and SET factors (Social, Economic, Technology) that may be driving change, or can be used to drive change (entrepreneurs capitalize on change, or drive change)
- Look for three customer groups – underserved (or not served at all except for DIY solutions), non-consuming, and over served (these are the customer groups that can power disruptive innovations)
- Identify which jobs need to be done differently – by identifying their importance and the lack of satisfaction of the executors with current solutions in the market of interest to the entrepreneur/innovator
- Forecast to project the future – observe, question, experiment, network, connect the dots (brainstorm, use 6 Hat Thinking[22] or other ideation exercises, interview experts, crowd source, etc.).

Step Two – Identifying the Competitive Set, or Competitive Battles

- Who has the "Sword and the Shield" to fight competitive battles? Which incumbents or others in the competitive set are expected to choose "flight" or to fight?
- Utilize RPV (Resources, Processes and Values) to analyze likely competitive

responses – Porter's 5 forces shape the industry competitive landscape) [23,24]

R – tangible and intangible, controlled or accessible
P – ways of doing business, skills to transform assets into value
V – values, motivations, and culture of the organization as noted above

- Analyze the industry structure:
  - The rate of product diffusion along the Product Life Cycle (PLC) for this industry. Is it long cycle or slow cycle? (c.f. Figure 8.)
  - Is it regulated? Are there industry standards?
  - Are there channel access issues?
  - Are there costs/barriers when switching from present solutions? How slow or fast have other innovations been adopted?
  - What other barriers to entry may exist?
  - If you are contemplating competing with a platform in a networked ecosystem, how are you going to build collaborations with the existing power players and their stable ecosystem of users, customers, complementary products and services?

Step Three – Making Strategic Choices

- Analyze the value chain to determine where the most value can be created and differentiated
  - As appropriate consider partnerships and alliances as you choose your place in the value chain.
- Identify the target entry market, i. e. where is the best market fit (most compelling need) for a potential product or service fit (the market entry point – MEP)?
  - What is your Minimum Viable Product (or Service) for the MEP?

At this point the innovator should be focused on creating a highly-differentiated product with a sustainable competitive advantage. Thiel[15] refers to this as "creating a monopoly", and he lists 4 methods for doing so:

- Proprietary technology, e. g. patents
- Network Effects to drive large scale adoption, and that leverage the platform and its ecosystem
- Economics of scale on the supply side, or demand side
- Branding

To the above list, we also suggest for consideration: customer/user switching costs; high capital barriers; and, channel access control.

CHAPTER TWO - THE LEAN (AND AGILE), NEEDS-DRIVEN INNOVATION PROCESS AND APPROACH

In this section we address a process that can be employed to address the question – what do customers (and users) want, whether or not they can articulate their need. We use two frameworks in this regard. The first is the design thinking approach, from the work of Brown,[11] Martin[10] and others. The second is the lean startup process promoted by Ries,[25, 26] Blank[27, 28] and others. These lean principles are applicable to any company, or any size, and in any industry - of course with some level of adaptation appropriate for the complexity of the industry, e.g. life sciences, energy, etc. The overall perspective is user/customer-centricity and application of agile or adaptive methods, to achieve capital efficient innovation. Following Brown, see Figure 4, we recommend a first step of divergence, where choices or options are identified (in lean startup methodology, these are hypotheses regarding the business model components, customer need, product features – product/market fit. The second and next step is then convergence, where choices are made or hypotheses validated.

The approach that we have developed can occur in multiple stages or iterations as shown in Figure 5 (ITERATIVE INNOVATION), and in a more "cartoon-like fashion" in Figure 5a. In Figure 5 we also include several tools used by designers that can be used at each stage as one progresses thru the evolution from an idea to a validated opportunity (see the sidebar in a subsequent

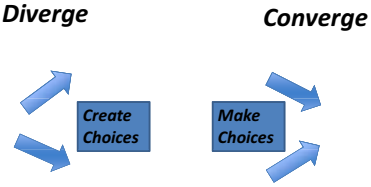

Figure 4: Convergent and Divergent Thinking [Ref - Tim Brown, "Change by Design" (2009)]

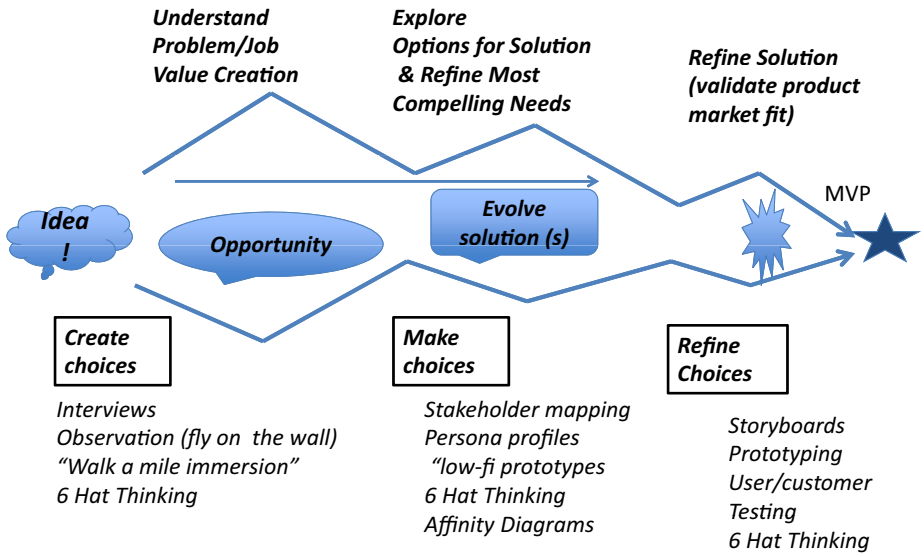

Figure 5: Iterative, Lean Innovation

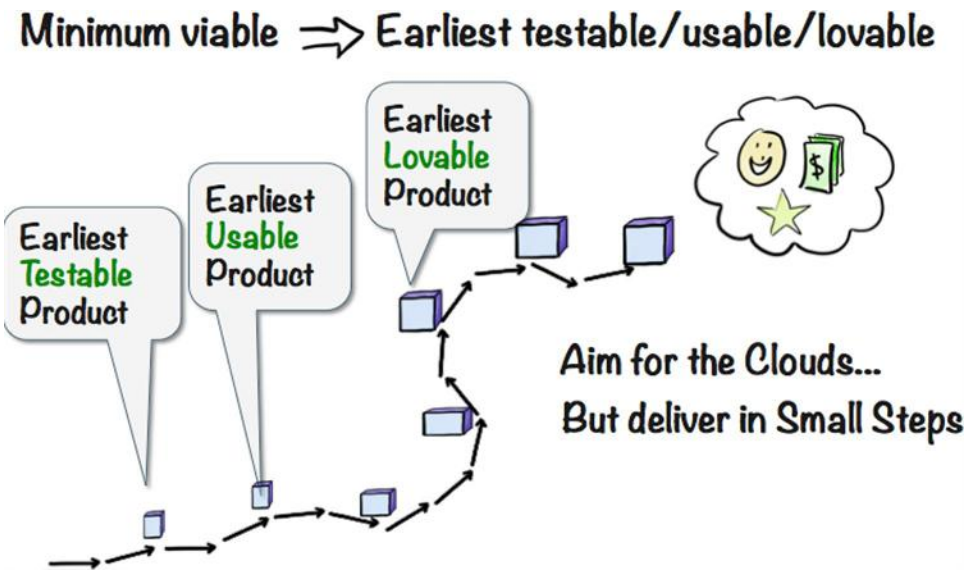

Figure 5a: Path to the Minimum Viable Product
Source: http://blog.crisp.se/2016/01/25/henrikkniberg/making-sense-of-mvp

section for more detail on the design tool kit and methodologies available).

Key elements of the lean approach include:

- Strategy is hypothesis driven
  - Use business model canvas for testing critical elements of the business model early before spending on the development of solutions that the marketplace will not value
- Validated, customer-centric learning
  - Product and customer selection to validate product/market fit
  - Iterative product releases to test MVP
  - Supports development of a repeatable and scalable business model

The approach in effect utilizes the scientific method of making and validating hypotheses sequentially, and then progresses by validating or invalidating these hypotheses via customer/user interaction. Invalid hypotheses are then reframed via the feedback for subsequent validation thru retesting, i.e. pivoting. Short and repeated cycles are

then taken as noted above and as suggested in Figures 4 and 5.

The iterative process shown in Figure 5, 5a, provides our framework for identifying compelling customer/user validated need, a Minimum Viable Product or service (MVP) to fill that need, and a target market entry point (MEP) that comprises the target entry market where the customer/user need if greatest – who has the most "pain" and is willing to pay. All of these can be iterated and validated by use of the Business Model Canvas of Osterwalder to develop and validate the business model elements needed for creating, delivering and capturing value (see below).

A few precautions are in order here regarding the MVP concept that is used extensively in the literature, especially within the lean startup community. While both MVP and MEP are conceptually simple concepts, they comprise the essential elements of the customer validation process. What comprises a validated entry product and market segment for the specific innovation? We suggest that the jobs to be done concept is very useful here. Once the job to be done is identified and validated via user interviews and/or observations, a product/solution that contains the minimum feature set required to do the most important job components would comprise the MVP. Those job executors that have the most compelling need to get this job done comprise the entry market (MEP). Our advice is don't try to get the whole job done with a complete product upon first product launch. Use the entry product to validate the business model prior to expanding the features and market segments comprising a broader set of job executors. Recall one of the Google principles: "ship and iterate – get it to market and then improve".

In contemplating these concepts, we suggest considering the points made in a very useful blog site for (http://blog.crisp.se/2016/01/25/henrikkniberg/making-sense-of-mvp). The author suggests that you should aim high, but deliver incrementally (and iteratively). The following summary is extracted from the blog (Fig. 5a). The authors of the referenced blog provide the following good advice:

"Avoid "Big Bang" delivery for complex, innovative product development. Big Bang here refers to building a complete product and then delivering it! Do it iteratively and incrementally with the needs of the customer/user in mind. You knew that already. But are you actually doing it?"

"Start by identifying your 'skateboard' – the earliest testable product. Aim for the clouds, but swallow your pride and start by delivering the skateboard. (The skateboard is used here as a metaphor for an incremental path to a multi-wheel vehicle as the eventual product envisioned)."

"Avoid the term MVP". Or at least, be more explicit about what you're actually talking about. Earliest testable/usable/lovable is just one example; use whatever terms are least confusing to your stakeholders."

Similarly, MEP should be reserved for that market segment identified as the Market Entry Point (MEP) thru customer interviews and testing where the earliest testable product overlaps with and fills the most compelling need of the customer or user. In effect the MEP is identified thru the customer or user development process and is again iterative.

Once the MVP and MEP are identified, we move to identify strategies for entering and dominating the target market and then growing to subsequent market segments and evolving the offering to dominate downstream segments. Our perspective, as noted is to approach this from the entrepreneurial mindset in partnership with the design community to really understand the user perspective. However, at this stage it is important to develop a strategy for growing the market, so we will next go on to summarize the principal strategies that can be employed to create and grow a sustainable competitive advantage. Below, in Chapter Four, we include brief summaries of Disruptive Innovation and Sustained Innovation, Blue Ocean Strategy, and Open Innovation. We also follow the Outcome Driven Innovation approach promoted by Ulwick[1] and referred to earlier in the article.

CHAPTER THREE LEVERAGING DESIGN THINKING TO UNDERSTAND ARTICULATED AND UNARTICULATED CUSTOMER AND USER NEED

Consider two views of innovation from two perspectives – design and business. From a design perspective, Brown [11]defines innovation as a system described by three overlapping spaces. Along the way, iterative processes are employed by designers that loop back through each of these stages in a multistage, convergent and divergent process. The three stages are succinctly summarized as:

- **Inspiration** - the motivation to find a solution to fill an identified unsolved problem or need, ideation, and implementation
- **Ideation** - generation and testing of various ideas or solutions
- **Implementation** – defining the path that leads to the market

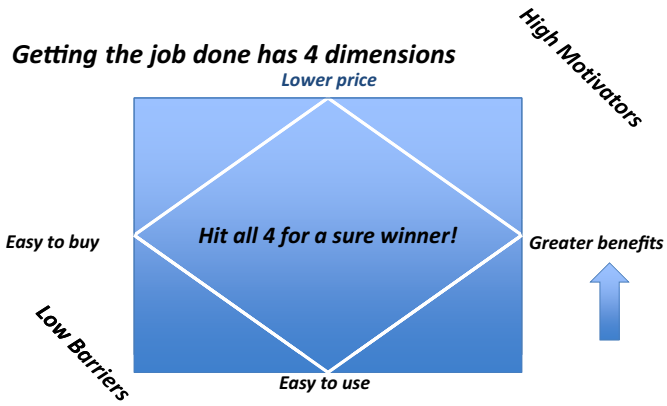

Figure 6: How to pick a sure winner! From Eric Mankin (Christensen group) - HBS

Innovation, from a business perspective, is a process for devising a product or service that profitably addresses unmet customer and user needs, whether they are articulated or unarticulated. So, we can also see three stages here:

- Identifying an unmet market need (both articulated and unarticulated)
- Developing a differentiated solution with a sustained competitive advantage
- Creating a Business Model that creates, delivers to the market, and captures value for the stakeholders of the firm

We have suggested a similar iterative approach to validate each of these stages. An integrated view would suggest that innovation is an outcome whose goal is the creation of significant change and value in new or existing markets.

As we have already discussed, the market is defined as follows:

Market = job to be done + the executor(s) + the context

The market segmentation using this approach utilizes identification of jobs, then the executor(s) that may include multiple parties, and then the context within which the job is done, e.g. in the home, office, automobile, hospital, etc. While doing that, we first identify the components of value that customers/users expect, and how to fill the need and the characteristics of a successful product. Eric Mankin[29] from the Christensen group has developed a very useful model for testing the viability of "a potential winning product" – also applicable to services. While it is appealing to look to a single "goodness factor" or value for which one offering is clearly superior, e. g. price, performance, etc., in reality it's more complex and the value proposition (or value curve) has many dimensions as will be covered later in our summary of Blue Ocean Strategy (BOS). Mankin[29] proposes that if a proposed solution can be shown to excel in 4 dimensions, then the product has the potential to be a winner, c. f. Figure 6. The right-hand side of this chart contains two **motivators for purchase** or adoption- performance, and price or cost. The left-hand side captures two **barriers of adoption**- ease of use, and ease/convenience of purchase. Note that performance can itself have multiple dimensions where value can be created via a value curve a la Blue Ocean Strategy (see below). This "Mankin framework", however, does not effectively address the non-quantifiable factors associated with adoption of a really compelling design or **emotional component** of the adoption decision. We point out the importance of this dimension later in this article.

The iterative approach used in the lean startup process can be used to develop and validate hypotheses as they evolve for each section of the Business Model Canvas c. f. Figure 7. In this section, we'll focus on the "customer" facing side of the Business Model Canvas dealing with target market, value proposition, channels, customer relations, and the revenue model. We'll also consider partnerships that may be required to develop a go-to-market strategy, in addition to the resources, processes, values and costs.

The following pathway for hypothesis development and validation might look like the following, and is adapted from the approach advocated by Aulet[30] in his recent book titled "Disciplined Entrepreneurship":

1. Who is your customer? {Customers}
   - Segment your market by job to be done
   - Select a beachhead market or target market (MEP) – see **Figure 8**
   - What is the size of the MEP market?
   - What is the end user profile and persona of the customer/user?

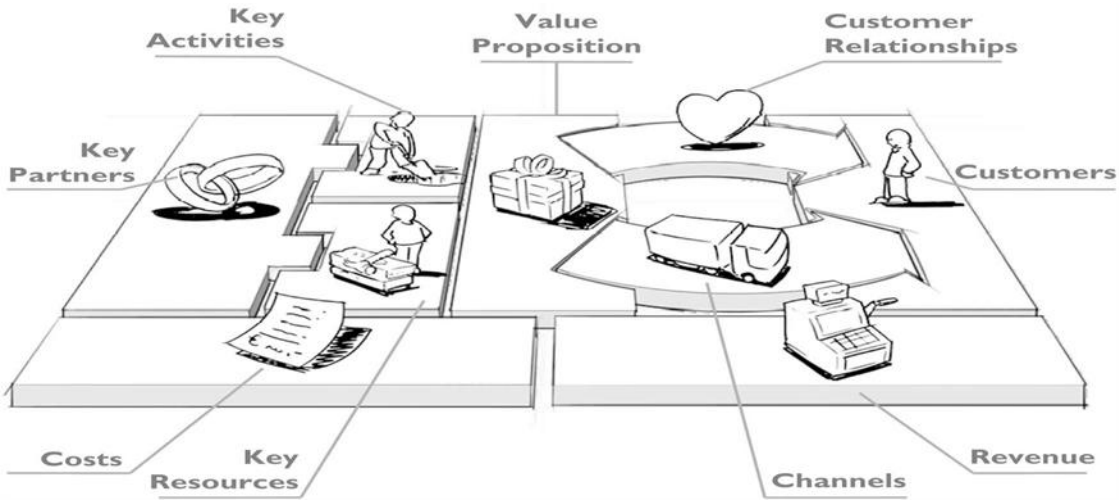

Figure 7: Use the business model canvas to create, deliver, and capture value (Ref: Osterwalder)
Note: Use is as a tool to supplement the BSC and align the business model with strategic goals

2. What can you do for your customer? {Value proposition/ offering}
   - Construct a value proposition and positioning statement
   - What is your key differentiator and sustainable competitive advantage?
   - Construct a high-level specification of your solution and define the features and benefits needed for a minimum viable product (MVP) that addresses the job to be done
   - Develop a life cycle use case for how your solution enables your customer to get the job done
   - Construct a product life cycle (PLC) – see **Figure 8**, and forecast how you will dominate the entry market and then cross the chasm?

3. How does your customer acquire your product? {Channel and Customer Relations}
   - What channels will you use to reach the customer?
   - How do you acquire customers (awareness, consideration, choice, repeat)?

4. How do you make money from your product or service? {Revenue Model}
   - Lay out the elements of your revenue model, ref to Osterwalder, Business Model Generation for various revenue model options for products, services, and platforms.

5. How do you design and build your product? {Resources, Key Processes, Key Activities, Costs}
   - This is dealt with in subsequent sections of this article dealing with the RPV and culture.

6. How do you scale or grow your business into mainstream markets (and cross the chasm)?

Note that the list above does not explicitly address the **Partnership component** of the BMC. Since we adopt and advocate an open innovation approach to building a fully integrated value chain to the market, partnerships can come into many of the stages since partnerships can be used to source technology for innovation, access market channels, manufacture, distribute, provide complementary products or services, etc. *So, partnerships should be identified in parallel with the evolution of each element of the business model canvas.*

Next, we consider the impact of consumer emotions and behaviors on new product adoption - We have identified a number of factors that lead to gaps in the development and adoption of new products and services. We have also presented valid *quantitative decision criteria* for promoting or discouraging adoption, e.g. performance, price, ease of use and ease of purchase. However, even though the developer may "hit" on all of these dimensions, there are emotional and behavioral factors involved in making decisions. So, one should question the rationality of economic decision-making, since the

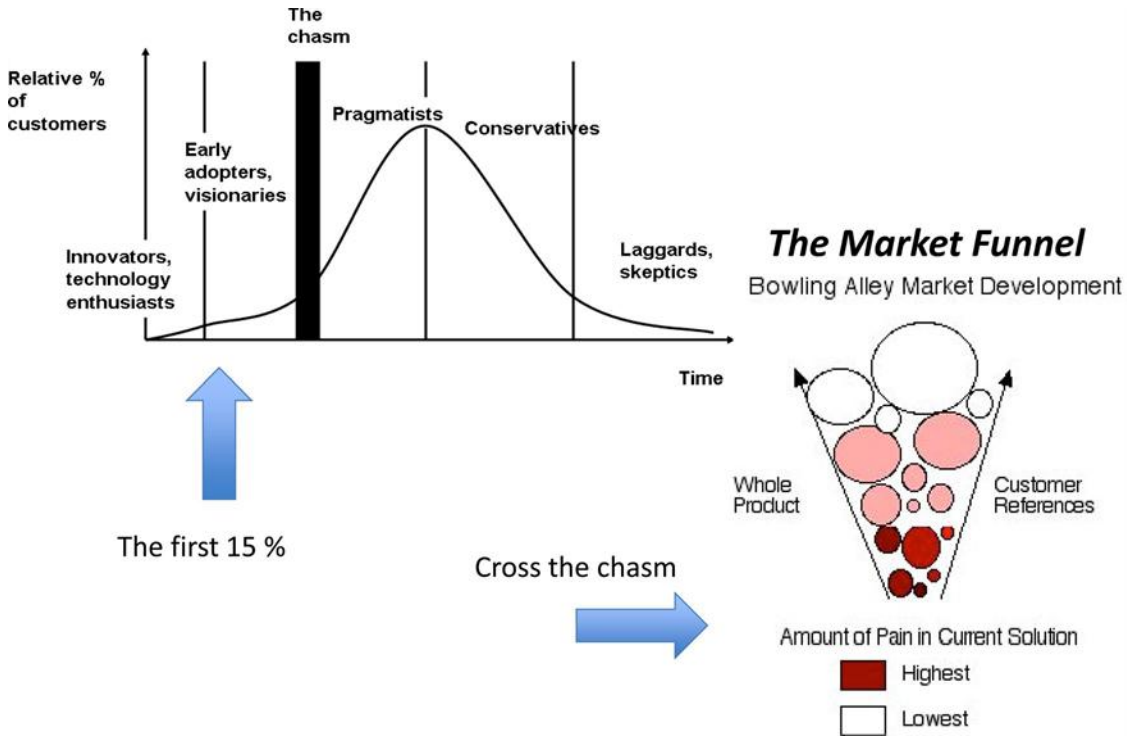

Figure 8: The market funnel and product life cycle (adapted from Moore, crossing the chasm)

literature would support the perspective that more often than not, adoption decisions may be more emotional than based on rational or quantitative criteria – particularly in business to consumer (B2C) markets. Or even in the biomedical markets dealing with the human interface with the product or service, e. g. patient, physician, or support ecosystem.

In order to better understand both rationale and emotional criteria, we suggest that product developers and managers be better connected with the potential customers and/or users in a target market (recall the importance of observation, questioning and experimenting). While many developers indeed develop products successfully for which they have a personal need, their desire for something new and better may not be the same as a third party without those same biases and experiences with their jobs to be done. So, involve the customer in the process and measure not just quantitative reasons for adoption, but identify those more emotional factors as well. Behaviors do not change easily, and in many cases decisions are made "fast, not slow" and the biases are not conscious – c. f. Kahneman,[39] "Thinking, Fast and Slow"! Kahneman[39] provides a framework for the decision-making model as consisting of System One (fast and intuitive), and System Two (slow and analytical) as follows:

- System One – fast, automatic, intuitive, and largely unconscious mode of thinking
  - Uses association and metaphor to produce a quick and dirty decision
  - System One "proposes"
- System Two – slow, deliberative, analytical and consciously effortful mode of reasoning
  - Draws on reasoned choices to make a well informed (analytical) answer or decision
  - This system is also lazy (easy to accept the System One answer)
  - System Two "disposes"

Boatwright and Cagan[40] in their recent book "Built to Love – Creating Products that Captivate Customers", suggest that product emotions should be designed into products and services in parallel with the products or services themselves. Product designers must determine appropriate emotions for their new products (what resonates with the customer/user?); craft an emotion strategy; and, translate the strategy into emotion-based features (emotion touch points). These principles also apply to the design of services as well as products (perhaps even organizations). Donna Sturgess, former Global Head of Innovation at GlaxoSmithKline cited in the forward of the Boatwright and Cagan[40] book

that "consumer response to rational features account for only 15% of all the decisions that we face". She then points out that most decisions are subconscious, and that emotions dominate decision-making. She states that the result of traditional marketing results in a "sense gap". Some key considerations are summarized below:

- Emotion matters in every type of business
- More sensory interaction in customer experience is better than less
- Emotion has to be managed strategically
- Emotion results in increased profit

Kevin Roberts, an "advertising guru" and CEO of Saatchi & Saatchi supports this perspective and states that 80% of buying decisions are made emotionally, not rationally. In the book, "Emotionomics- Leveraging Emotions for Business Success", Dan Hill[41] also demonstrates that emotions do indeed matter and that we must face the rational/emotional split. Managing emotions is a strategic competence that organizations need "to make stronger emotional connections with their customers to achieve long-term, sustainable success".

As noted earlier in this article, innovators and early adopters behave differently than do early majority and late majority or mainstream customers/users. Therefore, building both rational (quantitative) factors and emotional (qualitative) responses into the adoption value proposition must be considered as the product evolves and transitions to mainstream markets. Go-to-market strategies must recognize that adoption follows the sequence: consideration, trying, choice, and repeat or retain. Exposure to multiple customers/users is recommended to explore the reasons for rejection, that may be overcome with perseverance and really understanding the motivation for adoption of a new product or service. Are the biases of the developers the same as the adopter of a new product or service? Perhaps the more innovative product will present more resistance for adoption because it is so different? Smart innovators should prepare for initial rejection. Involve multiple parties in early product testing, and build the emotional connections as suggested by Hill[41.]

CHAPTER FOUR - OVERVIEW OF SELECTED, EXTANT THEORIES FOR BRINGING INNOVATIONS TO THE MARKET AND BUILDING SUSTAINED COMPETITIVE ADVANTAGE

We have previously discussed our perspective and contributions on customer/user centric innovation, the jobs to be done methodology, and use of the coupled design thinking/lean entrepreneurship model to understand market need and opportunity for value creation. These insights set the stage for opportunity identification and development whether the organization is a startup, growing concern, or mature. It is also incumbent on the organization to use an appropriate strategy to create differentiated value, and build a sustained competitive advantage. These objectives are best pursued using validated strategic frameworks that have appeared in the literature over the last few decades.

Most of these theories on innovation are well documented in the literature, but we include brief descriptions of those that we find most useful below for those unfamiliar with them. Consider this to be a literature review with citations provided to those who desire more comprehensive descriptions and for further study.

For creating new markets, the work of Christensen[2,7] and of Kim and Mauborgne[32] may be employed to create **Disruptive Innovations**, or new markets in uncontested space (**Blue Oceans**). The work of Chesbrough[33,34] is noteworthy in the creation of **Open Innovation** business models that can be used to augment and leverage the strengths of the organization with outside sources – inside out, and outside in innovation. Building and leveraging a **Platform Strategy** can be used to create and sustain a sustained competitive advantage. Platforms beyond single products are described most recently by Cusumano[35] as "an architecture" or, technology surrounded by networks consisting of; complementary products and services; a set of users/customers in multiple markets; and, partners.

Disruptive Innovation (DI) in Brief

Christensen and Raynor [36] have published recent articles in the Harvard Business Review to remind the community that the principles and underpinnings of DI are often misunderstood. In fact, many confuse the term disruptive with a new, or "disruptive technology" rather than a disruptive (low cost) business model that employs existing technology, even though that technology is expected to advance over time to enable new features and benefits.

A disruptive innovation provides a "good enough" solution (to be defined by market testing as discussed earlier) that offers new benefits (or values) around simplicity, convenience, and low prices to customers who were overshot at the high end by existing offerings, or who would not consume at all because they lacked skills, wealth, or easy access to available solutions. In order to enter the market from the lower (and less profitable end), the new entrant is required to create a new business model that supports the lower cost and provides access to the new market.

So, disruptive innovations originate in low-end markets, or new-market entry points. Performance can then be increased over time to move "up market" where profitability can increase as new value is added, and eventually challenge the incumbents. Disruptive innovations take time (evolution along the product life cycle to reach mainstream late majority markets).

In the recent Christensen and Raynor[36] articles, they also suggest that neither Uber nor Tesla fit the DI model since, among a few other reasons, they do not target either low end or new market entry points. However, as we discuss below, both Uber and Tesla may be viewed as "changing meaning" as the Design-Driven Innovation community might argue. So perhaps they fit best into that category.

The definitions outlined above can be used to identify hypotheses for customer segments that might be appropriate targets for a disruptive innovator. Overshot at the high end, means that the performance provided by the current solution is more than they are willing to pay for, and/or the solution is too complex to use. Those customers are targets for disruption. Additional targets are those who are not consuming at all, have created "workarounds" to get the job done and therefore do not purchase (or use) the existing solution. Those "who are overshot" at the high end, might be seeking a simpler, less expensive solution, easy to use solution – i.e. they strip out the features and benefits that are not of interest to them or used by them.

So, in summary there are 3 principles involved in DI:

1. **Overshooting Creates Conditions for Disruption**
   - Too much performance for average customer to use
   - Product or service may be too complex or expensive

2. **Disruption Comes from Breaking Rules**
   - Consider offering not good enough along **traditional lines of performance** in mainstream market: simplicity, accessibility, affordability for (less demanding, or unserved) target market

3. **Business Model Innovation Most Often Powers Disruption**
   - Low price point required to serve target market (non-mainstream market) profitably
   - Utilize different value chain (partners, suppliers, channels)

Sustaining innovations are typically pursued by incumbents (established in the market), and target the demanding, higher-end customer. These continue until the high end is "overshot" and those customers may be ripe for disruption.

5 Questions can be asked for Spotting Disruption; c. f. Christensen et al [36]

1. Is the target customer a non-consumer or an overshot customer who will embrace performance tradeoffs for a lower price?

2. Is the company starting as simply as possible instead of trying to solve multiple, complex problems simultaneously?

   a. Think simplicity, convenience, accessibility, affordability
   b. Concept of minimum viable product (MVP)
   c. Can the incumbent improve performance fast enough to keep pace with customer expectations?

3. Does the approach look unattractive to incumbents when compared to other options? Does it disrupt all incumbents or can an existing player enter this market?

4. Has the company found motivated partners and market channels for its strategy?

   a. Does it create new value networks?

5. Is the company keeping fixed costs low to allow flexibility in finding a winning strategy and business model?

Christensen has also developed 6 steps to a "Black Belt" for disruptive innovators. Adoption of these steps (or factors) enable organizations to become "self-disrupters, and are incorporated into our Innovation Dashboard below. One interesting quote is - "an organization's capabilities become disabilities when disruption is afoot." Disruption in any organization needs to cover the following organizational features in order to be successful:

1. An autonomous business unit: the "innovators solution"
2. Leaders have previously led change: experience with commercializing disruptions is important
3. A separate resource allocation process: similar to startup funding tranches and milestones)
4. Independent sales channels: appropriate to reach new markets in a cost-effective manner)
5. A new profit (business) model: need a low cost solution for new markets
6. Unwavering commitment by CEO: leadership at the top is important to enable and facilitate execution

In effect these steps suggest that *entrepreneurial behavior is the key to innovation (as well as understanding that culture is also important – see below).* Start up a new unit, led by an experienced team and CEO, develop and validate a new business model, allocate resources like a venture capitalist (milestone based and with appropriate metrics, e. g. customer validation of product/market fit), etc. For a corporate spinoff, independent sales channels, and a lower cost revenue model would be necessary, and the CEO of the parent organization must be fully on board and supportive of the strategy.

Blue Ocean Strategy (BOS) in Brief

Blue Ocean Strategy was developed and popularized by Chan and Mauborgne [32] in their book published in 2005. The innovator can use the analytical frameworks and tools that they have developed and validated to seek non-customers (their term) thereby creating uncontested market space (the Blue Ocean) rather than competing with incumbents in existing markets for customers (the Red Ocean). To compete in the uncontested market space, a leap in value is created for the company and the customers in the new market space, while reducing cost for the customer. Having just covered DI, the Value Innovation approach should sound like a familiar mantra, but with a different set of tools and methodologies.

Value Innovation requires the simultaneous pursuit of differentiation and creating value along new dimensions in addition to the low cost. The BOS framework builds on that theme which in some sense is like the Verganti approach to create new meaning (see below). However, BOS provides a set of tools that we find are very useful. They include a four-action framework, the eliminate/reduce/raise/create grid to assist the innovator for development of an appropriate value curve from which "a unique selling proposition" (USP) can be created. They then pursue a path similar to the framework that we have developed and described earlier in this paper. That is to find a suitable market entry point and subsequent market funnel. They create new demand by identifying and pursuing three tiers of "non-customers" who are pursued by an USP and pricing/cost strategy that is appropriate for that tier. The market tiers may be described as follows, and may be considered as "layers" or segments of our market funnel (Figure 8):

- Tier 1 – soon to be non-customers
- Tier 2 – refusing non-customers (i.e. those using other solutions already)
- Tier 3 – unexplored non-customers

The market entry point (Tier 1) is defined by those customers/users where the USP is most compelling for those who have little alternative to get the job done. Tier 2 contains customers/users who have already adopted alternative solutions, thereby demonstrated the importance of getting the job done, and might be willing to adopt a new solution that can provide better performance at a lower cost and that is easy to use of buy. The last market tier is more of a red ocean market to be pursued after the product (or platform, as we'll describe below) has been developed to compete against the now emerging competition. In effect progressing from Tier 1 thru Tier 3 (which may contain multiple sub-segments) follows the PLC concept that we described previously.

The utility curve can be developed for each market segment using the Buyer Utility Map to identify the various steps to do the entire job (in "job to be done" language), and which part (or parts) of the job is most important and "least well done" (in Ulwick's ODI framework) [1]. The reader can identify similarities, and differences in all of the frameworks described herein. So, we provide all of those that have been useful to us in framing the issue of how to pursue innovation successfully and where the pitfalls, or potholes may lay.

In summary, the BOS strategy is a compilation of tools and frameworks that can be used to develop a compelling market entry and growth strategy by identifying uncontested market space (DI does that as well). However, the BOS provided tools and frameworks that can assist the innovator to construct a strategic framework. These tools should be invaluable to the entrepreneurial team that is constructing a go to market strategy. They should also be useful to the corporation that chooses to create a Blue Ocean Strategy for a new initiative. We have described earlier that there are political and cognitive barriers when allocating resources, redefining processes, and having the commitment to pursue such innovations. There are many ways to block change in existing organizations.

The BOS book[32] describes a number of innovations that have been brought to market using BOS principles.

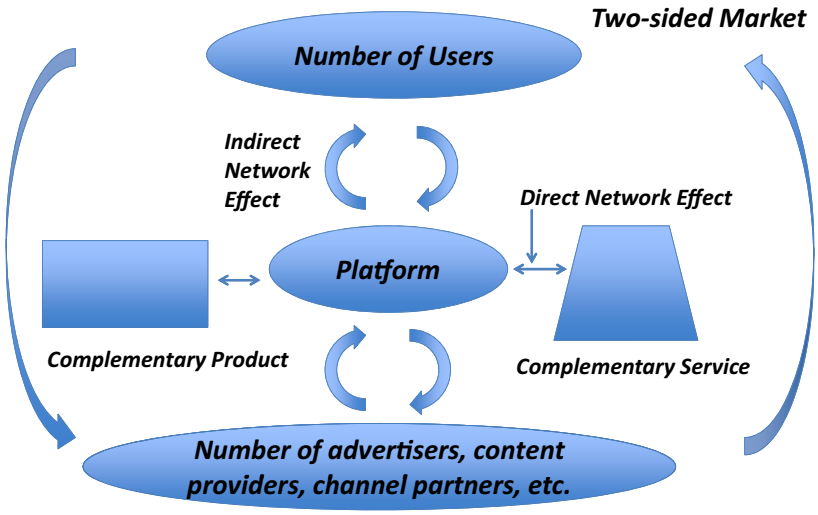

Figure 9: The platform ecosystem (Ref. Cusumano, 2012)

They include: Cirque de Soleil, Southwest Airlines, and Home Depot. We have also studied Salesforce.com (using HBS cases available thru their web portal) to illustrate the application of BOS. We suggest use of the BOS model for commercialization of 3D bioprinting in Section Two of this monograph.

Platform Strategy (PS) in Brief

Cusumano [35] and others have outlined the framework and strategy to pursue the development of platforms and networks to produce sustained competitive advantage (c. f. Figure 9). The platform and its supporting ecosystem and network by be used to build and sustain a market leadership position vs. a single product with a much less powerful network utilizing" Metcalf's Law".[37] However, the early stage company may start from a single product, like Salesforce.com, Box, Google and others, who have then grown and dominated multiple market segments by developing a supporting ecosystem and network. Alternately, and depending on the industry and competitive landscape it may be necessary for the early stage company to join existing networks of power players as complementary products or services. In today's innovation landscape, platforms are most often thought of in the context of information technology (IT). However, the concept of a platform has been around for years.

A platform is the common foundation (or, technological) base from which one can create a family of products (and services), including targeting different customer segments. Historical examples include railroad networks, electric power grids, automobiles/airplanes, and then more recently digital products, e.g. computers.

More recently we have seen the evolution of platforms where competition actually occurs at the platform level. For example:

- Transportation Power Systems
  - Gasoline, Natural Gas/derivatives, hydrogen, hybrid, electric
- Batteries
  - Sony, Panasonic, Sanyo, A123, Aquion Energy, Tesla
- Social Networks
  - Facebook, Linked In, Twitter, —-
- Video Games and the emerging area of Virtual Reality
  - Sony, Nintendo, Microsoft, —-
- Enterprise Software
  - SAP, Oracle/Sun, Microsoft, IBM
- Mobile Computing
  - Apple (OS and IOS), Android, Blackberry (?)

Platforms are incorporated into business models with the potential to create, deliver, and capture more value than a single product or service, sustainably. They can also be used to allow multiple parties ("market sides") to transact across the platform. These parties can include users, partners, complementers, and service providers. Direct network effect link products and services associated with the platform to add value directly. Indirect network effects provide access to a broader set of users via the larger network. The value of the platform increases non-linearly with the addition of more users, complementary products, services, partners, etc. utilizing Metcalf's Law[37] which states that "the power of the network is proportional to the

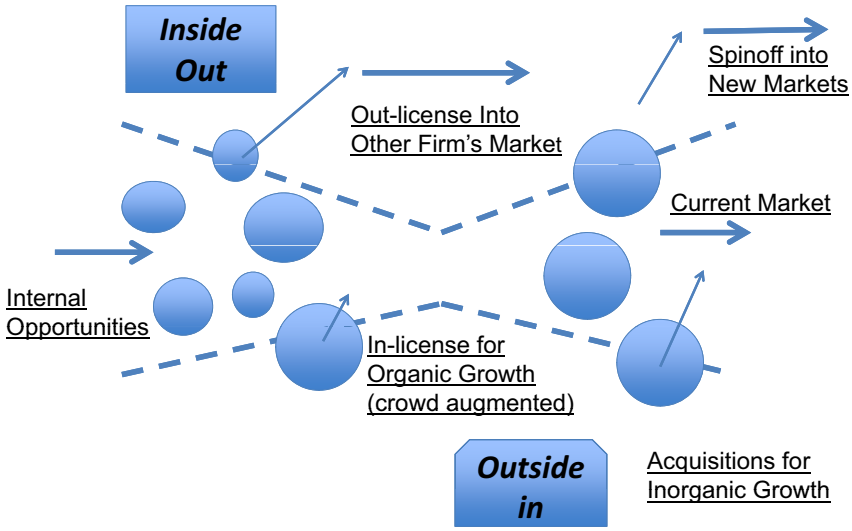

Figure 10: Open innovation is bidirectional
Internal culture and approach designed to support both directions

square of the number of connected users of the system". A network in equilibrium is difficult to disrupt once established, since multiple parties must to agree to switch simultaneously.

Going to market with a highly differentiated single product using Disruptive Innovation or Blue Ocean Strategy is a necessary, but not sufficient condition to build sustained competitive advantage. We have also pointed out that there are other components of a sustained competitive advantage, including building a superior platform and network around it. This also suggests the importance of partners to increasing the value of the business model. Therefore, our next and last part of this section is focused on the pursuit of the principles of open innovation.

Open Innovation (OI) in Brief

Open innovation has been promoted and developed by Chesbrough [33, 34, 38] starting with work at Harvard in the 1990's and then extending to his leadership at the University of California, Berkeley. **Dr. Henry Chesbrough** is a professor at the Haas Business School (Garwood Center for Corporate Innovation), and executive director for The Center for Open Innovation. Chesbrough and his collaborators cover the work extensively in a series of articles and books, so as with the above theories and concepts we provide a concise summary here, and refer those interested to the more extensive open literature references available.

At its essence, OI opens up the value chain of the organization to leverage both external and internal resources for innovation. It includes an "outside in" component and an "inside out" component (Chesbrough and Garman)[38] to provide an augmentation of the firm's resources and processes to expand the innovation capacity of the firm. "Outside in" components can include: ideas; licenses; acquisitions; and partnerships to expand those available in the firm's business model, including use of firm channels and customer relations components. Conversely, the firm can choose to use the "inside out" path to include: spinoffs, partnerships, out-licenses. This may provide the potential for access to new channels and lower cost business model components for disruptive or Blue Ocean innovation.

The OI paradigm is shown in Figure 10, as adapted from Chesbrough. Some of the interesting uses of OI in recent years include crowd sourcing for new ideas (see later section for Procter and Gamble's Connect and Develop approach). OI can also be used to access the firms existing customer/user base to test product or service ideas throughout the customer development phases. Collaborative development of products and services is also possible.

We have presented above the use of a platform strategy and that can also be employed in the OI business model. The firm can become a partner on an outside platform, or partner with other to build the firm's platform.

There may also be some disadvantages to OI, but in most cases these can be managed. These may include: unintentional sharing of information that is proprietary (trade secrets or premature and inadvertent disclosure of intellectual property prior to patenting); formation and management of complex licenses between multiple

parties; finding suitable and compatible partners for sourcing and developing ideas.

Chesbrough and Garman[38] have developed an interesting checklist focused on incorporating "inside out" strategies for firms considering implementation of OI strategies. They refer to these as "5 moves for successful OI":

- Become a customer (or supplier)
- Let others develop your non-strategic objectives
- Make your IP work harder for you and others
- Grow your ecosystem
- Create open domains to reduce cost & expand participation

Design-Driven Innovation (DDI) in Brief

We have discussed previously in this article, that innovation can be characterized along the dimensions of technological breakthroughs, and business model innovation. DI, BOS and OI are all focused on the latter category. Verganti[6] as a member of the design community brings a different perspective beyond the domain of the entrepreneur or technologically oriented innovator. He supports the thesis that "people do not buy products, they adopt meanings". Beyond utility, meanings include "profound, emotional, psychological, and sociocultural factors that promote adoption". Every product or service can add meaning beyond features, functions, and benefits (performance) as we have discussed in a previous section. These are intrinsic and given by the design, so the innovator does not provide them per se, but must understand them and build the product or solution to incorporate these "emotional needs" into the solution – in a sense these may be "unarticulated needs" (note that this concept was included in our previous section and attributed to the work of Cagan and Boatwright[40,] and also Hill[41]. Marketing and branding are often used to promote these meanings as part of the customer relations' component of the business model. Therefore, DDI can be categorized as a "radical innovation in meaning". The new product or service elicits an unsolicited response of what the user was "waiting for", but may not be able to articulate a priori (the proverbial unarticulated need).

In our innovation map (c. f. Figure 2) we show this domain in the upper right hand corner. A list of examples provided by Verganti[6] may be used to "visualize" what is meant by a change in meaning. Consider Apple, Ferrari, Herman Miller, Intuit, Nintendo, Starbucks, and Whole Foods as prime examples of recent products and services that fit this category (perhaps, we could we add Uber and Tesla to this group of examples?).

A central concept of the DDI framework suggests that firms should "step back from users and take a broader perspective". In effect, they should explore the context in which people's lives evolve – perhaps as suggested in the Innovators DNA, firms should not only question users, but also observe them. What "could be made to occur" or how might the context of life be made better. Verganti[6] suggests that "interpreters" can play a role in this regard, in effect as experts that can be asked for their insights. In our opinion, this interpreter role is comparable to our use of expert interviews to accompany more typical market research tools used in the business community. These interpreters or experts may include designers, suppliers, the media, artists, developers, and firms in other industries. Verganti's Interpreter Collective Research Laboratory ecosystem surrounds the firm interested in innovation (another use of Open Innovation). The ecosystem should cover the technology, cultural and social system surrounding the firm.

The process of design-driven innovation according to Verganti[6] is as follows:

Listening –gaining the knowledge (as described above, and including the Questioning and Observing component of the Innovators DNA)

Interpreting – we might suggest that this comprises the "Experimenting" component of the Innovators DNA

Addressing – leverage the power of the interpreters (acquired by Networking) and have a collaborative interdisciplinary team capable of Associative Thinking).

CHAPTER FIVE - THE DESIGN CULTURE - CHARACTERISTICS OF DESIGNERS AND THEIR THINKING

We have put considerable emphasis on the use of design thinking. Therefore, at this point it would be appropriate to provide our perspective and basis for building a business model that is incorporated into the innovation culture of the organization. Building an innovation culture would necessitate acquiring a team and cultivating the behavioral skills needed for innovators.

Existing literature, e. g. Dyer, Gregerson and Christensen has identified the 5 discovery skills exhibited and needed for disruptive innovators – c. f. "The innovators DNA".[17] These 5 traits or skills are Observation, Questioning, Experimentation, Networking, and Association (or, associative thinking via diverse, interdisciplinary innovation teams).

Our work, both prior to and subsequent to that publication has stressed the need to include design thinking

as an integral part of the innovation process and culture. So, we ask, how can that be used to complement or supplement the Innovators DNA insights? We have had the opportunity to expose our MBA graduate students to a number of firms in Silicon Valley over the last 4 years as part of our annual Designing and Leading a Business Capstone course based in the Bay Area at the Carnegie Mellon Mountain View campus (the students move to Silicon Valley for the last mini semester of the MBA program. This program provides an in-depth immersion into the unique innovation ecosystem there. In addition to exposure to VCs, founders, and accelerators, the program incorporates a series of interviews and sessions with a number of design firms and product firms that have incorporated design thinking into their innovation process. Design firms would include: Adaptive Path, Big Tomorrow, Bould Design, Cooper, Frog Design, IDEO, Lime Design, and Lunar. Firms adopting design thinking into their cultures include: Air BnB, Capital One, Citrix, DocuSign, Google, Intuit, and You Tube. We have also included the Stanford D-School, and of course the School of Design at Carnegie Mellon University. See Sidebar article on Citrix to illustrate the approach that they used and the culture that was created there as a traditional engineering company built a design-driven culture to become more customer centric and responsive.

CITRIX – LIFECYCLE OF DESIGN THINKING ADOPTION IN A TRADITIONAL ENGINEERING-DRIVEN SOFTWARE ORGANIZATION – THE IMPORTANCE OF TOP MANAGEMENT SUPPORT (OR NOT)

COMPANY DESCRIPTION:

Citrix designs, develops and markets technology solutions that give people new ways to work from any location with seamless and secure access to the apps, files and services they need on any device, wherever they go. A number of technology trends including cloud, mobile, and now the evolution of software-defined environments are changing the role of IT in business, and Citrix is a leader in that evolution. Networks, desktops, data, and even in-person meetings have all been decoupled from physical locations and transformed into fully digital mobile workspaces that provide complete business mobility. Citrix is leading the transition to software-defining the workplace. Citrix powers business mobility through secure, mobile workspaces that provide people with instant access to apps, desktops, data and communications on any device, over any network and cloud. The company was founded in 1989 and has grown substantially thru organic growth and by acquisitions to become a multi-billion dollar, public company with global operations. Citrix is headquartered in Fort Lauderdale, FL and has major US operations in Santa Clara, CA. Ref. https://www.citrix.com/about.html.

Citrix (applied design thinking in its evolution to become an industry leader with full support of the CEO. In that regard Catherine Courage former senior vice president of customer experience at Citrix had used the following definition. *Her team was responsible for company-wide brand, advertising, social, web, product design, information experience, and business process reinvention. Their mission is to partner with functions across the company to deliver an outstanding experience for customers and employees.*

…"an approach to innovation that can be applied to all areas of business. Design thinking does not refer to a formal step-by-step process, but to a framework and mindset. It is focused on a bias towards action, a human-centered viewpoint and a mode of continual experimentation. The core idea is that by deeply understanding customer needs, opportunities for innovation will emerge. These ideas can be further refined through rapid prototypes and iterations to result in breakthrough outcomes"

CITRIX DESIGN THINKING PRINCIPLES

1. **Focus on users:** Who is your customer? We all have a customer… whether they are internal or external… it's your job to meet their needs.
2. **Make it simple:** Do the hard work, so your users don't have to. Customers will eagerly adopt products and processes that make doing their job easy.
3. **Inspire delight:** Exceed your user's expectations. We want people to actually enjoy - even love – their every experience with all things Citrix.
4. **Exhibit craftsmanship:** Attend to fit and finish, and take pride in the quality of your work.
5. **Deliver unique value**: We can all be innovators. We want to do things in new and better ways. Citrix stands for excellence, not the status quo.

Ref. http://www.youtube.com/watch?v=CJT340fooKA

DESIGN HISTORY AT CITRIX:

In 2009, Citrix then CEO Mark Templeton issued a challenge: Make Citrix a leader of design excellence by transforming the traditional engineering-driven company into one whose very DNA is built on the fundamentals of design thinking and doing. … Mark believed that, in addition to traditional means of growth, his company's success in exceeding the $2 billion mark would depend heavily on its ability to focus on improving the end-to-end user experience of its products, services, and partnerships.

Ref. http://www.managementexchange.com/story/reweaving-corporate-dna-building-culture-design-thinking-citrix

SOURCES/REFERENCES:

Reweaving Corporate DNA: Building A Culture of Design Thinking at Citrix by Catherine Courage – Senior Vice President, Customer Experience at Citrix July 14, 2013

Citrix established an extensive set of goals, implementation checkpoints and metrics for measuring progress associated with development and implementation of a design thinking culture in an established engineering-driven culture. These are summarized below in two major categories:

1. The first set of goals start with the development of a distributed design thinking approach throughout the organization for the solution of all business problems and challenges. This requires a top down corporate strategy on par with product development, marketing, sales, and support.

    a. Enable the development of design leadership throughout the organization. Create a mindset *to embrace a customer-centric product or service development.*

2. Additionally, develop and implement a set of succinct methods for implementing the discovery of user's core needs, finding ways to meet those needs, and implementing impactful change

    a. To shorten the product development cycle with quick iteration and feedback loops to enable you to build the right solution
    b. To build a mindset with a bias toward action (small concrete steps that move the project forward), accepting that innovation requires iteration, and encouraging disparate viewpoints

3. Make design thinking visible and measurable to the organization and it's customers and partners

    a. Make design thinking a competency to be measure toed in individual annual reviews
    b. Publicize design thinking content on company websites explaining its value, impact, implementation
    c. Utilize employee forums and other events to present the value of design thinking
    d. Send key employees to design thinking workshops both internal and external
    e. Create PR that educates customers and peers about user experience successes

KEY IMPLEMENTATION CHECKPOINTS INCLUDE:

1. Seek out and partner with experts to help with design strategy implementation particularly in the early stages of building competency within the organization (Citrix used the Stanford D school, IDEO, Lime Design, founder Maureen Carroll, Ph. D.)

    a. Continue to leverage outside support to achieve early successes as competency is developed
    b. Begin implementation with projects that will quickly make a visible significant impact
    c. Start with empathy for the user (applies to any customer interaction) then move to generating ideas and prototyping

2. Celebrate all successes in putting experience first both externally and internally (publicize quarterly)

    a. Pick impactful collaborators for big project investments
    b. Don't assume that all parts of the organization will understand the value of design thinking concurrently
    c. Be empathetic and remember, it's a journey not a destination

3. Brand the Design Thinking Program so it is recognized throughout the organization (Citrix – *Design Matters to Me)*

    a. Create an intranet to share design thinking information and approaches throughout the organization

b. Insure that every project starts with an implementation plan which includes a picture of the current landscape (journey map), a core team, extended team, and senior management support (executive sponsor), and target users (analogous & extreme)
c. Build a strong ecosystem of support, including distributed spaces that allow for flexible working and innovation (ambient design thinking with pop-up design studios)
d. Create rewards and recognition for those that successfully implement design thinking on the job (PR for teams, team "heroes"

METRICS SHORTLIST

1. How many:

   a. employees have been exposed and trained in design thinking?
   b. projects are actively using design thinking in their development?
   c. departments are using design thinking (Product, Finance, HR, Sales, Legal, Marketing, etc.)?
   d. workshops and courses on design thinking have been presented / attended?
   e. leaders have been trained in design and are spreading (evangelizing) design-thinking methods throughout the organization?
   f. industry awards have products influenced by design thinking won?
   g. business articles in top tier publications have recognized the organization for its design approach?
   h. educational institutions or other companies reaching out to partner and share best practices.

2. What is the ROI on products using design thinking in their development?

3. Internal support and visibility:

   a. Support and encouragement by executive
   b. Centralization of design thinking organizationally
   c. Budget for design
   d. Demand for design support across the organization (wait list)
   e. Design studios and innovation spaces distributed throughout the organization?
   f. Have educational institutions reached out to partner on design thinking research?

OUTCOME IN SHORT

Change came to Citrix in 2015 as a result of criticism from an outside investment group (Elliott Management) unhappy with recent financial performance of the company. Elliott also strongly suggested that Citrix leadership of lacking focus, claiming the company made several overpriced, nonstrategic investments and focused on hyping noncore products and concepts. As a result the CEO stepped down and a new strategy was put into place. The refocusing led to a de-emphasis on design thinking and as a result Catherine Courage left and is now at DocuSign building a design culture there. Lesson to be learned – top level (board level and CEO) support is an essential component of any corporate strategy, as is bottoms up engagement. While the lessons learned at Citrix are valuable, we can look to other leading Silicon Valley and Bay Area firms for similar approaches to building a customer-centric culture. Our Top 10 list of design traits and skills has been developed from the best practices for sustainable customer-centric cultures from leading Bay Area firms. Additionally we recognize the recent trend for a number of management consulting firms to acquire design companies to complement their traditional "quantitative strategy practices"; e. g.McKinsey/Lunar, Accenture/Fjord.

Based on our work we have synthesized our ***"Top 10 list"*** of the behaviors that characterize the design thinking culture.

1. Critique
Designers thrive in open, no holds barred critiques. Critiques are visual exercises where ideas are represented (sketches, models, mockups – boundary objects) in front of a casual cohort of peers for evaluation and comment. Ideas, concepts and possible directions obtained from observation, interviews and insights are explained and debated. Often naive critics are involved – those with no knowledge of the project or subject matter, but with lively creative minds that can readily react and explain their reactions to what they see. In addition, expert critics are involved in order to draw out their particular domain knowledge for the project. The purpose is to stimulate a wider and better range of solutions or approaches to a particular problem.

2. Action
Designers like to make things that represent the physical world and context, as it is known at the moment. Low-tech mockups and models represent the relationship of the components, no matter how incomplete the specification. This allows designers to move forward with partial solutions, which can be tested and evaluated.

3. Collaboration
The visual tools used by designers invite collaboration. Ideas represented with drawings and all parties regardless of their specialty can grasp mockups. Often designers can represent new ideas as they are discussed with simple sketches to further the conversation. Collaborators that don't easily gravitate to using visual means to express ideas can be easily trained to use napkin sketches and simple desktop modeling skills to further their ideas.

4. Ambiguity
Designers are comfortable with ambiguity. They often see more than one meaning or solution for a problem. "What if" comes easily to the designer that poses multiple solutions in the early stages of the design process. The goal is to identify the real constraints of the project. What are the real user needs and how can they be best addressed?

5. Constraints
Designers actively seek out constraints and see them as aids to creativity. Constraints can include any number of tangible or intangible expectations based on physical or emotional factors such as price, look, feel, balance, etc. Often a constraint can be used to communicate knowledge across disciplines. They become nodes for discussion where understanding and agreement can be achieved. Design thinkers creatively challenge and work around each constraint to fashion a unique product that goes beyond solving for a list of needs.

6. Reactivity
Designers try to place people in a reactive mode, by visualizing new ideas that people can evaluate with all their senses using drawings, models and prototypes. When people are asked what they want they have a hard time thinking beyond what they already know and use. When confronted with an artifact, users can readily evaluate it, react and respond as to why or why not it has merit. When presented with a series of concepts potential users have no trouble combining ideas (a little of this and a little of that) to produce a new concept

7. Iteration
The design process is not linear but iterative. As concepts (hypotheses) are proposed more is learned that informs earlier directions, causing the process to loop back on its self, creating the need to rethink earlier proposals. The cycle of analysis, synthesis, visualization, assessment, and evaluation is repeated with more background and insight, while moving to a suitable solution. Designers tend to postpone judgment as long as they can, preferring to consider and search for alternatives throughout the process.

8. Creativity
The designer's creativity revolves around inspiration. As opposed to artists, a designer always has a client's needs in mind. Solutions are not created out of "whole cloth" as might a sculpture, but rather in response to needs and constraints imposed by the user. The discovery of needs and constraints inspires resolution.

9. Empathy
Designers cultivate the ability to step into another's shoes. Empathy is key to designing for people. By exercising their curiosity, refining their observations, and offering their partial understandings designers realize preferred solutions that fit their audience.

10. Delight
In their book, "Built to Love, Creating Products That Captivate Customers", CMU faculty Jonathan Cagan and Peter Boatwright observe that "if companies want to energize the marketplace, their products and services must make customers feel better".[40] Emotions and loyalties are thus enhanced when market offerings are designed to elicit emotions. So, it is not just functionality that counts, it's the ability to anticipate and incorporate the emotional component into products and services.

Designers also incorporate a number of ***methods*** into their process. We may add this as number 11 above, but we consider methods more appropriate as a set of tools rather than as behaviors per se. The design process and methods are user-centered and are based on making ideas visible and discovering insights from this visibility via the use of iterative techniques. Designers classify ***users*** into categories adapting ideas from anthropology:

- Those that are not conscious of their needs;
- Those who can be asked about their needs;
- Those that can be observed to discover their needs; and,
- Those that can articulate their needs.

Many tools and techniques can then be employed to gain an understanding of latent needs and to discover what users really need and want. They would include Interviews (including expert interviews), Knowledge Mining, Storytelling, Guided Tour, "Fly on the Wall", AEIOU, Shadowing, Think Aloud Protocol, Behavioral Mapping etc.). 6 Hat Thinking is also a recommended process for building consensus during the iterative process.[22]

How might these 10 "designer behaviors" be included in the Innovators DNA studied by Dyer, Gregerson and Christensen? We suggest considering the following:

1. **Observation** – creativity
2. **Questioning** – constraints, empathy
3. **Experimentation** - ambiguity, reactivity, iteration, delight
4. **Networking** - collaboration
5. **Association** (or associative thinking) – critique, action (and methods or utilization of tools – our 11th attribute of design culture)

In closing this section, we note that the Roman architect Vitruvius in his treatise on architecture, De Architectura, asserted that there were three principles of good architecture:

- **Firmatis** (Firmness / Durability) – It should stand up robustly and remain in good condition.
- **Utilitas** (Utility / Commodity) – It should be useful and function well for the people using it.
- **Venustatis** (Delight / Beauty) – It should delight people and raise their spirits.

Successful design is a combination of all of these principles. An elegant solution evokes an immediate esthetic, or emotional response in the viewer well before function and robustness can be ascertained (recall the work of Verganti). The artifact becomes desirable or covetable through its delight and beauty (think of Apple's offerings, and Nest's and Tesla's). It is our contention that the utilization of design-thinking methodologies provides a better understanding of what customers want and need. In addition, they also provide a means to incorporate emotional factors into economic decision-making associated with innovation, thereby augmenting more quantitative marketing tools. Building an innovation culture that balances quantitative and qualitative methods provide a more optimal method for creating and delivering value (functional as well as emotional) to customers and for capturing a greater fractional portion of that value for the firm via the emotional components.

CHAPTER SIX - INCORPORATING CULTURE AND METRICS INTO AN INNOVATION DASHBOARD

Kaplan and Norton[13] pioneered the development and expansion of the Balanced Scorecard (BSC) and their work has provided a very complete documentation and demonstration of the utility of their approach in the open literature. Very succinctly, the BSC provides a framework for tracking all of the important elements of a company's strategy from continuous improvement, to partnerships, to teamwork, and global scaling. *The BSC can and has been used to focus on how companies can excel at creating value for shareholders, partners, and employees as constituents of the organization.* It can also provide a convenient and powerful framework used to align the business activities of the organization to achieve, align and communicate its strategic goals. The BSC is centered around the Vision and Strategy of the organization and incorporates 4 dimensions (c. f. Figure 11):

- Financial
- Internal Business
- Learning and Growth
- Customer

The BSC framework provides a unified framework for the organization to summarize its strategy, and specific targets, initiatives, and metrics in each of the 4 dimensions listed above.

In this work, we have utilized the Business Model Canvas approach developed and promoted by Osterwalder et al[14] to provide a centralized framework for developing and articulating how the business model of the organization evolves to create, deliver and capture value for the organization and for its external partners and suppliers. We have emphasized in prior sections that it is important to realize that each of the 4 innovation categories may and probably will require some modification or creation of the business model for existing and for new organizations. Therefore, we suggest that the BMC should be used as part of any innovation management program to complement and supplement the Balanced Scorecard. Reviewing and reconstructing an appropriate business model canvas will point out where changes may be required to capitalize on that innovation, or where new components must be added.

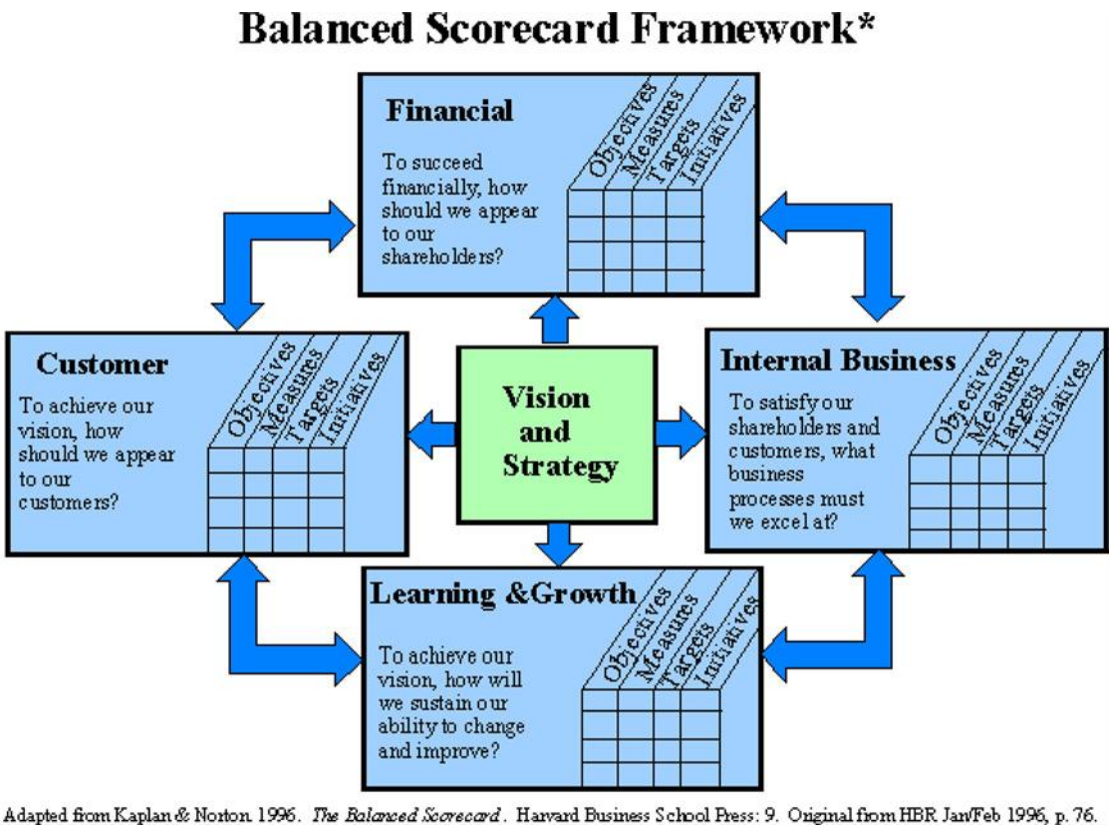

Figure 11: The balanced scorecard

While the Business Model Canvas and the Balanced Scorecard can be used independently, we have attempted to synthesize these two approaches into a single ***Innovation Dashboard*** that can be used to focus the organization on innovation and how to evolve its business model and its culture to capitalize on becoming and remaining an innovation leader. Our proposed Innovation Dashboard framework is shown in Figure 12. Note that we have used the same 4 dimensions of the BSC, but also adapted the framework of the BMC into the BSC approach, and broadened the scorecard to include the organizational culture explicitly:

Financial - incorporates the Revenue and Cost elements of the BMC (current, historical, projected). This component measures the capture of value by the corporation and sets up some metrics for measuring same.

- Revenue & Profitability (leverage the Revenue and Cost elements of the BMC)
- P/E (or market cap if appropriate)
- Market Share and Rank in markets served
- New products and services per $ of R&D investment (ROI, IRR or NPV)
- Cycle time for creating products (extensions/sustained innovations, disruptions, by acquisition)
  - Organic growth vs. outside in sources for innovations including acquisitions
  - Inside out - spinoffs
- Compare each of these metrics with industry leaders

Business Processes/Culture – Resources, Processes, Values and Partnerships from the BMC

- Open Innovation Best Practices Employed – Inside Out and Outside In
  - 5 moves recommended by Chesbrough and Garman for inside out, plus outside-in via licenses, partnerships, collaboration, acquisitions
  - Partnerships formed along the value chain from the BMC
  - Processes for assimilation of acquisitions into the company culture
- Lean, Iterative, Collaborative processes for innovations as appropriate for all innovation categories

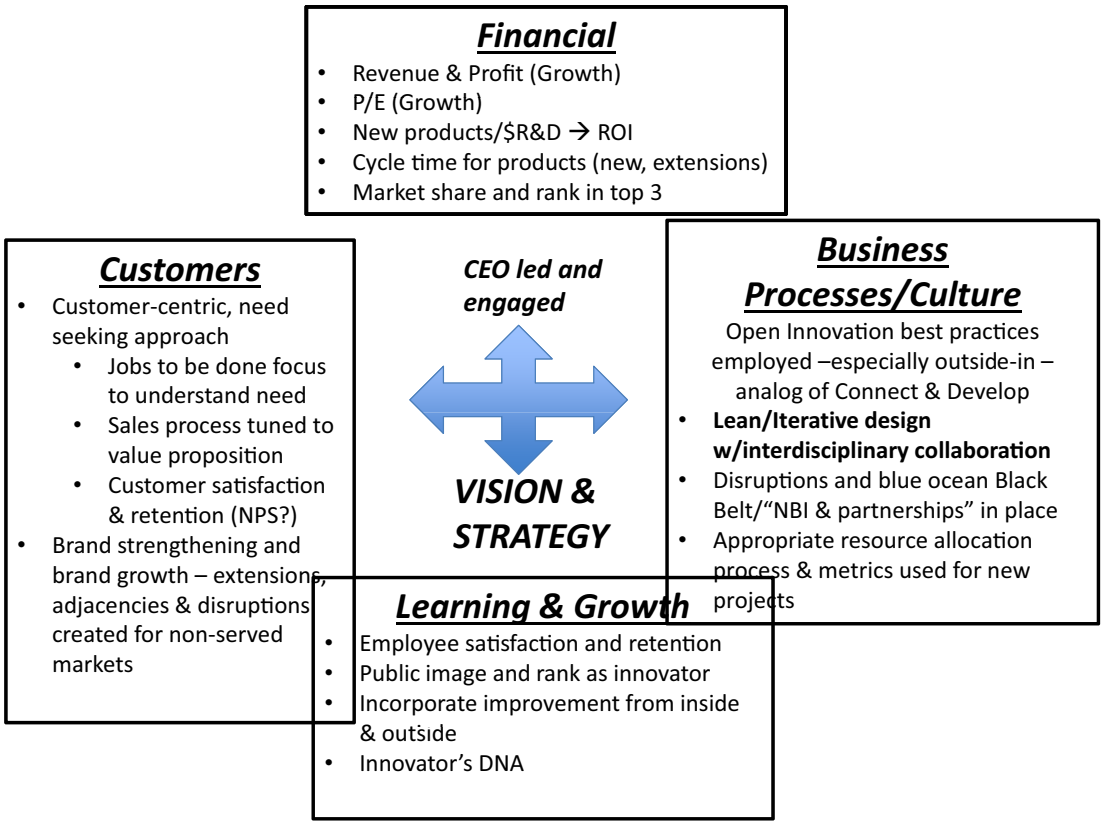

Figure 12: The innovation dashboard

- Development and progress of building design-thinking culture – see Citrix sidebar for examples of metrics
- Use of design thinking tools listed as listed on Fig. 5 and in section titled Design Culture as appropriate
- Processes for managing "virtual teams" that are not co-located and come from multiple organizations – e. g. crowd sourcing, consortia, partnerships, in licensing, etc.

- Utilization of Disruptive Innovation principles (and/or Blue Ocean Strategy Design Driven Innovation)
  - Innovators Black Belt of Christensen applied (especially CEO engagement and appropriate financing allocations and metrics for advancing disruptive innovations)

Customers – uses the elements of the customer facing side of the BMC (market segments/customers, value proposition and offerings, customer relations, and market channels)

- Customer/user centric, needs driven approach
- Sales proposition aligned with value proposition
- Customer satisfaction and retention
  - Adopt and develop key performance indicators (KPI's) and, net promoter score (NPS)
- Brand strengthening and growth – extensions, adjacencies, disruptions and new markets entered

Learning and Growth- a separate component that deals with growing and maintaining the organization as a globally recognized innovator

- Employee satisfaction and retention
- Public image and rank as an innovator
- Continuous incorporation of improvements adapted from inside & also adopted from the outside
- Innovator's DNA embraced and adopted and cultivated internally

Many organizations have been successful in evolving and developing their innovation processes and cultures,

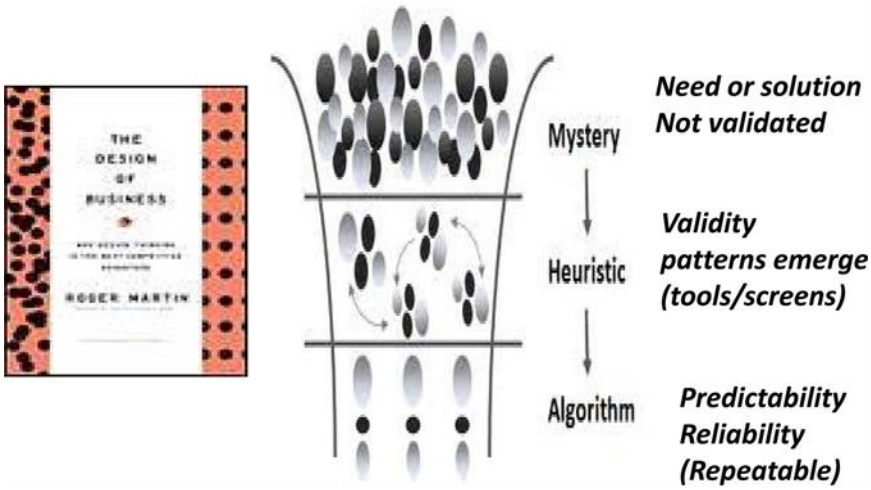

Figure 13: The knowledge funnel [adapted from Roger Martin, Business by Design (2012)]

and we have highlighted some of them in earlier sections of this paper, e.g. see Citrix sidebar, and Top 10 Design Characteristics. Many more organizations are also obvious, such as for example Apple, Google/Alphabet, Amazon, Facebook and others. In the CPG industry, P&G stands out and has been highlighted in a chapter of the book by Martin,[10] "The Design of Business: Why Design Thinking is the Next Completive Advantage". We also refer to a recent HBS case study on P&G, authored by Larry Huston and Nabil Sakkab, "Connect and Develop: Inside Procter & Gamble's New Model for Innovation" – HBS R0603C[31]. This latter article posits that innovation is the engine that drives top-line growth; that internal R&D is insufficient; and that a better approach can be achieved thru open innovation methods. P&G termed this model "connect and develop". Connect includes partnerships with external organizations such as universities and national laboratories, web-based talent markets (e.g. crowd sourcing), suppliers and even competitors. A partnership with Nine Sigma facilitated the Connect part of the open innovation strategy. The Develop framework "evolves these ideas into profitable new or refined products – swiftly and cheaply – using the firm's core competencies; R&D, manufacturing; and marketing prowess". As pointed out by Brown[11], A.G. Laffley the CEO at the time (and now again) took a top-down approach to transform P&G into a design-thinking organization, and to drive opportunities down the knowledge funnel (a Brown construct illustrated in Figure 13). He set a goal that half of the innovations should come from outside of P&G, and to shave costs and gain speed to market. They also focused on the "mystery to heuristic" part of the knowledge funnel, where P&G was observed to be weak. The results spoke for themselves: 13 of 15 brands increased market; expanded brands to 20; within 6 years achieved 10% year over year profit growth. Also, it should be note that Connect and Develop drove 35% of the company's innovations

In short, the P&G approach focuses on where to look (how to identify customer needs and to identify adjacencies), how to leverage their networks (their suppliers and leverage of Nine Sigma); how to distribute and screen ideas; and, how to promote openness to external ideas. A great role model for others to emulate, and which incorporates virtually all of what this article has covered and recommended for implementation.

CHAPTER SEVEN - CONCLUSIONS AND POST SCRIPTS

We conclude and summarize Section One with a reinforcement and expansion of several key points made in the text regarding best practices in commercialization and innovation.

First regarding innovation, consider building a business that meets several essential "screening criteria". We have previously articulated five anchors of a good business: 1) a compelling market need; 2) creation of significant value for the target market; 3) creation of a significant differentiation and a sustainable competitive advantage; 4) identifying the potential for good profit margins with high return on investment potential; and, 5) creating a good fit for all constituents with good market timing; c.f. Boni.[42]

In order to develop and exploit the winning business opportunity, it is then necessary to create a winning business model needed to exploit the type of innovation being pursued;

- For existing technologies – disruptive innovation or blue ocean (new model required); sustained innovation (extension of existing model)
- For breakthrough-technological advances – radical or exponential (extension of existing model); or architectural/design driven innovations (new business model)

In Section One we emphasized several points made by Peter Thiel[15] who stressed the importance of building a company that no one else is building (uniqueness), and also building a sustained competitive advantage (monopoly in his terms). The building of a platform was included therein as a potential key element for success (see more on this below).

Also, Roger Martin and A. G. Laffley[43] in a recent issue of Harvard Business Review have developed 5 components of a "playing to win" strategy, which was developed principally for innovation in more mature organizations (but which in our opinion, is also applicable for smaller, emerging organizations). These are consistent with our five anchors noted above:

1. What's our winning aspiration? (e. g. what is the purpose of the organization? where is the unfilled need that we can fill uniquely?)
2. Where do we play? (e. g. customer segment, distribution channel, customer relations)
3. How do we win? e. g. value proposition based on understanding customer need – low cost and differentiation solution; plus, a sustained competitive advantage
4. What capabilities do we need? e. g. internal, or accessed thru open innovation
5. What systems are required? e. g. processes, rules, and structures (and we would add culture)

All of these points are related to the business model, and would benefit from use of the Business Model Canvas to identify and validate hypotheses. Items 4 and 5 above from Martin and Laffley fit into the RPV (resources, processes and values) as discussed by Christensen in "Seeing What's Next".[7]

The recent Harvard Business Review articles published by Van Alstyne, Parker, and Choudary[44] in April 2016 stressed that "platforms bring together producers and consumers to trump differentiation as a competitive advantage". The critical asset is the community, and the resources of all the members that are orchestrated through the platform and its network effects. Platforms therefore, create a sustained competitive advantage that pure pipeline/product businesses generally do not. In a previous publication titled "Project, Product, Company" in J. Commercial Biotechnology, we argued similarly that the "pipeline Company is essential to creating a sustainable business for growth and profitability.[42] A Platform is even better! However, Hagiu and Rothman[45] argue that attracting a critical mass of buyers and sellers in a networked market is in itself not sufficient to "win". Before scaling, all problems with the business model must be "fixed" (or created), e. g. trust and incentives aligned amongst all constituents of the network, and, regulatory issues. This latter issue is important in both tech and most certainly even more so for the biopharma/medtech businesses. In the latter case payment/reimburse issues are also important business model elements (revenue model) to resolve before scaling. So, business model validation is critical before transitioning from a startup to the growth company as we have noted previously.

Finally, Zhu and Furr,[46] argue in "Products to Platforms: Making the Leap", that there are four best practices to ensure success:

1. Start with a defensible product and a critical mass of users
2. Apply a hybrid business model focused on creating and sharing new value
3. Drive rapid conversion to the platform
4. Identify and act on opportunities to deter competitive imitation

In our paper "Project, Product, or Company" we suggest that creating a successful product first can permit later transition to the Company metaphor – either a "product pipeline company", or if possible a "platform company" [42]. Dominating product entry market thru the innovators and early adopters stage may well signal the ability to transition into growth with subsequent products or to transition into a platform company.

As noted at the beginning of Section One, commercialization deals with the resources, processes, and values needed to bring a new opportunity to market. We have advocated integration of design thinking skills into the team maintain customer and user centricity, i. t. to understand and exploit opportunities in the marketplace, and to fine tune products, services, or solutions thru validation of product/market fit (in lean startup jargon).

The jobs to be done (JTBD) approach is a very useful and essential construct by which to understand market need that is being unsatisfied or met sub optimally thru "workaround solutions". The JTBD approach not only validates need and value creation opportunities, but also identifies the minimum viable product or solution that can be brought to the market entry point (recall market is defined at JTBD + Executors + Context). Questioning and observing should be used to identify quantitative value as well as the emotional components of value to

be created. Together with experimentation, the team can identify both articulated and unarticulated need. Experimentation then validates and the hypotheses. Disruptive innovations require understanding of the unfilled need and the value to be conveyed that fills that need in the selected target market. Similarly, for Blue Ocean innovation, a new value curve is require to be developed, validated and articulated.

One product/market fit is validated, then we move on to develop the go to market strategy that will lead to market dominance in sequential markets starting with innovators, early adopters, early majority (crossing the chasm), and growth beyond into mainstream market segments. Or, in Blue Ocean Strategy language moving from Tier 1, to 2, to 3. For design driven innovations the innovator must identify the new meaning and how to articulate that to the target market. All of the above fills out the customer facing side of the business model canvas – except for the revenue model which requires further experimentation as to how much and who will pay for the value being created.

One further important innovation strategy that should be highlighted relates to the ability to pursue commercialization and innovation in a capital efficient manner. While that is not covered explicitly in this monograph, it is apparent that resources (especially money) are required to pursue commercialization and innovation. We advocate utilizing the power of open innovation to leverage the resources of others and to reduce risk (as in the discussion on building platforms above). Boni and Moehle[47] have recently published an article on the topic which has identified several key components of the DNA for collaborative innovation:

- Leveraging a set of open innovation networks exploiting "outside in" and "inside out" tactics as per Chesbrough and Garman[38]
- Building collaborative, interdisciplinary teams working across the product life cycle (emergence of the 'virtual team')
- Building an innovation culture around the 5 behavioral traits ("5 base pairs") of the Innovators DNA examined by Dyer, Gregerson, and Christensen[17]

These concluding messages and post scripts provided above should be applicable to guide the startup, evolution and growth/expansion of any business whether they are hardware, or software, tech or med tech/biopharma. We have already included selected examples most pertinent to tech and software in Section One. In Section Two of this monograph we include examples/case studies leveraging these principles for healthcare innovation. There, we focus on illustrating the development of commercialization and innovation strategies in biopharma, med tech, and digital medicine. And, with some examples of design thinking, including service design as applied in these industry segments.

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Section Two

Innovation Practices in Biopharma, MedTech, and Digital Medicine

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Section two applies the principles presented and summarized in Section One to the production side of the healthcare industry, and consists of 7 chapters (or contributed articles). Our focus is on biopharma (the converged pharma and biotech segments), MedTech, and digital medicine. We also include a discussion on areas of convergence of technology, healthcare, and biopharma as the broader industry has begun adoption of a customer-centric business model that incorporates solutions that merge drugs, devices, and digital technology to impact the entire healthcare system. The 7 Chapters are summarized below:

1. **Innovation Principles in the Pharma 3.0 Business Model Paradigm: User-Centric Applications to Biopharma, MedTech, Digital Medicine with Cross Sector Convergence** – This article is an overview that summarizes the challenges of innovating in biopharma and MedTech, and the emergence/evolution of digital health, and convergence of technology and MedTech. Contrast differences and similarities (B2B or B2C in tech vs. B2/5P in healthcare (patient, physician, provider, payer, and partner –the 5Ps) in a science-driven, regulated market; lean thinking applied to Biopharma; and, managing additional risk factors associated with healthcare innovation such as IP, regulatory, reimbursement, privacy and cyber security. *Arthur A. Boni*

2. **The R&D Marketing Interface in Biopharma and MedTech.** - This article highlights the importance of building an extended team that incorporates the expertise needed to guide product development, strategy, and marketing during the development process for biopharma and medtech products. We focus on the importance of marketing at the earliest stages of company formation and product development to shape the product life cycle. Marketing focuses on creating an appealing target product profile (TPP) as a means for ensuring commercial success. We describe a methodology and rationale for creating the TPP to achieve better outcomes for products brought to market. Thanigavelan Jambulingham, Professor, Haub School of Business, Saint Joseph's University.

3. **Design Thinking at Daedalus**. Developing solutions for biopharma/medtech/digital medicine products and services requires a cross disciplinary team to engage a broad cross section of the healthcare ecosystem. Unlike technology products, the ecosystem is more complex and involves patients, physicians, providers, payers, and partners. Each of these parties must be engaged to understand overall market need, requirements, and constraints. This article focuses on design thinking as part of the overall strategic and marketing resources that can be used to observe, question, and understand the needs of the entire ecosystem. The interdisciplinary commercialization team can thereby reach a common understanding of the outcome of each component of the job to be done from the perspectives of each party, and thereby achieve overall product/market fit for the product design and overall business model components. This article outlines the perspective and approach of Daedalus, a full-service, interdisciplinary product development firm with decades of experience working with medtech companies. The article is complementary and supplementary to the materials on design thinking in Part One of this monograph/special edition. It also covers several examples as mini cases that are pertinent to healthcare from projects undertaken by Daedalus, Inc. from their industry

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portfolio of achievements. *Matt Beale, President of Daedalus, Inc., and Tim Cunningham, Founder and former President of Daedalus Design, and Adjunct Professor at Carnegie Mellon University.*

4. **Service design for delivery of user-centered products and services in healthcare.** In this article, the essential elements of service design are covered, since service is an important element in the evolving Pharma 3.0 business model where patient centricity is important. Also, we recognize that the evolving healthcare system stresses the importance of interaction throughout the ecosystem. We discuss Service Design in the evolving healthcare ecosystem, recognizing the importance of interactions throughout the system – patients, providers, physicians, extended care networks, etc. The discipline's value is then illustrated through various applications in several mini case studies. *Sarah-Marie Foley, Master of Science in Interaction Design, School of Design, Carnegie Mellon University*

5. **Innovation, Commercialization and Business Development Strategies for Three-Dimensional-Bioprinting Technology: A Lean Business Model Perspective.** This article focuses on translational medicine in regenerative medicine based on research and commercialization at Carnegie Mellon University and the University of Pittsburgh. It covers the commercialization and innovation approach for a novel 3D Bioprinting invention originating at CMU with multiple applications including tissue-based drug discovery. *Prakash Thakur, Dario Don Cabrera, Nate DeCarolis, and Arthur A. Boni.*

6. **Medrad Innovation Journey - from start-up to Industry Standard: Mountain Climbing, Spelunking, Over the Horizon Home Runs, and creating a "DC-3 Effect"**. Medrad was a pioneer and is now a current leader in the medical imaging industry; which, after acquisition is now part of Bayer Radiology. In this article (or case study), we describe the customer and user centric processes employed by the company to identify underserved and unserved markets, and to commercialize its technology. Also, the company culture is described along with their adoption principles before they were popularized. *Ned Uber, Fellow at Bayer in Pittsburgh*.

7. **Case study of Molecura Labs**. This article is a case study that focuses on Moleculera Labs, an emerging biotechnology R&D company developing clinical diagnostics and identifying new therapeutic targets. The article covers commercialization and innovation strategy applicable to an emerging biotech company that has utilized patient-centric, capital efficient, and lean principles for development, validation, and go-to-market execution. This case study includes key factors that are essential for successful biotechnology companies. These range from management of technology, market, and team/leadership risks to dealing with financing, regulatory, IP, and reimbursement issues. *Craig Shimasaki, President and CEO.*

Article

Innovation Challenges and Opportunities in Biopharma, MedTech, Digital Medicine, and Their Emerging Convergence: User & Patient Centric Applications in the "Pharma 3.0 Business Model Paradigm"

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INTRODUCTION

In the first section of this monograph, titled "***Bridging Theory and Practice for Commercialization and Innovation – a market-centered perspective for cross-industry applications",*** we outlined a number of overlapping theories or models dealing with innovation. Theories, when well stated and proven, are basically statements of causality. Scientists and technologists use them all the time to predict physical or chemical phenomenon for example. However, whether or not we explicitly recognize them as such, theories also exist in the business world and can be useful as guides to behavior and decision making. These models serve as lenses through which "the world" is viewed and that enable predictions, or forecasts to be made. However, they may also act as "blinders", limiting our ability to see that which may not fit into our existing models. As the famous statistician, George Box said in an often-repeated quote, "essentially, all models (theories) are wrong, but some are useful." [1]

In regard to models in the "business of healthcare", we view these innovation theories or principles much like *pattern recognition methodologies* and less like the theories or algorithms that precisely describe and predict physical or chemical phenomenon. Box also pointed out that according to Occam's (or Ockham's) Razor, we should seek the simplest description available to describe the phenomena or pattern[2]. When two descriptions may be used to explain the same phenomena, the simplest generally works best - simpler theories are preferable to more complex ones because they are more testable.

In this regard, I am struck to point out the obvious similarities between Disruptive Innovation Theory and Blue Ocean Strategy (as outlined in Section One)! Both are used to understand and exploit new market opportunities where competition does not currently exist. So, the creation of a market with no competition can be represented by the blue ocean (creating a new value curve), or as a disruptive innovation that provides a low-cost solution for a job to be done, i. e. to meet the need of an unserved market space. So, we as entrepreneurs and innovators are generally advised to use the simplest description that works, and to be satisfied with the ability to recognize and use patterns (or screens) to guide the iterative product development/market fit stage of the innovation process. The lean startup model, or methodology is in its essence, an insightful utilization of the scientific method to find need, solutions, and then iteratively validate the product/market fit prior to scaling. Of course, in the biomedical space there are multiple parties involved in validating product/market fit as will be discussed below.

Recognition of patterns leading to understanding and predictability is nicely illustrated by the knowledge funnel in Roger Martin's book, "The Design of Business" discussed previously in this monograph[3]. He framed a funnel that starts off with a state of "mystery, chaos,

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or lack of any explanation "– whichever term you prefer. However, with further observation, questioning, experimentation, networking, and associative thinking, i. e. examination and analysis comprising the Innovators DNA of Dyer, Gregerson and Christensen[4], we can proceed to a state of understanding where some rational explanations appear; these are the patterns, screens or heuristics that have been identified. The final stage of evolution occurs at the end of the funnel; where further analysis leads to an outcome and potentially to the development of an algorithm, or an ability to predict outcomes accurately. This last stage, seldom achieved in business, is the desired end point, or the ability to predict the outcome precisely. Christensen in his book "The Innovator's Prescription"[5] focuses on disruptive innovation in healthcare, and frames disruptive innovation in a similar way where experts (highly trained surgeons for example) are required at the earliest stage since they have been trained to see patterns to guide their jobs to be done, but that they can be progressively displaced (or disrupted) as predictability becomes possible - by less trained professionals and potentially by machine learning derived algorithms (less expensive and good enough solutions for certain jobs to be done).[5] He goes on to discuss disruptions of the healthcare system along two dimensions:

Migrate provider

- Expensive specialists → less skilled practitioners → self-care

Migrate disease treatment/point of care

- Teaching hospitals → general hospitals → outpatient clinics → home-care

Opportunities exist and evolve over time along both of these dimensions as technology evolves and business models are developed.

In Section Two of this monograph (current section), we discuss the emerging challenges and opportunities in the healthcare industry and on the development and implementation of strategies for innovation. We focus on the "producers of goods and services" in the broader healthcare market, e.g. Pharmaceuticals, Biotechnology (collectively Biopharma), Medical Devices, and Digital Medicine (informatics, digital medicine). Each of these industry segments have seen similar transitions as covered below, and have led to the current emergence of digital, personalized medicine, including the ability to edit genes. The broader industry segments are driven by the invention and emergence of revolutionary technologies, but evolves under market focus, the ability to manage risks, and to compete in a capital efficient mode, while dealing with high levels of government involvement (e. g. with regulatory approvals, intellectual property, and reimbursement for products sold to end users.

BIOPHARMA EVOLUTION

The pharmaceutical industry has adapted and evolved over the years. The industry is enabled by emerging technology, from small molecule discovery and development, to the emergence of biotechnology, genomics and personalized medicine. The business model continues to evolve and change with the objective of continuing to create, deliver and capture value. The challenge of continuing to innovate is one that the industry faces now and into the foreseeable future.

Ernst & Young, in their annual "state of the industry report, "Beyond Borders"[6]. E&Y has termed these three models as Pharma 1.0, Pharma 2.0, and Pharma 3.0. Pharma 1.0 was prevalent early on in the pharmaceutical company evolution. Pharmaceutical therapeutics were largely small (organic) molecules and the business model was termed the Blockbuster Drug era, i.e. using the term to describe the potential "billion-dollar molecule" that could be used to sustain the organization during its period of market exclusivity possible largely thru patents (and their extensions).

Drivers of change signaling the end of the Pharma 1.0 era (beginning in the 1980s) included: patent cliffs, R&D productivity challenges, globalization, demographics, and pricing/reimbursement/regulatory issues (this driver of change persists to this day). During this era the biotechnology industry evolved, and this segment was much more entrepreneurial in its approach to drug development and financing strategies. We saw scientific advances in discovery as the Biotech Industry emerged with protein based therapies. And industry convergence was anticipated as genomics and associated technologies foretold the coming of personalized medicine.

The next era in the 1990's and early 2000-time frame focused on disease state, looking for the best solutions available for therapeutic treatment and to balanced or diversified portfolios. This era, termed Pharma 2.0 by E&Y, was characterized by the creation of Diversified Portfolios some developed internally, but many brought into the firm by open innovation. We saw extensive M&A activity leading to consolidation of the pharma and biotech industries, e. g. biopharma.

The drivers of change the end of that period beginning in the new millennia included: healthcare reform, the emergence of healthcare IT, value mining, and the serious emergence of consumerism (direct to consumer advertising) – and still awaiting the business model for personalized medicine to emerge. This leads us to the

next and current era which is referred to as Pharma 3.0. That current era is characterized by Healthy Outcomes. In the adoption and evolution of Pharma 3.0 , we are observing a shift from a physician, and provider- centric model to one where consumers and payers have emerged with more power in the ecosystem.

In the Pharma 3.0 era the focus is on Health Outcomes and we expect to see focus on wellness and prevention and perhaps for personalized medicine to move from the innovators and early adopters into mainstream markets. We also expect to see: new collaborative business models and partners; disruptive and sustained innovation; social media; mobile health; open innovation, and extensive networked collaborations and partnerships cross industry. It is our belief that many of the innovation principles covered in Section One are appropriate for the Biopharma industry in the context of its current challenges and constraints. This is also shared by E&Y (and the quote from Glen Giovannetti, one of the principal authors of "Beyond Borders":

"In this capital-constrained environment, we can no longer afford inefficiency and duplication in drug R&D. The industry needs to remove duplication, encourage pre-competitive collaboration, pool data, and let researchers learn in real time."

We recommend that the same principles from the Pharma 3.0 business model, utilizing an "outside-in" approach can be extended to include MedTech and to the evolving field of digital medicine. Digital transformation is now accelerating and leading to Convergence: where healthcare, traditional biopharma, and technology (the tech industry) collaborate as the industry moves to a customer and user-centric business model (Pharma 3.0). There is much to learn from industries "beyond life sciences" and to leverage strengths of a diverse range of entities (patients, providers, social networks, data analytics firms. What if big data could be harnessed to develop quicker, real-time insights about candidates in the pipeline? What if entrepreneurs, venture capitalists, and pharma worked together instead of in series?

As a result, in the near future we could see more and more examples of "converged" solutions that merge drugs & diagnostics (combined Rx-Dx) and devices, and digital technologies (including social media) to impact and connect the entire healthcare ecosystem which is customer/user centric. But, keep in mind that all of this will be occurring under the influences of globalization, the emergence of biosimilar biotech therapeutics, pending healthcare reform in the US, and drug pricing challenges. All formidable challenges individually and certainly collectively. We will cover some of these emerging opportunities in the next sections.

The goal going forward, as always will be to create, deliver and capture value to enhance the well-being of individuals (patients) while also serving the needs of the entire healthcare ecosystem (physicians, providers, payers, and even partners). Since design thinking is inherently a customer/user centric methodology, there will be many ways to incorporate design thinking into the culture and approach to innovation to identify, understand, and validate need and "jobs to be done". This would also include service design, where the utility of design thinking can be extended into providing an exceptional experience for services associated with healthcare and its delivery. All of these communities are under transformation as the industry shifts to the customer/user centric business model (Pharma 3.0) – more power in hands of patient and payers, less in hands of providers and physicians. Satisfying the needs of the "multiple P's" is indeed a challenge for this industry unlike any other. We contrast the differences and similarities into these markets from Business to Business (B2B), to Business to Consumer (B2C). Or for healthcare "B2/5P" (patient, physician, provider, payer, and partner – the 5Ps). This later is a more appropriate way for businesses to interact in a science/technology-enabled, regulated healthcare market – much different and more complex that the tech industry or most other industries. Later in this chapter we will outline some of the emerging business models that are being developed.

The industry segments above represent a very significant part of the value chain of the broader HealthCare industry which in the United States accounts for more than ~$2Trillion of expense or about 17.5% of US GDP (and growing) according to Burns, "The Business of Healthcare Innovation"[7]. Cost containment and risk management is an ever-present challenge. Burns further indicates the following breakdown for the industry illustrating that the concentration of value occurs in just a few diseases:

- 50% of value in 33 diseases
- 75% of value in 70 diseases
- 90% of value in 116 diseases

The Top 7 diseases, treated by a combination of small molecule and biotech drugs are summarized below, with each category ranging from $20B to $60B annually:

1. Obesity
2. Heart disease
3. Diabetes
4. Cancer (breast, lung, colorectal, prostate)
5. Infectious diseases (HIV/AIDS, other)
6. Central Nervous System – CNS (Alzheimer's, age associated memory, psychoses, anxiety)

7. Arthritis

Med Tech Summary

The MedTech market is also undergoing transformation under similar pressures outlined above for biopharma (and below for Digital Medicine). The market segment is smaller than biopharma, but growing profitably. The broader market is segmented into: medical devices, diagnostics, and medical imaging (we include mini case studies in each of these below). The largest market segments address cardiovascular, orthopedic, and neurological issues. Additional market segments include:

- mobility assisted technologies, bio-implants, diagnostic imaging, micro-arrays, minimally invasive & noninvasive surgery devices, biomaterials, mobile health & telemedicine, molecular diagnostics, drug discovery & drug delivery devices
- The industry is dominated by a handful of diversified companies (20,000 companies, most <$100 M annual revenue) – and, a few major players (30 to 50) with annual revenues exceeding $1B. Given this structure, M&A is most likely future for startups and emerging companies. The market is characterized by faster innovation and adoption (compared to biopharma), but is still slow compared to the non-medical technology market. Higher profitability/margins prevail (industry average P/E of 13+ in 2009 vs, P/E of 10 for pharma. However, new products are fueled by new technology and unmet market need. In this case, the physician exerts considerable power in the market adoption since they are most often the users of the technology. So, user centricity is equally as important as customer centricity. Sustainable growth is driven by the aging population. While there is price competition, commoditization is less common for devices (unlike generics or biosimilar therapeutics in the biopharma world). Sustaining innovation drives overall market growth, but disruptive innovation creates new market segments as noted above. "Procedure penetration" is also a growth mechanism since (once approved by the FDA), "if it works (safe and effective) it will be used even more broadly than expected (ex. stents, minimally invasive surgeries). A caveat here is that payment depends on performance according to "meaningful use interpretations".

We summarize below some of the continued innovations in MIS (minimally invasive surgery):

- Cardiovascular Percutaneous valve replacements
- Vascular assist devices & artificial hearts/ lungs
- Neurovascular/stroke occlusion
- Neuro-modulation
- Orthopedics – extremities (hips and shoulders)
- Prosthetics
- Robotics
- Artificial limbs, assisted walking, exoskeletons, etc.
- Diabetes pumps and continuous glucose monitoring

So, what else is coming next?

- More drug/device combinations
- Non-hospital based telemonitoring, telemedicine
- Digital radiology (already here), digital pathology (emerging), virtual colonoscopies (in development)
- Targeted diagnostics (therapeutics)
- Convergence of devices and drugs
- Stents, implants (orthopedic – spines, knees, hips)

We would suggest that perhaps the medtech segment would benefit by "taking a page from the biopharma playbook by creating business development strategies that partner with smaller, emerging medtech companies and even academia collaborations earlier in the life cycle prior to M&A consideration.

As a final issue, we point out that from a competitive perspective, patents are as important in medtech as they are in biopharma. But, we ask the question - "can emerging companies really use patents as the primary competitive advantage for the single product companies that they build to get to market and demonstrate value"? Beyond patents, how do you build competitive advantage in this space? (look at the Medrad case study written by Ned Uber later in this volume). We would

suggest building a platform strategy, or alternatively partnering with one of the larger players to leverage existing platforms. Platforms provide advantages for leveraging all players in the ecosystem, while connecting users and customers with the products and services that they need.

Digital Transformation Summary

The emergence of digital medicine promises to transform and disrupt healthcare over the next several decades. To accomplish this transformation will require cross industry collaboration and convergence around one common set of goals – affordable and available healthcare that creates value for all parties (patients, providers, physicians, payers, partners – and, now the public (an important 6th P, important in the current quest to improve and provide affordable healthcare to the entire economic spectrum). Convergence (covered below) deals with the intersection of multiple industries to provide products and services with higher value. With digital medicine or digital health, we see evidence of convergence of technology and medicine. We also extend this to include convergence to include development of appropriate business models, e. g. technology, medicine, and business. Consider the following areas of evolution:

- **Technology** - Artificial Intelligence, Machine Learning, Digital imaging, digital health (consumer-facing wearables), 3D printing/manufacturing, robotics
- **Medicine** – Telemedicine, Genomics, Gene Editing, Personalized Medicine or Precision Medicine
- **Open Innovation Partnerships** and **Convergences** have begun to emerge **cross industry** – The technology industry is bringing new perspective and capability to the healthcare industry. Just to name a few: Google/Alphabet/Verily (partnerships with J&J. GSK, Sanofi); IBM Watson (partnerships surrounding this AI/ML platform are too many to name); Apple; Microsoft; GE Healthcare. These alliances and partnerships are expected to fuel usability, efficacy, and capital efficiency, and to create a healthier population with responsibility for their own wellbeing.

The Product Life Cycle concept, and crossing the chasm model is useful to understand the evolution underway. In the case of consumer driven (technology) products, one might expect a short life cycle of adoption and diffusion. We see perhaps two-year life cycles for consumer electronics devices such as cell phones and personal computers/laptops. In healthcare, given the dynamics and non-market factors that drive adoption, we might expect a much longer progressive evolution and market penetration covering three phases perhaps over a 15-year time frame.

Phase 1 - We are still in Phase I of the evolution (focused on innovators and early adopters), for example with individualized fitness trackers and health monitoring devices. There is a need to develop scalable solutions with demonstrated product/market fit over the next 5 years or so. Also, for integration of population data for personalized insights, decentralization of the care delivery model, ingestible sensors, patches, etc.

Phase 2 - Enter the Chasm, and or the downside of the Gartner Hype Cycle[8] as appropriate technological advances occur, & business models are developed and validated during the next 5 years or so.

Phase 3 - Then Transition into the early and late majority markets where wearables move from outside the body to targeted therapies and chronic disease management, convergence of wearables with digital health platforms

This area provides significant opportunity/need, an abundance of technology options, but plenty of threats including privacy, data security, regulatory and reimbursement (pricing), and challenges with technology adoption commensurate with value creation and delivery.

A takeaway message is that the emergence of **digital medicine will transform and disrupt healthcare** over the next several decades – just like digital and mobile technology has changed our lives over the last two decades thru the internet, search, social media, etc. To accomplish this transformation will require **cross industry collaboration and convergence** around one common set of goals – affordable and available healthcare that creates value for all parties (patients, providers, physicians, payers, public) –and partners!

Convergence – the Future of Healthcare Innovation Cross Sector

Following the theme of digital medicine above, we include a brief summary of some current examples of disruptive technologies (still seeking disruptive business models to enter the upper right quadrant of innovation titled Architectural Innovation or Epiphany of

Meaning/Design Driven Innovation, c. g. Figure 2 of Section One in this monograph). We refer the interested reader for much more detail on the topic of emerging technologies to "Monetizing the Future: Business Model Transformation in Healthcare" (ref. Frost & Sullivan, 2016).[9]

- Watson for oncology, robots to assist autistic children, drug delivery patches, ingestible sensors and devices to assist with medical adherence, virtual colonoscopies, robotic surgeries, tele-radiology/pathology, etc.).
- Use of brain-computer interface to connect the visually challenged → wearable electronics, sensor fusion, energy harvesting.
- Computer-driven intelligence for automated decision making → smart sensors, M2M communication, 3D printing, big data, predictive analytics, context aware computing.
- Next gen connected care for continuous and personalized care.
- Augmented, Reality-based surgery – real-time information sharing during surgery ("everything as a service" business model – a takeoff from the software as a service cloud based model popular in the tech space).

EMERGING BUSINESS MODELS IN BIOPHARMA

Previous work by Boni and co-workers has recently summarized the emergence of new business models in biopharma and also identified some challenges faced by the industry. The interested reader is referred to recent papers published in the Journal of Commercial Biotechnology by Boni & Moehle[10], and also Boni[11].

We then consider the implications regarding emerging business models in biopharma, especially related to the near-universal trend to move from a closed innovation model (vertical integration within the firm), to an open innovation model with partnering occurring across the value chain; Boni and Moehle[10].

The lean thinking/lean startup model is then applied to Biopharma as a further strategy to achieve capital efficiency and converging on product/market fit, especially while also managing additional risk factors associated with healthcare innovation such as IP, regulatory, reimbursement, privacy and cyber security, Boni[11].

Specific strategies that Boni and Moehle[10] suggest include the following:

1. A focus on **creative value sharing** along the value chain with academic and commercial partners (open innovation, as opposed to vertical integration).

    a. The use of staged, creative, partnerships and consortia to create a networked innovation model for creating, delivering and sharing value.
    b. Leverage academia, emerging companies, and industry to form extended teams across the value chain.
    c. Examples here include the FIP Net concept developed by Eli Lilly and Co. The consortium approach pursued by Pure Tech Ventures in creating the Enlight Biosciences model in partnership with multiple biopharma tech companies

2. Use of **"stage appropriate" financing vehicles** for translating thru each stage of commercialization from the laboratory to the clinic to commercial product (service) – government, private equity (angel, angel consortia, VC, and private equity), public funding.

    a. Using the concept of "bio dollars" (milestone-based payments that progress as risk is reduced along the path to market) as an integral part of the financial deal structure as a way of balancing risk and reward.
    b. The use of public-private partnerships to finance higher risk, early stage investments and enhance downstream partnerships
    c. Examples here include various ab initio formation of platform companies utilizing breakthrough technologies by Rock Health (e. g. Foundation Medicine), and the Harrington Project that couples academic medicine to BioMotiv to accelerate discoveries to the market leading to breakthrough medicines.

3. Developing and growing **"seasoned" management teams** with expertise and network access across the value chain to match technology with market need.

    a. Utilization of **virtual management teams** that can add value to **a portfolio of opportunities**, and with the expertise and ability to cross the "valley of death"

from the inspiration and ideation phase of innovation, thru the execution phase to commercialization. ***We are quick to point of that this approach will require the development and adoption of new management skills and processes to manage these sometimes "self-managed", open and virtual teams that span the globe.***

b. Adopting the use of **networked "accelerators"** to move seamlessly thru the commercialization pathway (translational research to cross multiple "valleys of death" from the laboratory, thru clinical testing, to FDA approval and to the marketplace).
c. Examples include Jlabs, QB3, and Rock Health.

In summary, the following principles are recommended by startups and emerging companies:

- ***Operate Lean and Use Agile Development Processes***
- Keep the cost of capital low while addressing product/market fit
- Scale team business and technology expertise adaptively as the market is developing

- ***Use Creative Financing***
- Use for profit and not-for profit sources and partnerships

- ***Create and Grow Innovation Teams***
- Collaborative and diverse interdisciplinary teams evolve thru the commercialization phases when scaling from startup to "platform company" to market
- But, some of the "DNA" embedded at the earliest stages must persist

Summary

We have provided a short summary and **visibility** into the technologies impacting the future of health and medicine, and to the business model challenges that exist to exploit these advancing technologies and lead to commercialization of the technology and bring the outcome of innovation to customers and users. Technologies include Artificial Intelligence (AI) and Machine Learning (ML), Machine Vision (ML), to big data, robotics, and digital devices, and low-cost genomics on the physical technology side. Technologies on the biotechnology side would include synthetic biology, gene editing, regenerative medicine, and beyond — these breakthrough technologies are reshaping prevention, diagnosis, therapy, discovery, and beyond. However, all of these disruptive or transformational technologies must be incorporated into business models that, in addition to creating value, must deliver that value to all participants in the value chain. And, to bring about wellbeing in an affordable and accessible manner, while retaining a sufficient fraction of that value for the stakeholders and partners in the venture. And, as an additional challenge: to deal with intellectual property issues; regulatory challenges; and, reimbursement/pricing issues! Healthcare innovation is indeed a challenge.

So, how do we apply the commercialization and innovation approaches and innovation theories outlined in Section One to innovating in biopharma, med tech and digital medicine given the evolution and current challenges of this industry?

First, Boni, in a previous article has written briefly about the role of design thinking in biopharma[12]. We have covered design thinking in Section One of this monograph, and also have included articles specifically for biomedical applications later in Section Two (see articles by Sarah Marie Foley, Matt Beale and Ned Uber). The interested reader is referred to those materials in this Monograph.

Secondly, and in closing, I am reminded of a book written by Gary Pisano, "Science Business: The Promise, the Reality, and the Future of Biotech"[13]. At the time this book was written, many were questioning whether or not biotech would meet the expectations of its promise, despite all of the money that had been invested by the venture capital community and the pharmaceutical companies over the previous several decades. This book discusses the challenges associated with turning the growing biotechnology field into a business, e.g. "how can biotechnology science be a business". As stated by Pisano, the hypothesis is that nimble, entrepreneurial businesses based on (science), protein-derived leads, would provide more drugs, more profit, and greater reward to investors (and partners). The observation is that few biotechnology companies ever reach profitability, even with exits possible by IPO in some cases – principally for the purpose of accessing more capital publicly. Most biotech companies end up being acquired by pharma which has fueled the emergence of the biopharma ecosystem as discussed above. Access to the pharma business model is important, e. g. channels, clinical expertise, resources, etc. We are just now beginning to see the emergence of paradigm shifting technologies based on genetically modified immunotherapies for example obtaining FDA approval (even though the debate continues on reimbursement)

Table 1: "Learning objectives" for commercialization and innovation in biopharma, medtech and digital medicine

Observations and Challenges Associated with Innovating in this Industry	Learning Objectives
The industry is driven by science and technology; however, the ideas originating from scientific advances are only as good as the business model that create, delivers and capture value.	Identify unmet needs and value creation opportunities that are unique. Create new value curves for unserved jobs/executors/ contexts, with lower cost and higher performance solutions. And, select a position in the value chain for your organization and innovation that optimizes risk, reward, and capital efficiency.
Create and implement novel, open innovation business models to accelerate innovation from discovery thru the clinic to the market.	Create or participate in a significant platform serving an ecosystem to create and sustain a competitive advantage. Platforms win vs. products!
Traditional Venture Capital investments must be leveraged by government and other private sources of capital, since VC capital taken alone is insufficient to capitalize emerging ventures in healthcare.	Finance entities with significant capital, over long time, high risk hurdles across the regulated development lifecycle using corporate partnerships and alliances, and to exit via IPO, or Mergers and Acquisitions (M&A) – and, to get reimbursed. Use lean entrepreneurship principles to address the early stages of venture development prior to growth and scaling.
Disruptive innovation (or blue ocean strategies) for innovation must be adapted to accommodate market and non-market factors that drive or impede innovation.	Leverage the skills of the design community to innovate in an ecosystem where the interests of consumers, customers and payers (patients, physicians, providers and payers – the 4, or 5 P's) must be aligned, and where non-market factors add additional complexity and risk dimensions, c. f. Boni12

– and the business models are just recently being developed and implemented.

We have learned over time how the Industry structure, or anatomy that was borrowed from Silicon Valley (tech) has some "flaws" when applied to biotech –or at least has some serious challenges.

Biotechnology in particular is not analogous to technology (software, computers, semiconductors). - What is different for biotech?

- The uncertainty inherent in human biology and processes leads to very high technology risk profiles since it is difficult to predict that the technology will "work". We all remember that at most, only 1 of 10,000 initial New Molecular Entities, e. g. drug candidates, or NMEs) reaches the market with FDA approval (the number varies depending on drug type, e. g. small molecule, monoclonal antibody, etc.)
- Complicated and overlapping intellectual property (IP) exacerbates the problem, since patents with strong freedom to operate are essential.
- The capital intensity and development life cycle are much higher and longer and that is not necessarily compatible with the life time of venture capital funds (notwithstanding the limited size of funds).
- The business model challenges are much more complex as we have already discussed - think about the 5Ps. It's a much more complex set of dynamics for bringing products to market and getting paid with sufficient ROI.
- We have previously written about the challenges faced by the bio-entrepreneur as they decide "how much of the business model do they build internally" vs. by "renting parts of that business model from others". Do we try initially to build a platform and a single product, and then build a platform downstream (or join another). This decision impacts financing and team building decisions and of course the risk/reward balance. Refer to our article titled "Project, Product or Company" as metaphors for selection of paths to the market.14
- Successful drug R&D needs to be highly integrated (and learned from experience). This has considerable implications regarding the team composition across the development life cycle from laboratory to market

- Finally, harnessing and leveraging collective and cumulative (institutional) learning is a huge and expensive challenge

In summary, in effect all of this presents a serious an open innovation challenge for biopharma, and to a certain extent med tech and digital medicine.

We have developed a set of "learning objectives, or takeaways" shown in Table 1 that might be a helpful guide for the bio-entrepreneur.

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Article

The R&D Marketing Interface in Biopharma and MedTech

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ABSTRACT

This article highlights the importance of building a marketing led cross-functional team that integrates the R&D, and commercialization process in an early stage Biopharma and MedTech company. Marketing should play a prominent role in the cross-functional team at the earliest stages of company formation and product development to identify unmet need, design the development plan, shape the product life cycle, position the product in the competitive set, and understand all market drivers and competitive factors that are essential to ensure commercial success. In particular, in this paper, the focus is on the importance of creating an appealing target product profile (TPP) and describe the rational and methodology for creating the TPP. Drug development is a high risk, high cost, high reward undertaking, and the TPP provides a market-guided approach to development of drugs more quickly, inexpensively, and with a higher rate of success.

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INTRODUCTION

Earlier in this Monograph, Boni has discussed emerging trends in Biopharma, MedTech and digital medicine (see Chapter One of Part Two titled "Innovation Principles in the Pharma 3.0 Business Model Paradigm: User-Centric Applications to Biopharma, MedTech and Digital Medicine with Cross-Sector Convergence). Differentiated product, patient centricity, access, cost control, and price transparency are important factors for commercial success as the Pharma 3.0 business model emerges and is being implemented by the industry. With increasing sensitivity to the cost of medicines, power is shifting to patients and payers, so the importance of value and outcomes is increasing. Alternative delivery models and partnerships are emerging, and digital transformation is enhancing patient engagement in the health care ecosystem. All of these factors are centered in the domain of marketing, the focus of this Chapter. First, we discuss briefly the life sciences drug development environment followed by the role of marketing in shaping the Target Product Profile and how TPP can improve commercial success of a product.

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LIFE SCIENCES ENVIRONMENT

When a life sciences product (pharmaceutical, biotech, MedTech) is discovered, invented or conceived major commercialization challenges include the cost risk, and time to develop the product for the market. For example, in the case of pharmaceutical and biotechnology products, the cost and time required to develop the product for FDA approval is a very expensive and lengthy process. According to the research from the Tuft's Center for the Study of Drug Development, it is estimated that the cost to develop a pharmaceutical drug is $2.6 billion (2013 dollars)[1]. The $2.558 billion figure per approved compound is based on estimated average out-of-pocket costs of $1.395 billion and time value of money (expected returns that investors forego while a drug is in development) of $1.163 billion. The average length to develop a drug is about 12-15 years (Pre-IND 5-7 years, Post IND 6-7 years and approval 10 months).[1] For every 10,000 drug candidates developed about 250 enter clinical trials and one gets approved. These very low approval rates highlight the risk involved in drug development. Then the drug, upon commercialization, has to recoup the cost of all the failed projects to be reinvested to support further drug development. To minimize these risky drug development projects, pharmaceutical companies have created an options model of drug development that includes partnership(s) with early stage companies thereby investing simultaneously in a multitude of technologies, monitoring the

research outcomes over time, and also partnering or acquiring technologies that are promising for the market at later stages of development, e. g. Phase II a, b, or Phase III in the FDA schema. Also with the advent of biologic drugs the cost of investment capital and manufacturing are both high. So, it is imperative that the company should have a good understanding of the market potential, timeline and cost of development before investing significant resources in developing the drug.

Even after the FDA approval, only a third of the drug launches meet the forecasted sales[2]. One of the reasons for lack of market adoption is the lack of clarity of differentiation of the products vs. current standard of care alternative treatments. For example, a recent study classified the pharmaceutical products into three categories: 37% of the market falls into the commodity category; 35% would be consider as differentiated products; and, the remaining 28% would be "transitional", i. e. between commodity and differentiated products[3]. In another study, only 24% of the total number of products launched are considered strongly differentiated in the market.[4] Because of the increasing cost of healthcare, the payers are increasingly focusing on the value and outcome of products in their reimbursement strategy. Rajkumar et al have identified four categories of the CMS (Center for the Medicare and Medicaid Services) framework for payment or reimbursement to providers.[5]

- Category 1 – Fee for Service – no link to value
- Category 2 – Fee for Service – link to value
- Category 3 – Alternative Payment Models Built on Fee-for-Service Architecture
- Category 4 – Population-based Payment – where physicians and organizations are responsible for the care of individuals for an extended period of time.

By 2018, 50% of payments are expected to be alternative payment models (Categories 3, 4), and 90% are Fee for Service linked to value (Categories 2,3, 4). So, a measurement of value created and delivered is becoming an increasingly important component of the commercial success of biomedical products, i. e. the value captured. CMS indicated in early 2016 that they have already achieved the goal of 30% of payments based on alternative payment models set for 2016 and are on track to achieve the 2018 goals. The message is that the value-based reimbursement models will increase the need for pharmaceutical companies to show evidence of value for their newly launched products.

An additional trend that is stressing the importance of marketing is the loss of exclusivity for pharma products with the emergence of generics and biosimilars in recent years. The patent expirations are expected to be 50% more in the next five years[6]. An estimated $140 billion dollars of branded products are going to losing patent exclusivity between 2017-2021[6]. Therefore, there is increasing need to bring to market high value products to replace the loss of revenue due to the patent expirations.

In summary, the medical product development process is a high-risk model. Given the changing life sciences industry landscape both startup and established companies alike have to create innovative products to serve markets with high unmet need and deliver value to those markets. The start-up companies, being resource constrained, have to be especially prudent in their choices of products to develop for the market. In this context, the role of marketing within the companies can assist in identification and development of high value products.

MARKETING

By definition, marketing comprises the activity and processes for creating (Product), communicating (Promotion), delivering (Place or distribution), and exchanging offerings that have value (right Price) for customers, clients, partners, and society at large[7]. Marketing facilitates developing an acceptable product that satisfies an unmet need, creates awareness of the product by communicating the value of the product to the stakeholders such as physicians, patient and payers via promotion, makes the product accessible by executing a distribution strategy also called place, and finally offer the product to the customers capturing the value created using appropriate pricing strategy (See Table1 below).

High-performance marketing in an organization can create the ability to leverage customer insights, demonstrate superior cross-functional collaboration, and achieve strategic focus. Accordingly, marketing needs to be empowered to generate and share its knowledge of customers (and of the overall constituents/competitive set outside of the organization) with all other functional aspects of the innovation team in the life sciences company: from research, preclinical, clinical, regulatory, manufacturing, finance, health economics & outcomes research (HEOR), analytics, and sales, so that the knowledge can be reflected and incorporated into everything the company does (c. f. Fig. 1). In this Chapter, we discuss how marketing can help to create, commercialize, and offer an innovative product with high potential to obtain a significant market share.

An innovative Product is by definition a differentiated product (solution) that offers a meaningful advantage (value) over existing treatments for a given condition. Marketing can shape (or frame) a differentiated product using the target product profile (TPP) developed for

Table 1: 4 Ps, A's and Objectives of Marketing

4 Ps	4 As	Objectives
Product	Acceptability	Address unmet needs
Promotion	Awareness	Communication of value
Place	Accessibility	Create convenience
Price	Affordability	Value to payers

Figure 1: Marketing facilitate cross-functional decisions

the purpose of creating a competitive advantage for the product.

TARGET PRODUCT PROFILE

In 2007, FDA developed a target product profile (TPP) guidance document as a strategic tool to facilitate effective constructive dialogue between the FDA review staff and the sponsors (companies), thus potentially reducing the drug development timeline and minimizing the risk of late stage failures of the drug for a targeted indication.[8] Three common reasons for pharmaceutical failures in phase III trials are efficacy (failure to meet the primary endpoint), safety (unexpected adverse or serious adverse events) and commercial/financial (failure to demonstrate value compared to existing therapies) value of the products.[9] TPPs can

improve the probability of optimal safety and efficacy data in a timely manner, thus enhancing the commercial value of the product. The sponsor would begin developing the TPP with the end goal of creating the best possible label in mind, and to specify the drug development program and specific studies to support the proposed label; and, to guide the design, conduct and analysis of the clinical trials. Ultimately, the TPP should allow for an improved label, decrease the total amount of time spent on the entire drug development process, and reduce the cost as well.

ATTRIBUTES OF A TPP

A Target Product profile (TPP) is an important strategic document that provides a detailed summary of the product being developed, product's desired characteristics and features, developmental plan that demonstrate the product performance and the features that would provide competitive advantage. Sponsors should start with the TPP with the commercial objectives of the product in mind. How should the final label describe the product that will meet customer needs? Here the customer includes (patient, payer, pharmacist, and provider). It is important to conduct market research thru questioning to gain insights and to understand the needs of all these constituencies. The TPP would include: indication, dosage form and frequency, and differentiation (efficacy safety, economics). The attributes shaped by marketing would include (indication and usage, dosage and administration, dosage forms and strengths, contraindications, warning and precautions, adverse reactions, drug interactions, use in specific population, drug abuse and dependence, clinical pharmacology, nonclinical toxicology formulation, trade dress, efficacy/superiority, safety, pediatric dose and pharmacoeconomic data). All parties (research, development, marketing, regulatory, and clinical testing are required to work together to develop and execute a strong development plan that demonstrates superior clinical performance, patient benefit, and health economic value. Note that in startup companies and in companies practicing open innovation, some of these parties may be obtained from outside sources obtained by contract and/or partnership.

The resulting document should contain an optimized realistic view of the objectives of drug development. This document ideally contains a synopsis of what will end up on the drug label, listed for each of three scenarios: the ideal product description ("best-case"), a minimally acceptable product description ("worst-case"), and a realistic description that falls in between these best- and worst-case scenarios that will likely resemble the actual commercial product label after approval (Target or "likely-case"). The best case should be the goal: what the sponsor hopes to claim on the final label, which will be used to guide the design, conduct, and analyses of clinical trials to provide maximum efficiency to the overall development program (see Table 2). An annotations or comments section can be added to provide information on proposed, planned or completed studies that will support the target, including protocol numbers and relevant dates. A TTP is a dynamic living document which can be updated as the drug development program progresses and knowledge of the drug increases. Thus, TPP provides a structure for the scientific, technical, clinical, and market information that is required to achieve a desired commercial outcome. It provides all stakeholders with a clear vision of the product objectives and helps guide research and development decisions. It is a dynamic strategic document that should be reviewed and updated throughout the development process.

As noted earlier, significant sunk costs during R&D, and poor market acceptance upon launch does not lead to a favorable financial outcome for the developer. We posit that early stage and continuous marketing input can change this equation. Recall in the lean startup model where continuous feedback from all constituents during the development process is needed for successful demonstration of product/market fit upon the product launch and growth stages. In the biomedical arena market feedback is required from all of these (multiple) constituencies: patients, physicians, providers, payers, partners, regulators, (and investors)! Close collaboration of all these constituencies is required to achieve an integrated commercial model, i. e. product/market fit in lean startup jargon. In addition, we note that marketing is too important to be left to marketers alone, all cross functional team members should be engaged in creating the marketing message and TPP.

STRATEGIC FRAMEWORK

Tebbey and Rink[10] have provided the following strategic framework in three levels:

1. **Target Market Profile (TMP)** – to delineate the unmet needs of the market for which the product is viable. The TMP will capture information regarding the therapeutic areas/diseases including unmet need, patient populations, drivers of use, competitive assessment and the economic cost of the disease.

Table 2: Sample TPP

	Description	Example		
Product Description	Brief description and/or current product name.	CTSI-001		
Mechanism of Action (MOA)	The mechanism by which the product produces an effect on a living organism.	Blocks the interaction between		
Clinical Pharmacology	Pharmacokinetic information, distribution and pathways for transformation.	• Intravenous (IV) administration of CTSI-001 to subjects was well tolerated in the ascending single-dose (0.002-10 mg/kg) and multiple-dose (0.5-5 mg/kg) studies. • The pharmacokinetic profile is roughly linear at doses above 2 mg/kg and the mean half-life is around 28 days. • Safety and PK profiles from the subcutaneous tolerability study are expected to be comparable to that seen in IV studies and PK/PD profile in treatment population will be supportive of monthly closing regimen.		
Indication	Target disease or manifestation of a disease and/or population.	Moderate to severe patients inadequately controlled on inhaled corticosteroids (ICS).		
Primary Efficacy Endpoints	The most important clinical outcome measure. Ideally should be easy to interpret and sensitive to treatment differences.	***Optimistic***: >50% exacerbation rate reduction vs. inhaled corticosteroids.	***Target***: 50% exacerbation rate reduction vs. inhaled corticosteroids.	***Minimal***: 35% exacerbation rate redution vs. inhaled corticosteroids.
Secondary Efficacy Endpoints	Additional criteria that may be met during a clinical trial, but that are not required to obtain a successful positive clinical trial result.	***Optimistic***: Four (4) months asthma control measured by Asthma Control Questionnaire (ACQ)	***Target***: Three (3) months asthma control measured by ACQ	***Minimal***: Two (2) months asthma control measured by ACQ

Source: Launchpad.ucsf.com

2. **Strategic Target Profile (STP)** – a vision of how the product should meet the needs of the market. The STP includes the target attributes (desired profile) along with value drivers/positioning, global reach, pricing/reimbursement, revenue/profitability, investment, cost of goods, and any licenses/royalties that may be required. This material is developed prior to clinical testing and then would be updated as needed as the clinical trials advance.
3. **Target Product Profile (TPP)** – a dynamic summary of the drug that is most likely to launch. This would include indications and usage (label) including: dosing and administration, contraindications, warnings, adverse reactions, description, clinical pharmacology, storage and handling. This information is updated as clinical trials advance and with the guidance of the regulatory authorities.

This strategic framework (TMP, STP) is used to shape the TPP and to define the clinical and commercial value of the product (see Table 3). Application of the framework encourages the right dialogue within the company and with the FDA to optimize label and commercial success. The framework enables the identification of key development milestones, critical times to assess the achievement of TPP and success criteria. Marketing is key for creating a "beyond the pill" solution, and shaping the label for the product.

Table 3: Strategic Framework

	Target Market Profile (TMP)	Strategic Target Profile (STP)	Target Product Profile (TPP)
Purpose	Captures all the key information about the market	A vision for a product that will meet the needs of the market	A record of the drug that is most likely to launch
Content	Therapeutic areas/diseases • Unmet Need • Patient Populations • Drivers of use • Competitive assessment • Economic cost of disease	Target attributes (desired profile) • Value drivers • Global • Pricing/Reimbursement • Patient Share • Revenue – Profitability • Pharmacoeconomics • Investments (R&D, COGS, SGA) • Cost of goods • Licenses, Royalties	Indications and usage (label) • Dosing and administration • Contraindications • Warnings and precautions • Adverse reactions • Description • Clinical Pharmacology • Clinical Studies • Storage and handling
Rigidity	Create before the STP or TPP Details are updated as findings emerge, but core facts change only in response to major market events	Set at the beginning of clinical development and updated only when necessitated by changes in the TMP	Updated as clinical and pharmacologic findings emerge and in response to guidance from regulatory authorities

Source: Tebbey, P. W. and Rink, C. (2009) "TPP: A Renaissance for its Definition and Use, Journal of Medical Marketing, Vol. 9 (4), 301–307

VALUE OF TPP

TPP can help the inventor to understand how the drug can be valuable to the customers' (patients, physicians and payers), differentiate from other competitive offerings and identify the critical value drivers and improve internal communication for product development. Specifically, TPP helps to identify the indications to pursue, obtain additional intellectual property (IP), develop publications and presentations to validate the technology, design clinical trials to get optimistic outcomes such as efficacy, specificity, reduce adverse events, decrease cost of goods sold, and explore novel mechanism of action (MOAs). TPP can potentially develop the label and the drug product insert from the global perspective. TPP can provide varying labeling scenarios and also estimate each scenario from the perspective of probability of success for regulatory approval, personnel needed, manufacturing, competitors and market penetration thus guiding the strategy development and decision making of the inventor. Investors have potentially many different alternatives to invest. Effective use of TPP can make the investors understand the importance of your technology.

However, recent research published in Nature has shown that while TPP is valuable, it is underused.[11] Our goal is to stress the importance and power of TPP as an influence to successful outcomes, and how it can lead to more efficient and successful drug development.

When used properly, the Target Product Profile can be an invaluable strategic planning tool. TPPs can assess potential pitfalls and create mitigation plans at all stages of the clinical development process. They can aid in planning through distribution to clinical and nonclinical research organizations in order to solicit advice and modify existing study plans to be more time- and cost-efficient. These documents also promote a team-based approach to drug development, by raising awareness of the marketing goals and the clinical programs among team members and promoting collaboration within the project.

The TPP can also be used to estimate the market potential and establish the net present value of a given product. By taking into consideration the optimal (best-case) scenario, the target (likely-case) scenario, and the minimal (worst-case scenario), a sponsor can provide develop the competitive strategies required to make a successful product; keeping in mind that a successful product is not only an approved product, but also one that is optimally profitable.

ROLE OF MARKETING -"BEYOND THE PILL SOLUTIONS"

Marketing shapes the core value of the product using TPP. But designing a differentiated value-based product require appropriate planning in shaping the data, service and financial dimensions of value in addition to the core product. These additional dimensions can provide "beyond the pill solutions" (see Fig. 2)

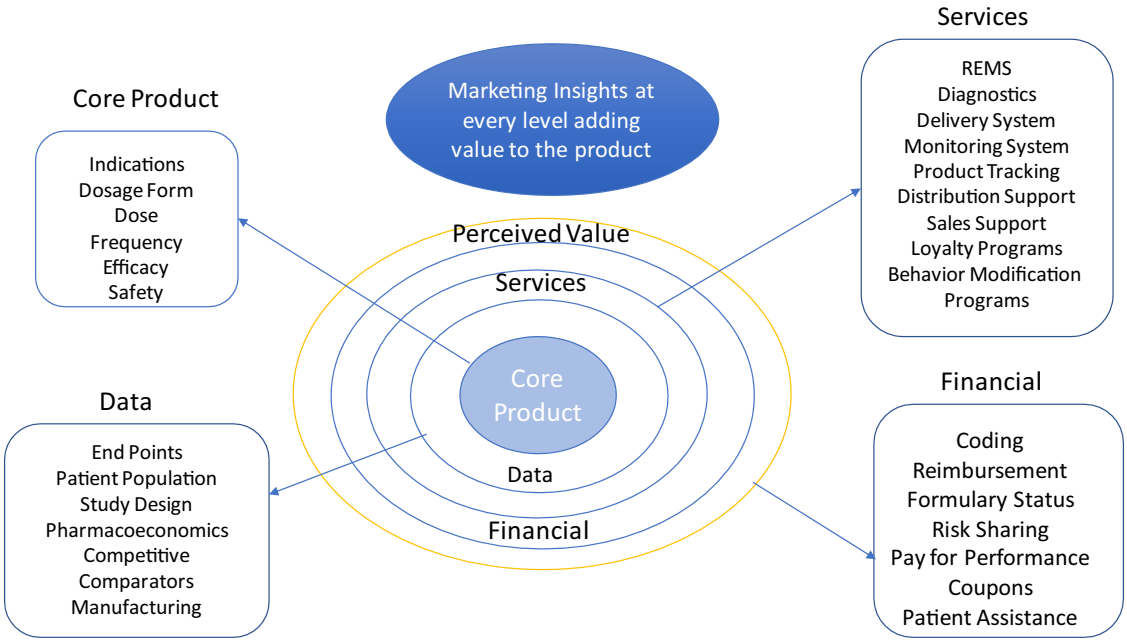

Figure 2: Marketing insights shaping the value of products

CONCLUDING REMARKS

Our message is that inclusion of marketing as an integral part of the R&D team is a critical component of ultimate commercial success. Market research and competitive intelligence is essential in clinical trial planning and label development. Cross functional teams work best to provide interdisciplinary perspective required to gather and incorporate all data and factors that will be important to ultimate commercial success of the intended product, and to understand the users (patients), payers, physicians, regulators, providers, partners.

So, start with the end in mind. That is to develop the ideal TPP and label that will win in the market. Then incrementally develop the drug to meet that TPP (which may evolve as more information and data are developed). A detailed Target Product Profile, when created early in the development program and updated as new information becomes available throughout the drug development process can be extremely helpful in mapping out the strategic marketing and scientific pathway. The TPP can not only facilitate interactions with the FDA, but also help in the strategic planning of the clinical and nonclinical programs and provide a valuable tool in the assessment of the market value of the product. TPP can also enable effective interaction with the payers to get valuable input on the commercial value of the product. It defines the goals of the drug development early in the process, focusing team efforts and streamlining program implementation. All of these advantages contribute to the ultimate goal of driving greater efficiencies and shorter timelines to the approval of an optimally marketable and profitable product. The success is when the final version of TPP is similar to the annotated draft labeling!

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Article

Design Thinking at Daedalus

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ABSTRACT

Developing solutions for biopharma/medtech/digital medicine products and services requires a cross-disciplinary team to engage a broad section of the healthcare ecosystem. Unlike technology products, this ecosystem is more complex and involves patients, physicians, providers, payers, and partners. Each of these parties must be engaged to understand overall market need, requirements, and constraints. This article focuses on design thinking as part of the overall strategic and marketing resources that can be used to observe, question, and understand the needs of the entire ecosystem. The interdisciplinary commercialization team can thereby reach a common understanding of the outcome of each component of the job to be done from the perspectives of each party, and thereby achieve overall product/market fit for the product design and overall business model components. This chapter outlines the perspective and approach of Daedalus, a full-service, interdisciplinary product development firm with decades of experience working with medtech companies. The article is complementary and supplementary to the materials on design thinking in Part One of this monograph/special edition. It also covers several examples as mini cases that are pertinent to healthcare from projects undertaken by Daedalus, Inc. from their industry portfolio of achievements.

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INTRODUCTION

Although our industrial design educations occurred in different eras and in different places, the authors learned a human-centered approach grounded in process. Because we had this in common, it was relatively easy for us to understand what we were working towards as a firm, even though we were often out-of-sync with the expectations of the kind of people and firms who hired us. Perhaps influenced by the automotive industry styling-oriented approach to design, we were often brought in late in the process to rescue the physical appearance of a virtually finished and completely engineered product. With the designer's hands tied, Tim Cunningham referred to this as "*painting on the design*", while a less diplomatic consultant might call it "*putting lipstick on a pig*".

Tim Cunningham founded Daedalus in 1979 as an industrial design firm. Matt Beale became his partner in 1995, and the firm's president in 2001. Together they executed the firm's transition from an industrial design firm to a full-service interdisciplinary product development firm with a staff of professionals representing ethnography, human factors, and a variety of design and engineering disciplines. Throughout their professional careers, Beale and Cunningham have worked as adjunct professors at Carnegie Mellon University and have contributed as lecturers and speakers at conferences and other universities. Since his retirement from Daedalus in 2011, Tim Cunningham has taught at Carnegie Mellon's Integrated Innovation Institute and Tepper School of Business in both Pittsburgh and Silicon Valley.

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In the advent of the firm, it took persuasion and perseverance and sometimes good luck, for us to find or make the then-rare opportunities to do design work that was more than skin deep. Whenever possible, we applied a process that teamed engineers, designers, and marketers together, with all of them having direct experiences with the people who would ultimately use the products we were creating. And, we kept a core interdisciplinary team intact and a part of the discussion

from project beginning to end, all of us focused on the people who would use the product and also the continuously changing mockups and prototypes of the latest product ideas.

To use more contemporary language, we applied design thinking thru an integrated, cross-disciplinary team from Daedalus and sponsoring company, who were intimately engaged with the product ecosystem. This approach is described more fully below.

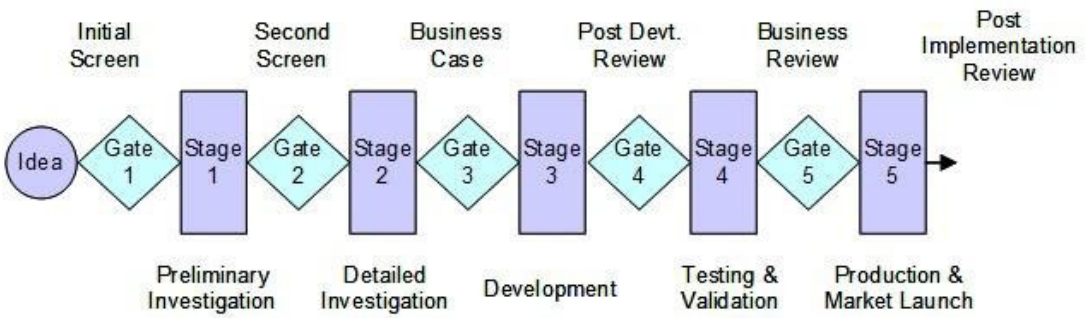
Design thinking has been popularized in the business world since the year 2000, especially through the work and writings of Tim Brown *(Change by Design)* and David Kelley *(The Art of Innovation, and The Ten Faces of Innovation)* of IDEO, and Roger Martin of the University of Toronto *(Business by Design)*. However, the term has existed in the industrial design profession since the late 1980s, while the concepts that underlie it have defined the industrial design profession since its inception early in the twentieth century.

Through a set of influences and experiences we arrived at our vision of design thinking. Three influencers stand out. The first was the father of applied human factors, industrial designer Henry Dreyfuss, who, in his 1955 book, *Designing for People*, defined industrial design as *a means of making sure the machine makes attractive commodities that work better because they are designed to work better.* The second was Victor Papanek, who, in *Design for the Real World*, advocated for the powerful social impact of design, and Edward De Bono, who taught us thinking can be done in a variety of different ways and these ways are teachable, *c. f. Six Thinking Hats and Lateral Thinking.* . Through these three influencers we came to understand that design was more than style, design could change society for the better, and that design was not only a way of doing but a way of thinking. We came to define design thinking as follows:

Design Thinking is a Way of Thinking that Understands, Explores, Simulates, and Implements Positive Change

To support that definition, we worked to define a design process. At root, our attempts at process were based on the 7-stages defined by Herb Simon in *The Sciences of the Artificial*. His process (define, research, ideate, prototype, choose/objectives, implement, and learn) could be applied in sequence, overlapping, with steps repeated, or in a unique order as a given project required. Although these processes were very useful as teaching tools, over time, as our clients became more savvier, they typically came to us with a process already defined. Most often, they came to us with some variation of Robert Cooper's *Stage-Gate* (or phase-gate) process.

Unlike the more free-form design thinking, or oriented processes developed by Herb Simon and others, the stage gate, or phase-gate processes tended toward linearity and required the completion of an onerous list of tasks within each phase. If the team failed to pass through the gate to the next phase, the team repeated a phase or the project ended. This process was good at killing projects and freeing up people to work on more valuable projects with better run teams, but the pressures to



https://www.linkedin.com/pulse/20141120080210-276368851-what-is-stage-gate-or-phase-gate-model

avoid failure and complete numerous drudgeries tended to quash the optimism and creativity at the heart of design thinking.

So, we developed a process that was very simple, high-level, and non-controversial, something that could overlay any process a client might require.

Unlike other linear processes, like Simon's 7-stages, these phases can be used in any order, repeated, overlapped, etcetera. But many teams, especially those under a phase-gate regime or its latent influence, will tend to work linearly. And this is the reason for the pairings within each phase. Steps that are often unwisely separated, such as the research and ideation (create) steps, are brought together, engaging designers with research and researchers with design. Even bringing in marketing or strategy perspectives; and users.

The first phase, **Learn & Create** combines marketing learning methods, including focus groups, surveys, and database studies, with ethnography and design research learning methods, including user observation, contextual inquiry, and Velcro modeling. As we are an interdisciplinary firm, we also draw on engineering learning methods in two ways. First, we list technologies that may apply to the project to use as building blocks. Second, we gauge the feasibility of any technically challenging requirement, so we know where we might need to relax requirements or invest additional research and development time. Relatively uniquely, we do not wait to apply design creativity until the learning is complete. As soon as a new finding triggers an idea we capture that idea in words, drawings, or even mockups. At times, later learnings mean these early ideas prove invalid, but more often the early ideas become the seed of something useful, or they become the basis of a research question. This feedback loop, between learning and creating, accelerates as the ideas multiply and diverge. Over time, more learnings are applied, and the ideas are reduced in number and converge, culminating in an initial product concept, thoroughly grounded in marketing, ethnographic, and technical learnings. Throughout this process, we are documenting decisions about what the product will do and how it will perform. Because of the greater rigor required (and FDA requirements), when we design medical devices, we also show how each decision we make traces back to what we learned about the needs of people.

The second phase, **Design & Develop**, sets up a different feedback loop, this time it is between design and engineering. While the industrial designer works to optimize the interface between the product and the person who will use it, the engineer works on what happens behind that interface, the technical functionality that enables the product's utility. As mentioned earlier, it was once typical for the industrial designer to be called in when a fully functional product was completed, to make that product appealing and usable for people. Over time, we developed a process where engineers gave industrial designers an understanding of the functional components inside the device housing and all the technical requirements that might constrain their placement. From this, the designer developed configurations of components and product concepts that they thought would work well for the customer, always interacting with the engineers to make sure requirements were being met. The give and take required to achieve the best possible design and engineering outcomes, simultaneously, is not easy, but it is pleasantly challenging

work, like a massively complex puzzle that no one person can solve. And how do you know if you've solved the puzzle? People who are representative of the ultimate product customers must tell you. Our approach is to take multiple product ideas out into the field for customers to use and evaluate. We do this more than once in the process, with the ideas shown to customers becoming more realistic and covering a narrower range of difference as we get closer to the solution.

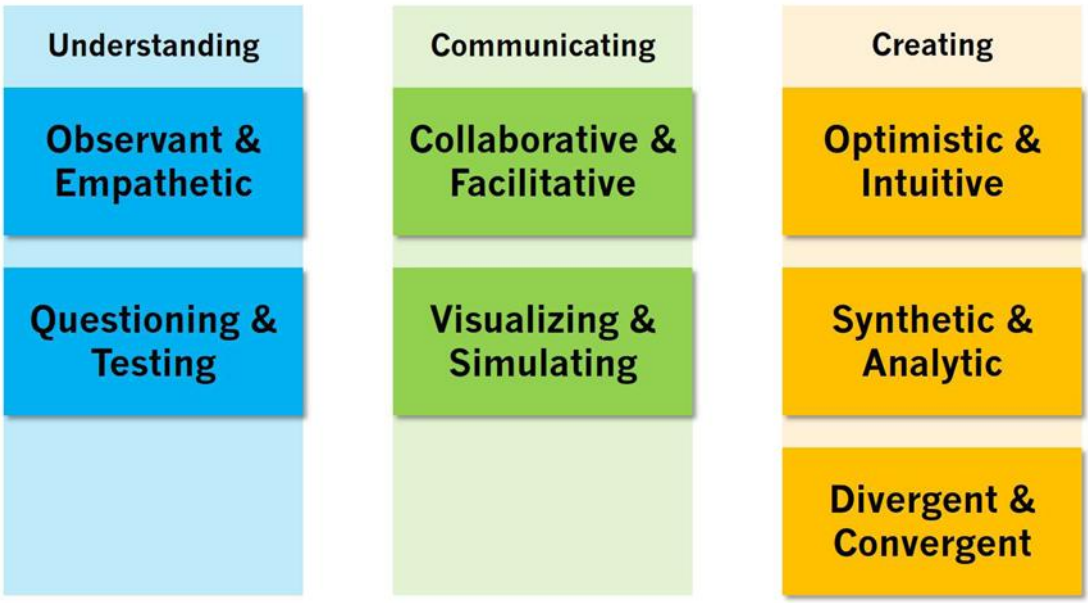
Finally, the third phase, **Prove & Deliver**, brings us back full circle to prove that our product does what the people using it will want it to do. In the language of the jobs to be done methodology, what are the outcomes expected by the job executors and others in the ecosystem? The job of the user or customer defines the value to be created. However, in medical product development, the terms referring to this proof process are *verification* and *validation*. *Verification* is a set of tests that evaluate whether the team designed a product that performs as the team decided it would perform at the outset – that it meets all of the utility (what the product will do) and performance (how well the product does it) decisions. But what if your decisions were incorrect? *Validation* tests the validity of your decisions by testing the product with representative users in a simulated or actual use environment to determine if it meets your defined user needs and intended purpose. To be successful, the metrics utilized define and quantify that the outcome satisfies the desired outcome of the job.

Through years of process development and project work, we began seeing design thinking not in competition with these processes but as a set of approaches that can influence or be used by a designer* at any step in any process. ***We found these approaches fell neatly into three categories: understanding, communicating, and creating.***

*Throughout this chapter, the term *designer* is used to mean *one who is designing* in the broadest sense and can apply to a person trained in any discipline. When a design professional is referred to in this chapter, a modifier will be included, e.g. *industrial designer* or *communications designer.*

Understanding

The ***understanding*** approaches enrich the designer's perspective on the work that they are doing. A product has impacts on people and the environment, so a truly holistic perspective requires secondary and primary research. Through this secondary and primary research, designers or specialized design researchers (or ethnographers or marketers) investigate the product's predecessor and similar products, the people who will experience the product, the environments in which the product will be used, the tasks the product will help people get done, and the product's life-cycle.



Unchecked, this process can result in a mountain of information for a designer to digest, let alone respond to thoroughly. However, designers and researchers in product development have developed a variety of techniques to help organize this information and make it accessible.

Observant & Empathetic

The first ***understanding*** approach calls on the designer to be **observant & empathetic.**

To be ***observant*,** the designer's instinct to influence and change must be restrained. By observing with an open mind, they can take the time to see things as they are and discover things what they didn't know. The core of being observant in product development is looking at (or video recording) real people and things in their true environments of use. And to be truly observant, we look at the whole and the parts. The whole includes the high-level feelings evoked and meanings discerned by and from the people, places, things, and actions being observed. The parts include each discrete, single-topic *visual observations* and overheard *quotations* from the research subjects.

To be ***empathetic***, one must be able to accurately understand and to some degree experience the feelings of another. To be productively empathetic in product development, you must not only go into the process believing that the right design can positively change someone's emotional response, but also you (and/or your team) must be able to create that right design. We'll talk more about how simple beliefs like these make for fertile design thinking later in this chapter, but for now, let's talk about what makes empathy happen. Our approach to gaining empathy involves three steps. First, we gather what information is available on the people we are researching through secondary research of fact-oriented telephone interviews. In this first step, we are essentially just learning those demographics that might be relevant to our research. Second, we engaged in some type of observational research, as outlined above, but here we will note that our observations also extend to emotional reactions, expressions, and utterances. Finally, we interview these people, asking them what they were feeling (not assuming we know what that grimace meant) and when, and how they feel on other days when we weren't observing.

MINI CASE EXAMPLE - *Daedalus researchers spent time with infants and toddlers whose blood flow was supported by implanted ventricular assist devices (VADs). We observed these children, their parents, family members, and other caregivers. The VAD pumps are small and inside the body, but they are controlled and powered by devices that are much larger and connected by short tubes to the child's body. Close observation led to an understanding of the needs of the various people involved and encouraged us to develop ideas that were easier to manage than what had come before. In addition, the empathy that arose in our team from observing emotional reactions of children and adults and then interviewing the adults involved both motivated and inspired us. That led to ideas that hadn't been tried before, like a fashionable VAD controller purse and a VAD controller backpack that could be worn by a stuffed animal.*

Questioning & Testing

The second ***understanding*** approach, calls on the designer to ***question*** **and** ***test***.

By questioning, we hope to understand situations as they are, what they were like in the past, and get some sense of what they might be like in the future. The questioning frame of mind is wary of received wisdom, group think, corporate "boosterism", and hearsay. Most importantly, as design thinkers, we question *our own* beliefs, opening ourselves up as much as we can to the possibility, even the likelihood, that the perspectives we are bringing to the opportunity may be outdated, incomplete, or incorrect. Recall that questioning is one of the additional traits of the innovator as discussed in The Innovators DNA, from Dyer, Gregerson, and Christensen, loc cit Part One).

Products are the result of many decisions, and these decisions are made based on an understanding of the reality that the product will inhabit. Someone once said that a product launched based on the then-current reality is typically far ahead of its competitors, because so much misinformation drives product development decisions. Our product development philosophy relies on this rule-of-thumb, and we do relatively little prognosticating about needs that may exist in the future. There are plenty of spoken and unspoken needs yet to be satisfied that our product designs can address.

By *testing*, we quickly translate our understandings of unmet needs into testable product mockups, images, or descriptions of solutions that we in turn test with

representative users. This testing is testing two things. First, it is testing the validity of our understanding of the unmet need, and second, it is testing the relative success of our solution.

For example, we might respond to a person's need for more of the nutrients in vegetables by developing a vegetable juicer. After asking a test subject to use the juice, he might say:

After trying it, we find that this vegetable juicer is easy to use, but we really don't like to drink vegetable juice.

At this point, we might realize that our understanding of the need was incomplete, that we designed and engineered a wonderful juicer, but for this subject at least, a juicer, wonderful or otherwise, wasn't what was needed.

Of course, this is a simple and obvious sounding example. Often revealed in testing are more subtle things, and you are very pleased that your testing was sophisticated enough to find them. Other times, however, the moment a misunderstanding is surfaced or a solution's flaw is revealed, that misunderstanding or flaw suddenly stands out as ridiculously obvious, and everyone on the team, and especially the people they report to, are bewildered that it hadn't been found before. The thousands of details that were implemented correctly disappear in the designers mind and everyone else's, and this mistake becomes everything. A mature team makes a careful correction and moves on, mindful of the other problems that may arise, and the team remains watchful. An immature team becomes obsessed with that *particular* error, at the expense of the constellation of solutions that must be well executed for the product to be successful. This obsession can be a challenge when a team is fixing a flaw uncovered *after* a product reaches the market, especially when that flaw leads to recalls, negative customer experiences, and/or significant cost to a company.

MINI CASE EXAMPLE *- Daedalus researchers were asked to evaluate the ease-of-use of a voice-controlled, body-worn computer that was to be used in warehouse environments The worker controlled the computer by issuing commands and asking and answering questions, with all of this language transmitted through a headset's earphone and microphone. This system allowed the worker to have her hands free to handle the packages she was moving. Our testing was conducted in a simulated use environment, complete with packages, shelving, sources of varying noise, people that interrupted the workers during tasks, busy periods, slow periods, and experienced and inexperienced users, with the latter hired from a laborer temp agency.*

The easiest functionality to control by voice was the basic device functionality, such as commands to turn the device off, adjust the device's speaking volume, or to pause device communication. And these functions were applicable to many industries, not just warehouse work, so our client had implemented them first. Other functionality, like the vocal interactions around directing a worker to retrieve a specific package or asking a worker to count the number of a type of package at a location, was developed later. In their lab environment, the engineers on our client team found it easy to move amongst these commands, generally getting the device settings just right before starting a shift and beginning to talk packages with the computer.

But in our simulated use environment, the need to adjust speaker volumes or pause communications came at unexpected times throughout a shift. Another person might interrupt a worker, or a loud noise might present itself requiring the earphone volume to be increased. These interruptions, and especially the associated adjustments, disrupted the flow of work-related information, and, as a result of these findings, the basic device controls were also engineered into the device housing as physical buttons that could be pressed with a finger or knuckle when the worker preferred not to use voice control.

While digital medicine was not a market for which the sponsor of this work was pursuing, it may be noted such jobs to be done may provide an appealing adjacent market. For example, a voice controlled computer could potentially assist a patient (or a physician/nurse) with this job to be done.

Communicating

The ***communicating*** approaches enable the whole to be at least as great as the sum of its parts. Hopefully, greater.

Imagine a brilliant product developer — we'll call her Anjali. She is paired with a not-so-brilliant product developer – we'll call him Dave. Who can generate more useful ideas for the project? Anjali? Or Dave and Anjali? The communicating approaches are about making certain that *Dave and Anjali* outperform just *Anjali* every time. These approaches are about making sure that the team's best thinking is communicated, that when facts are established everyone knows them, that the whole team's ideas are considered, and that the best ideas rise to the top.

Collaborative & Facilitative

The first ***communicating*** approach calls on the designer to **collaborate and facilitate.**

To be ***collaborative*****,** the designer employs tools that are as old as the profession, such as creating easy-to-understand drawings of ideas and pinning them on the wall for everyone to see. As technology has progressed, this process has become easier to do remotely but oddly enough is happening less and less in shared workplaces, where even the largest flat panel display is no substitute for a wall of ideas, especially when those ideas are competing for that display territory with all of your other workplace tasks. In our office, we have found ourselves again looking at design concepts serially, in a PowerPoint or Keynote presentation, which reduces our ability to simultaneously compare ideas.

Designers were also taught to work in teams long before it became a common approach in the university, so they expect to be working with others on the same problem, sharing ideas, and building on and improving the ideas of others. They are also taught to gather criticism from the team frequently as a way to improve their best ideas and eliminate bad ones, and finally, they are taught to engage representative consumers through *participatory design*. Participatory design gives consumers layman-usable tools to generate and share ideas and explain these ideas to product developers. These consumer-created ideas are almost never implemented as-is, but the process of designing and explaining surfaces consumer needs and feelings that we can't find any other way.

In collaboration style, we sometimes start to see the difference between a designer and a design thinker. For the most part, a trained designer is a design thinker, and designers have been design thinkers since long before the words *design* and *thinker* became such popular pairing. However, some designers who do not have the collaborative attribute of design thinkers. We believe this is because many of the people who are especially skilled at drawing from their imagination are encouraged to join the design professions. Not unlike creative writing, these skills are often developed during many long hours alone. These folks are, in a word, *introverts*. Whether the long hours drawing feeds their introversion or the other way around, the result is that the design professions include many high performers who need long periods alone and are not particularly interested in collaboration. They may have many of the other attributes of design thinkers, but this particular attribute they lack or they develop it over time.

To be ***facilitative***, the designer orchestrates, in ways small and large, visible and invisible, the productive work of the team. As firm managers, project managers and student team coaches, we are practiced at facilitating. While our management role entailed identifying the right team members and managing the deliverables and schedule, our facilitation role focused on information flow, team decision-making, and enhancing team performance (especially idea generation). That facilitation might entail something as simple as arranging for team members to work near each other, to identifying the need for an idea generation session and structuring that session.

And this facilitation role is not solely owned by the project's manager. Designers with a design-thinking orientation will look for opportunities to improve the same dynamics that the manager/facilitator does.

Visualizing & Simulating

The second ***communicating*** approach calls on the designer to **visualize and simulate.**

By *visualizing*, the designer enables herself and her team to see research results, possible solutions, or design constraints in an easy and fast to understand form. When involved in a project, we constantly ask ourselves *what information is important for the team to be thinking about and how do we make that information unavoidable?* Answering this question results in a constant flow of diagrams, drawings, 3D models, and photographs, all rich with meaning, but also quick to comprehend without extensive reading and study.

By *simulating*, the designer creates an experience that is a reasonable facsimile of the customer's eventual experience with the real product.

In our work, at the simpler end of the spectrum, we simulated the weight and size of a device with a four-hour battery life so we could compare it to a device with a sixteen-hour battery life. To do this simulation, we cut two different sized blocks of wood and filled them each with a different amount of lead shot. In minutes the team was able to decide that the sixteen hours of battery life was worth the extra size and weight, a decision that was not possible when looking at numbers on a piece of paper.

At the more complex end of the spectrum, we mocked-up partial bathrooms and provided sanitary prototype toothbrushes that allowed thirty representative consumers to brush their teeth while being observed by researchers. This testing and follow-up interviews ultimately gave a large multinational the confidence to select a specific design and then direct a seven-figure investment in manufacturing equipment to support its production.

A great deal of development simulation is being done with virtual simulation tools, both to evaluate engineering performance and to evaluate consumer preference. We use these virtual tools in our practice, but we are conscious of the differences between these virtual simulations and physical simulations and the advantages and disadvantages or each, and continue to find a place for physical simulations.

Creating

The ***creating*** approaches put us in a mode to be not only prolific but to be prolific in the right general direction. Some of us come to product development because they can't stop generating new ideas. Others who come to product development learn to be creative on the job, while still others never learn to be creative but contribute in other ways.

Facilitated ***knowledge-driven innovation*** *session.*

The design thinker doesn't create for the sake of creativity, and doesn't prize the bizarre and strange over the more ordinary and practical (or fear the bizarre and strange), but instead creates within bounds that have been established to exclude useless ideas but not exclude any useful ideas. The design thinker also knows how to help non-designers generate ideas and how to leverage the skills of others who are not likely to create ideas to both create fertile ground for idea generation or to evaluate the ideas that others originate.

Optimistic & Intuitive

The first ***creating*** approach calls on the designer to *be* ***optimistic*** **and** ***intuitive****.*

By being *optimistic,* the designer acts as a counterbalance to the caution inherent in the practice and reward systems of the other disciplines and fights for the projects highest potential. There are three arguments that we typically use, both with ourselves when we are thinking about projects and with the team when we want

to set the right tone at the outset or discourage excessive caution.

The first argument is intended to disabuse people of the notion that everything is a tradeoff. In our experience, we have found that although many beneficial design features come with costs, there are also many beneficial design features that come with no costs while there are still other beneficial design features that create additional benefits with no additional costs. There is no law in product development (or the universe) that every upside comes with a downside, or that every downside comes with an upside. We argue that the team should always seek the solution that creates additional benefits first, then the solution that has no downsides, and then and only then the solution that has the fewest downsides.

The second argument is about the inevitability of innovation. We ask team members, and ourselves, what the likelihood is that this product or service will radically change is the result of some person's insight or creativity. And then we ask them, "Why not us, why not now?"

The third argument is a counterargument. When proposing a new idea or improvement, the designer often receives a lecture about the immutable laws of the *Iron Triangle,* a rule of thumb of unknown origin that has been around for many decades. The Iron Triangle was originally about the fixed relationship between three variables in project management: cost, scope, and schedule. The claim is that any decrease in one variable will require an increase in at least one of the others. For example, if management wants the project budget reduced, then they must accept a longer schedule (due to a smaller and less qualified team working over a longer period) or a smaller project scope (due to a smaller and less qualified team working over the same period and in turn getting less done). In today's fast-paced work environment, the Iron Triangle is no longer called by its

	Michael	Jake	Julie	Tracy	Susan	Brian	Arthur
Age	6 months	3 years	6 years	17	33	35	63
Occupation	Infant	Pre-schooler	Kindergartner	Outside Caregiver	At Home Parent	Working Parent	Grandparent
Interaction	Day & night with parents and siblings	Day & night with parents and siblings	day with teachers & friends night & weekends with family	once a week with kids	All day with kids, breaks in evenings	evenings and weekends with family	bi-monthly to monthly visits
What they do	· Stationary (crib, lap, car seat) · No formal speech to communicate · Limited vision · Likes high contrast images faces · Poor fine motor control · Likes to mouth things · Rough on objects	· Recognize and say alphabet · Very mobile, running and jumping · Still messy, but not mouthing things · Still rough on objects · Better fine motor control · Can watch and understand TV · Can follow simple instructions · More independent · Sleeps in bed, but uses car seat · Inquisitive, "Why is.....?Why?"	· Read, write letters and simple words · Socializes · Coordinated · Can operate simple machines; VCR · Can be careful with objects · Has a longer attention span · Expects more from games and toys · Uses imagination when playing · Cares about personal appearance · Competitive; likes group games	· Sees kids on a weekly basis · Has computer and uses internet · Socially aware and conscious · Empathetic and caring · Bilingual · Likes children · Likes to have fun	· Concerned with child's development · Manages household · Runs errands with children · Light outside work at home · Coordinates activities and schedules · Plays the piano · Does not use computer, but would	· Works long hours @ start-up co. · Has laptop & workstation · Is color blind · Plays w/ kids @ night · Takes roadtrips with family	· Retired school teacher · Impaired sight and hearing · Intimidated by computers · Has Arthritis
What they want or need	· Tons of parental contact · Needs toy he can sleep with · Needs toy he can mouth or drool on · Needs stimulation to keep interest · Needs to have high contrast · Needs to set-in or hang-on crib · Sense of comfort/safeness	· Wants to use toy in bed · Wants to use toy alone · Also wants to use toy with parent · Wants to take toy in the car · Wants toy to be his; no sharing	· Wants to take toy to school · More control over toy's actions · Wants to personalize toy · Needs to save creations/artwork · Use toy to entertain herself/others	· Wants toy to keep the kids busy · Would like to participate with kids · Wants a toy that won't bore her	· Needs personal time · Wants a reliable, safe toy · Wants a well-recommended toy · Durable, low-maintenance toy · Toy with longevity · Toy will interest each of her kids · Good value · Educational merit	· Wants the latest/greatest for kids · Wants quality time with kids · Wants a tech-toy w/ lots of features · Wants a toy that upgrades ala laptop	· Wants a toy he can understand · Wants a toy he can share with kids · Wants a sitting vs. running toy · Wants to please the kids
Interests	· His parents and siblings · Lights, sounds and sensations · Eating and sleeping · People's faces and voices · Play music and lullabies · Grasping and tasting · Board/fabric books	· His parents and siblings · Pokémon, or latest fad · His friends · Arts and crafts projects · Music; listening and making · Being active; parks playgrounds · TV, videos and movies · Dr. Seuss books	· Her parents and siblings · Her friends · School and group activities · Swimming and dancing · Making art · Music; listening and making · TV, videos and movies · Internet; www.pbs.org (PBS kids) · Magic School Bus books	· Her family and friends · High school · Music, fashion and boys · Likes photography · Drama club	· Her family · Fitness and wellness · Socially active; community service · Continuing education · Music; playing and listening · Dancing; ballroom and Latin	· His Family · Online trading · Gadgets / hot technology · Music, live performances, clubs · Sports · sight-seeing with family	· His Grandkids · Golf · Talking about the Good ol' days · Travel · Politics
Contact with toy	Daily	Daily	Afterschool	Weekly	Daily	Evenings, weekends	Bi-monthly, monthly

Persona poster creates a visual representation of demographic information.

improve sometime in the future. Most people agree it is better than 50%, while others go so far as to say 100%. And then we ask them what made that change possible. People usually go first to new technologies not available today, but not far after that they say that that future name and is reduced to the sound bite *Good, Fast, Cheap: Pick Only Two.*

What the *Iron Triangle* and *Good, Fast, Cheap* ignore at least five important things: **First**, from company to company, project teams vary by multiples in relative efficiency. **Second**, the original project plan was created

by fallible human beings, so there may be too much or too little of any or all of the three variables. **Third**, many improvements are easier to implement than the poorer solutions they replace. **Fourth**, product development is work guided by decisions. In every project, there is work completed that is the result of decisions that are later reversed. We have seen projects where this work has been the majority of the work on a project. Some of this is inevitable, but not all of it. Sometimes, using the Iron Triangle to resist a new idea or a response to new information only delays a project redirection, actually resulting in more wasted work. And **fifth**, the new idea may result in greater profit, a number outside of the Iron Triangle that is a more important measure to most organizations.

By being *intuitive,* the design thinker makes use of non-analytical thinking to guide him or her to new ideas or areas of investigation. Although some believe that making use of intuition is irrational, science is beginning to show us that this nonconscious cognitive process can be useful.

When dealing with multiple variables to decide between ideas, we often use a *criteria matrix* to score the ideas. The criteria matrix allows an entire team to participate, and five or more variables to be manageable. We even weight the criteria by importance as a team, so we assure ourselves that we are giving all the issues the right amount of attention in our decision. The criteria matrix and its variants are great tools, but any decision made with a criteria matrix and a team takes some time, typically 15 to 30 minutes' minimum. Decisions that were going to result in the consumption of precious time or dollars were certainly a good use of the criteria matrix, but what about decisions during idea generation, particularly in the early stages?

We have come to believe that intuition allows humans to get beyond the five-variable limit of conscious processing (established at the University of Queensland* in 2005). We believe that the unconscious processing inherent in intuition is capable of processing many more variables than conscious processing, and that intuition can process multiple types of information (emotional, visual, language) that are ingredients of the same decision, something that is challenging for conscious processing or a criteria matrix. What intuition lacks, however, is perfect accuracy. Among other things, unconscious bias and human error can change our intuitions.

So, what do we do with it? We use it to generate ideas for solutions to problems and ideas for areas of research. These ideas are evaluated analytically before investing time and money, but very often the idea that came in a *eureka* is more on point than an idea that came from careful, conscious thought.

**How Many Variables Can Humans Process?, Graeme S. Halford, Rosemary Baker, Julie E. McCredden and John D. Bain of Griffith University, University of Queensland, Published January 2005, Psychological Science, American Psychological Society*

The traffic-cone/lighthouse form of the Industrial Scientific Radius Gas Monitor was the result of an intuitive eureka! Moment. The form tested well with customers and ultimately succeeded in the market.

Synthetic & Analytic

The second ***creating*** approach calls on the designer to be ***synthetic*** **and** ***analytic***.

When ***synthesizing***, designers pull ideas and information from many sources and integrate them into a cohesive whole. This is a strength of industrial designers, who also tend to immediately look at the change in a small aspect of a product in terms of its impact on the whole. The Gestalt psychology idea that "the whole is more than the sum of its parts," drives designers and is closely associated with the German Bauhaus school. Many consider the Bauhaus school to be the founding influence of modern design (and architecture), an influence spread when several instructors continued their teaching in the United States after the Nazis shut the school down in 1933. So, this focus on the whole and the desire to synthesize is deeply held, and at times, designers can be resistant to positive changes in smaller components that undermine a whole design that they have already envisioned. Within our office, designers are encouraged to be flexible and quickly create and share new embodiments of the whole that incorporate any proposed changes to concept components. And then the team can evaluate the advantages and disadvantages of the small component change in terms of its functional benefit and its impact on the whole.

When ***analyzing,*** we break down a problem or concept into its component parts, and study those parts. This break down and analysis tends to be a strength of engineers more so than designers, and engineers and designers can be great complements to each other, with the engineers analyzing and the designers synthesizing, *if* they recognize the value the other discipline is bringing. When they don't, this difference in approach can be the source of conflict. We find that the best method to resolve this issue is keep the engineering and design team members working in parallel and in regular communication. Designers also use analysis to understand the component parts that are being considered for incorporation into the new, synthesized, whole.

Divergent & Convergent

The third ***creating*** approach calls on the designer to **be divergent and convergent.**

By being *divergent*, designers create the opportunity to make good choices by creating many options to choose from. For some designers, ideas for solutions come easy, but their challenge is coverage of the solution space. They generate idea after idea in a narrow corner, keeping themselves busy but not covering all of the territories. We have spoken to entire teams that have struggled with this problem, and we have even heard it claimed that entire industries fall into this trap. For example, some say that the companies that are developing autonomous driving solutions are overinvesting in software innovation when it is a hardware innovation that is now needed to overcome the limitations of present-day systems.

A particularly prolific patenter in the medical device industry told us that he experiences the feeling of a door opening into a room full of ideas from time to time, after exhausting what he thought were all the possible rooms of ideas. It is usually one key that allows him to open this door, such as a new manufacturing technique, looking at the problem from a different stakeholder's perspective, or the relaxing of some requirement that had become doctrinal through the passage of time, a requirement that wasn't truly necessary after all.

One simple method we use to keep diverging is to build maps of existing concept and potential concept categories. Working solo, this can be done on a spreadsheet, while in groups, a whiteboard or a set of sticky notes works well.

By being **convergent,** the design thinker periodically prunes the garden. As Ed De Bono advises, we alternate between periods of relatively unrestricted idea generation and thoughtful elimination of the weaker ideas. What we are cautious to avoid is a process of serial idea creating and discarding, which is the tendency of many teams in product development. The serial approach is fatiguing because there is no creative momentum established, and it is fallible because the *acceptance yardstick* is applied so many times and always independently. By evaluating a large group of ideas against each other, the team not only applies the acceptance yardstick uniformly, the team also goes beyond mere acceptance by selecting the best among several ideas that have all satisfied the acceptance criteria, exceeding requirements. In a typical serial process, reaching acceptance is where the project stops.

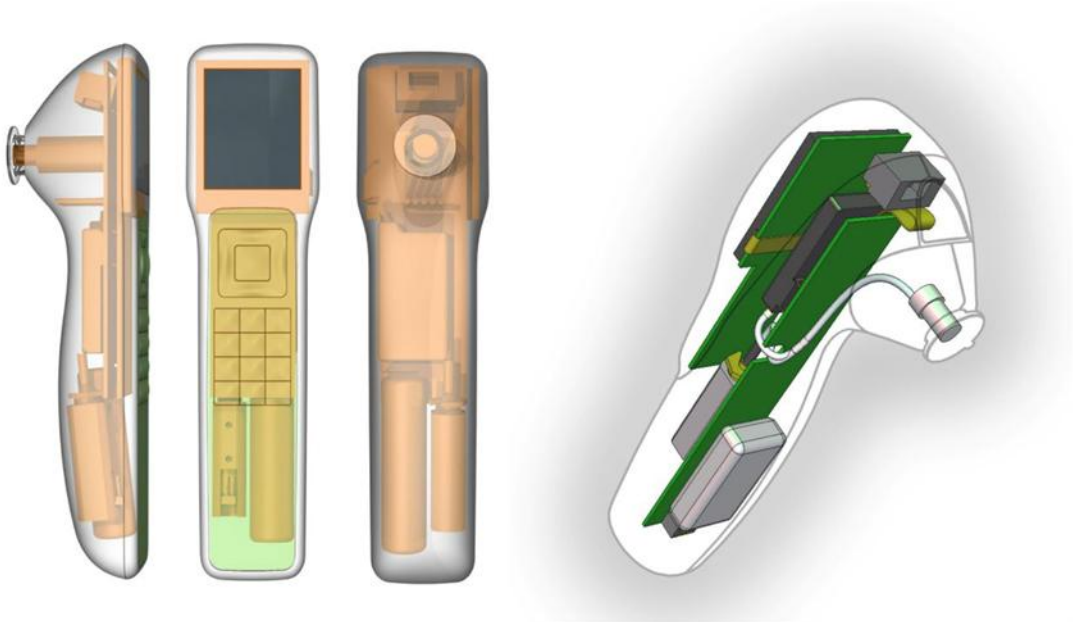
In our process, the selected idea or ideas from one round of convergence sets the approximate bounds for the next round of divergence. The design process could be described as a series of funnels, with work in each successive funnel addressing finer details.

CONCLUSION

In conclusion, we want to reinforce the concept that design thinking is as much a set of ***attitudes and approaches*** as it is a set of **skills and techniques.** There are many books and articles about the skills and techniques, and many business and design consultants who are willing to teach them to you. And among these folks are people we could highly recommend. We assume that the consultants from the business world overlook the attitudes and approaches entailed in design thinking because they are so different from the attitudes and approaches of business. The design consultants, on the other hand, like the fish who have no idea they are in water, have trouble communicating these more subjective aspects of design thinking as they are second nature to them and rarely verbalized. We expect to see all of this to evolve and change, especially as design firms and business consultancies increasingly merge.

Furthermore, we don't believe that the skills and techniques, as useful as they are on their own, reach their full power and potential without the attitudes and approaches we have outlined. Although we are a couple of fish which have spent their careers swimming in the design thinking water, we hope that we have done a reasonable job of capturing and explaining it here.

It is also our observation and articulated in many private discussions with Art Boni, as part of our work at Carnegie Mellon, that design thinking should be an essential part of any innovation team's approach. That is the

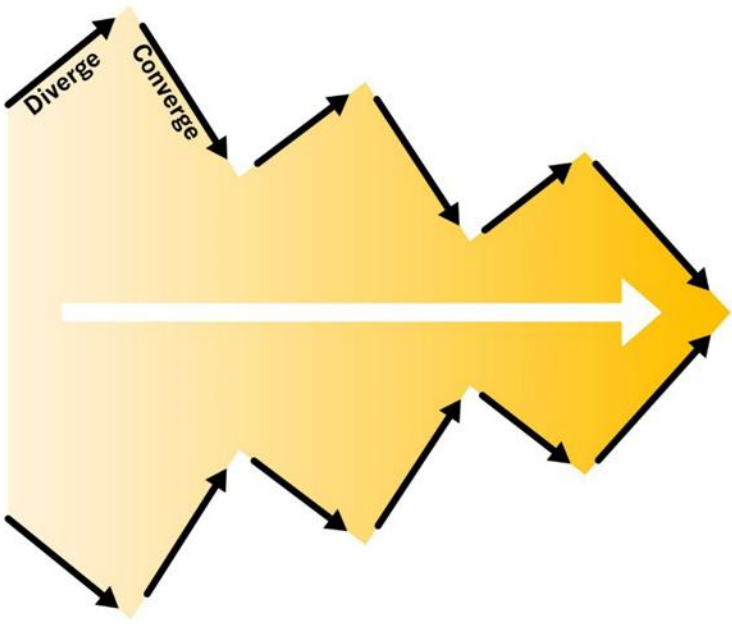


Visualization of the whole and the parts of a medical device.

basis for the Capstone Entrepreneurship Course, Desiging and Leading a Business. Integrated teams of MBAs, technologists and designers work together collaboratively in innovation project such as startup companies.

In Section One of this special edition/monograph, we note that design thinking has now permeated the world of technology (Apple, Google, Intuit, IDEO, etc.), business (Procter & Gamble, AirBnB, IBM, etc.). However, exampes in biotechnology are few. Medtech has begun to incorporate design thinking as part of their innovation team's approach and organizations like our own have worked in these fields. Also as discussed by Foley in her article on Service Design, design thinking is now permeating the incorporation of user experience in healthcare.

Boni (private communication, and Chapter One of this Section Two) has suggested that there are many more opportunities for design thinking to become part of the innovation team's approach in healthcare broadly. The most immediate opportunity involves the maturation of Pharma 3.0 and its focus on patient centricity – design the organization, the solution, and the user experience along with the "pill". Also, consider the possibilities associated with the emergence of Digital Medicine as industries converge. Design thinking is ripe for exploitation in Digital Medicine, not only to satisfy objective patient needs, but also in finding new meanings that serve emotional needs and in answering broader needs in the ecosystem. Technology (artificial intelligence, machine learning and virtual reality) + Business + Design is likely a winning combination as we tackle these problems. We encourage our readers to think creatively about the possibilities.



Divergence / Convergence Design Process Funnel

Article

Service Design for Delivery of User Centered Products and Services in Healthcare

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DEFINING SERVICE DESIGN

In the broader context of healthcare, hospitals have begun to adopt Service Design to understand and improve the patient experience.[1] The patient experience has increasingly become more important in the USA as hospital reimbursement is tied to patient satisfaction scores.[2] Beyond improving patient experiences, Service Design is extendable to helping care providers build relationships with individuals across different functions and silos to improve cooperation and communications internally and externally – while also improving outcomes.

This paper, will firstly cover the essentials of Service Design and observe that service is an important element in the evolving Pharma 3.0 business model where patient focus, or centricity is the emphasized (along with importance of the payer in adoption of healthcare solutions). From there is discussion of Service Design in the evolving healthcare ecosystem, recognizing the importance of interactions throughout the system – patients, providers, physicians, extended care networks, etc. The discipline's value is then illustrated through various applications in several mini case studies.

Margaret A. Breslin from the Mayo Clinic, states "[Service Design] is all about people. It is about taking them, their problems, their experiences, and their journey seriously".[3] Louise Downe, the Director of Design for the UK government defines Service Design as designing an action, and that "good services are verbs, not nouns".[4] The term literally means designing services, or designing something that is not tangible until the moment of its consumption'.[5]

Since the definition of Service Design is designing an action, this approach leads to relationship building by strengthening communications and advocating a common understanding across silos. Ben Reason, of Live/Work Studios, states "What Service Designers can bring to the table is a shared view of the patient and their needs that complex teams with mixed expertise can unite around. If everyone has the same picture of who the patient is and what is important to them, it is easier to align conflicting interests and processes."[6] Shared understanding leads to alignment and attainment of goals. Richard Buchanan, Professor of Design, Management, and Information Systems at Case Western Reserve University, states "the ultimate purpose of Service Design is to give people the *information* and *tools* needed to *act* — to be free to live as one would choose."[7]

Service Design is Human Centered Design applied at the systems level and looked at over time. At a systems level, it then attempts to connect broken parts of the systems by designing multiple points along a journey (called touchpoints) where a difference could be made in the execution of the job (or task) and its outcome. These touchpoints are designed to either enhance or streamline certain points in a process (of jobs to be done) so that this relationship is strengthened.

Service Design can empower patients by making them feel that they are contributing positively to their own health outcomes. In the book, *Service design: from Insight to implementation,* Andy Polaine, Lavrans Løvlie and Ben Reason talk about how Service Design can utilize its customers for labor and brand loyalty. They state "The most common lost opportunity is when enterprises neglect the resource that customers (patients) can be in terms of providing value back to the service. Customers

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are usually motivated to provide labor, knowledge, and data if these will help them get a better result (outcome), and when customers invest in the outcome they connect more strongly to the brand".[8] By these types of participation, customers and users (patients, physicians, caregivers, etc.) feel they have a stake in the product, and are more likely to utilize and integrate the solution into their life.

The patient experience is becoming a key performance indicator (KPI) for accessing the quality of care in hospitals in the UK[9] and in the USA, and there is a trend to shift the responsibility onto the individual. There is also a trend to move more healthcare out of "the institution" into the home where it is cheaper and more convenient, and more emotionally satisfying. Technology enables and allows monitoring to provide a larger picture of the patient in the home, and this picture can become a source of information to enhance the service and its design.[10]

As Service Design embraces Human Centered Design, a commonality dictates that it is critical to give patients a voice, because they are experts in their own life.[11] When shifting the responsibility to the individual, how a product or service fits into an individual's life is an important factor. Allowing individuals to take responsibility or ownership determines whether the product or service is utilized in the desired manner, adopted, and ultimately retained as a preferred solution. When considering the shift of labor to customers (patients), the move to the home is just this, a reduction in cost while potentially increasing the quality of life.

The examples used in this article are not intended to focus entirely on the replacement of labor, but rather enabling the labor to take place with focus on communication, relationship building and understanding the needs of the user, e.g. patient or provider, to provide improved outcomes. Service Design is about giving stakeholders what they need whether or not that need is articulated. The outcome is, that operations run in a way that alleviates bottlenecks and at the same time provide a compelling experience for all the stakeholders involved. In the next section, we extend the Service Design concept to the broader care ecosystem.

SERVICE DESIGN IN PRACTICE

Framing healthcare in the context of a system, care is delivered to patients via an ecosystem. Doctors, nurses, family/caregivers, and patients all need to interact and exchange information for the whole system or ecosystem to work effectively and efficiently.[12] Service Design aims to "connect the dots"[13] internal to this system. In connecting the dots, the experience allows care providers to "understand how they fit in the picture which then, in turn, helps them to do their jobs more effectively by increasing levels of communication" and interaction.[14] It is about making sure that all pertinent information gets to those who need it (the job executors), when and where they need it (the context).[15] Recall that the market is defined as the job, the executors, and the context, e. g. hospital, clinic, home.

Human Centered Design's core competency is understanding whom one is designing for, as well as understanding the other stakeholders who are involved. If one is designing for patients, it includes understanding their life before they entered the healthcare system, who they were, what mattered and was important to them, their emotional state, motivations, needs, constrictions, who is in their support system, etc. In contrast, Service Design also includes understanding their journey across the healthcare system, from diagnosis to treatment to recovery and back to day-to-day life. All of this must be acknowledged, appreciated, and incorporated into the solution. By thoroughly understanding all aspects that impact a patient's and all other stakeholders lives, the designer can then best integrate a solution over multiple touchpoints in a way that provides value, is seamless, and doesn't require individuals to impact their normal journey, i.e. to 'jump through additional hoops'.[16] Since the solution needs to fit into their lives, who is better to question (or observe) than the stakeholders themselves. They are the experts on their own life.[17]

Jessica Weeden, a service designer, gives an example of a project where she was asked to improve the exchange of information between hospital staff to better verify when the patient was ready of discharge. It was discovered that due to power dynamics, the nurses and the technicians were not communicating effectively among themselves. To understand how to get the job done more seamlessly, the designers "broke down these power structures in service of making sure the right information about the patient is being handed off to the right person at the correct time with the desired outcome being that the patient gets better care".[18] One needs to understand and break down social and political structures internal to the hospital to devise a system and a solution that doesn't add an additional burden to overworked nurses.

SERVICE DESIGN'S VALUE

Human Centered Designers often use the Double Diamond framework (see Fig. 1 below – taken and adapted from Dan Nessler) to describe the working process. The first diamond represents figuring out what the problem is, and the second represents figuring out how to address the problem (or to find an effective solution).

For each diamond, there is a divergent and a convergent phase. Divergent is going wide (identifying options), and convergent is narrowing in (selecting solutions).[19]

The value that design or service design delivers is in the divergent phase.[20] Other groups such as Process Improvement, or Quality Improvement, are very good at the convergent piece and where the problem is already known.[21] In the field of design, the framing of the problem or problem definition comes out of the research (discover) and its subsequent synthesis (define).

Service Design has this notion of the front stage and the back stage. The front stage is what is immediately apparent, what the customers see. The backstage is all the things going on behind the scenes that is necessary to make the front stage work. When one is 'connect the dots internal to a system' where it is looking at operations and relationship building, this is the back stage. The patient experience is the front stage.

Designers learn through doing. If there is an immovable impasse, designers use divergent thinking to go around or incorporate the impasse into the solution rather than needing to come to a halt.[22] Design is about testing the idea, learning from the idea, iterating and testing again. Service Design aims to prove the value first, and then to scale. Testing the idea is about breaking the problem into smaller assumptions, being creative in how one tests these assumptions, and testing things in a matter of days or weeks vs. a pilot that takes months or years. It is about quickly iterating towards success.[23] In validating the value on a small scale, one is in a better place to plan for the costlier approach of a Randomized Control Trial (RCT) at a later date.[24] Small scale testing is an example of validating product/market fit from the perspective of a service delivery system.

The following case studies are collected from various designers whose output was the design of a service that works efficiently and effectively for the entire care ecosystem. They deal with communication, relationship building, and letting the solution emerge from participants and their communities. They also deal with the understanding and providing for the qualitative, or emotional components of the job to be done which in this case is service oriented. Four mini case studies are provided for this article. There are two from the a Large Teaching Hospital in the Mid-Atlantic States Center for Healthcare Innovation Accelerator Program, one from Social Innovation Associates dealing with capacity building, and one is a spinout from Carnegie Mellon in Pittsburgh engaging and educating the community around the many challenges of alleviating childhood obesity.

CASE STUDIES

#1 Large Teaching Hospital in the Mid-Atlantic States- Emergency Department Project[25]

A Large Teaching Hospital's Health Care Innovation group has an accelerator program where designers internal to this group are matched with teams internal to this hospital. These teams seek to improve an aspect of their

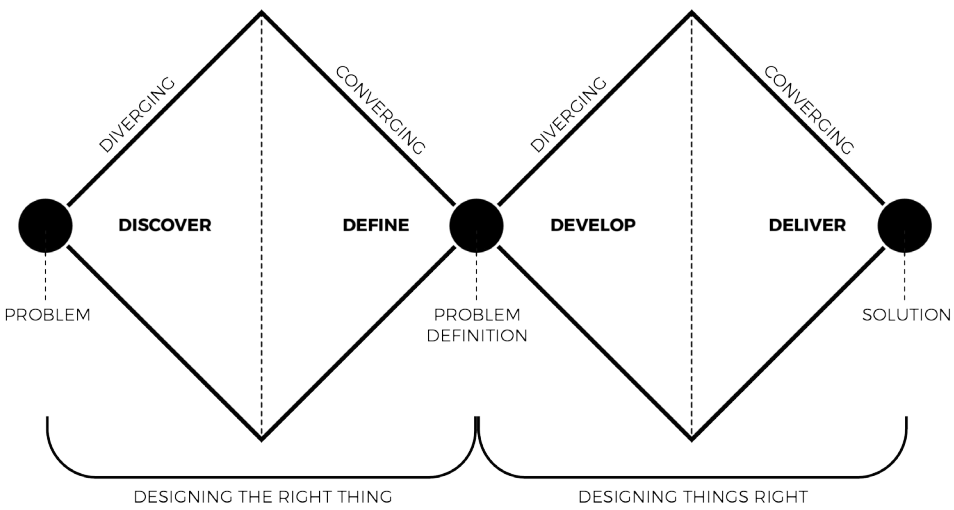

Figure 1: The double diamond framework

work (or achieving the job to be done), but need help solving a problem in a different or an innovative manner.

One of the projects came from their Emergency Department (ED) which recently became a Level 1 trauma center. Previously, these trauma cases were sent to an affiliated hospital site. The new status of this hospital as it learned to provide this service efficiently has resulted in bottlenecking and extended wait times for the non-urgent ED patients. Inefficiencies yet to be identified, gave result to the length of stay in the new emergency department being much longer than it was prior to the introduction of the Level 1 patients. To reduce this bottleneck, the hospital has already tried several things such as renovating to make the physical space more amenable to workflow.

Prior to this change to a Level 1 ED, the site was a community hospital in which the staff understood the needs of the patients coming into their ED frequently. However, with the arrival and intermixture of the new patient population, there was culture shock on both sides – patients, staff, and caregivers. The former patients wanted to know why it now takes so long to get examined and their problems resolved. The outcome is that there was a high percentage of people leaving without being seen or leaving without treatment being completed. Benchmarked next to other Level 1 hospitals, they were doing very poorly. Efforts were put into place to identify the source of the problem and to come up with an effective solution. Designers were asked to analyze the situation and to help optimize patient flow required to get people through the treatment process faster so they wouldn't leave before being seen.

Since solution of this problem was urgent, a "design sprint" (much like a hackathon-in that it is a quick, focused project) was utilized with the timeline drastically reduced – visualize the process from the perspective of the diamond in Figure 1. The first diamond (understanding the problem) lasted for two weeks. In the first week, the service designers did contextual inquiries, they spent time in the ED observing and asking questions to both patients and staff about why they were doing certain things. From this, they defined a scope for the project and then tried out many ideas for solutions (the second half of the first diamond) in the second week in the ED. These small-scale experiments led to the resulting framework and project brief: "How can you make the people feel like the wait isn't as long as it actually is?" – e. g. make the "wait" more enjoyable and engaging. The hypothesis was that if they could occupy non-critical patients (while caring for the trauma patients), time would seem to move quicker and the patients were less likely to leave.

Out of the small-scale experiments, the idea that was chosen to test further was a "care cart". A short pilot was run on this solution over a three-week period. A volunteer walked around with a cart and provide "distraction items" such as games and comfort items so that the patients will feel that they are being attended to and not just waiting. They are on the third iteration of the pilot as we speak, trying to test the solution while using the pilot as a tool to understand the deeper reasons people leave, e.g. "Kids need to be picked up from daycare, so I can't wait any longer" instead of just "the wait is too long".[26]

They will know a month later through patient satisfaction scores if patients feel better being attended to and stay until being treated. With positive results from patients and staff, the ideas will be turned over to the Accelerator for full development including looking into operational improvements.

#2 Large Teaching Hospital in the Mid-Atlantic States- Congestive Heart Failure Project[27]

Patients with congestive heart failure were not following through with the discharge instructions once leaving the hospital, e.g. adherence to medical prescriptions, exercises, etc. Lack of adherence was leading to repeat visits to the hospital – inconvenience for the patient and expense incurred by the hospital/provider (and potentially the payer). Hospitals are financially penalized for patient readmission within 30 days of discharge.[28] On discharge, the patients were given a 12-page follow-up booklet with instructions on how to care for themselves post hospital. A nutritionist sat down with the patient and went over the material and answered questions. This solution was not effective in reducing repeated readmission to the hospital. So, designers were brought in and asked to make the 12-page booklet more readable, effective, and easier for patients to understand and act upon the recommendations. Following the double diamond process, the designers tried to understand what else was at play before just jumping in to redesign this booklet. The designers dove deep with a cohort of patients through observations, interviews and contextual inquiries.

Human centered design involves looking at the patients' experience in all relevant contexts, both in the hospital and at home. It was important to understand how the patient used the information given to them, how the patient perceived the in-hospital patient education, as well as whether patients felt they could adapt this new routine to their life after discharge, and how this education was applied post discharge. During these interviews, the designer gained the trust of the patients. A few patients allowed the designers to visit their homes after

discharge to observe how this education was working and if there were any gaps that could be addressed.

People were pleasantly surprised about this approach. Originally, one designer tried to get patients to allow him to sleep in their home for 3 days to get the full picture of the problem. The designer's idea was to dive deep with a few people vs. a possibly ineffective 1000 person survey based on answers to questions on what patients say they want vs. observing first-hand what they need. The survey approach works best after "expert opinion or observation" has been explored to understand the issues and articulate them to others. Then proceed to achieve more statistical significance to the problem through a larger survey once options can be better articulated thru questioning.

Diving deep into the problem, designers learned what had previously been missed. For example, one patient had been in the hospital 5 times already for congestive heart failure. Her doctors were frustrated because she was not adhering to a low sodium diet. A dietitian came to speak with her about what foods to eat, what not to eat, and gave her a shopping list of healthy foods she likes. However, when the designers went to her house they realized she lived in a "food desert". The designers figured out that she ate mostly fast foods because she has those food menus attached to her refrigerator door. That was more convenient (and an established routine), so she didn't use the shopping list provided to her. She needed someone (a trusted coach or caregiver) to look at those menus and tell her what to eat, thereby establishing new patterns around eating habits. This is an example of how important it is to thoroughly understand a person's life and all the components of their life to adequately come up with solutions that ultimately work.

The resulting design for this service was delivering just-in-time education as a way of patient monitoring. This allowed for more sustainable behavior change by catching issues early and fixing them.[29] The end result was a significant reduction in the number patients being readmitted within the first 30 days' post-discharge. Design is about pulling back the layers of a problem to find the needs of the stakeholders by looking at the problem holistically. It is rarely re-designing an output such as improving the aesthetics of the post-op follow-up instruction manual but rather a re-design of the person-to-person interaction and resulting service.

#3 Changing the Conversation with Partners Services[30] (Philadelphia Department of Public Health (PDPH) Sexual Health Project with Social Innovation Associates)

The Philadelphia Department of Public Health (PDPH) is responsible for protecting the health of the city's citizens and preventing the spread of disease. The PDPH does not consider sexually transmitted diseases (STDs) to be fully treated until all exposed sex partners are treated. These partner services are delivered by a team of Disease Intervention Specialists (investigators) who engage people who test positive for reportable STDs, attempting to learn the identities of their partners, and offering all parties confidential services, including education about risk and prevention, referral, testing, and treatment. This then stops or slows the spread of disease among a population or network.

The sensitive nature of partner services often leads to stressful and inefficient interactions and uneasy relationships between PDPH investigators and the other players in the process. (e.g., persons testing positive, their partners, and related healthcare and social services workers). The PDPH contracted with Social Innovation Associates to lead a human centered design process to reduce the turbulence between individuals and organizations, increasing the effectiveness and timeliness of the PDPH's efforts to identify, reach, and, educate many of the city's most vulnerable citizens, which in turn advances the PDPH's efforts to stem the overall spread of STDs.

The Children's Hospital of Philadelphia's (CHOP) Adolescent Initiative (AI) is one of the community-based health provider organizations required to collaborate on partner service activities with the PDPH. The Adolescent Initiative provides medical treatment and social services support for teenagers who have tested positive for HIV. The Adolescent Initiative and the PDPH both work in the arena of public health to promote the health and wellness of Philadelphians. The organizations have different roles that, at times, require them to navigate competing goals and priorities. CHOP AI and the staff of other community-based organizations have reported they sometimes find their communications and interactions with PDPH investigators challenging.

The PDPH investigators follow-up with CHOP patients who have recently been diagnosed with a reportable STD, CHOP is committed to the individual patient, and the PDPH is charged to protect population health. In practice, this often leads to conflicting concerns and priorities between the two organizations. Human centered design was utilized to bridge this gap. A focus on patient experience provided the motivation and shared perspective necessary to build the relationships, work practices, and processes necessary for each organization to happily and effectively pursue their missions.

The workflow, as it currently stands, has the investigator for the PDPH investigators interview newly diagnosed teens at CHOP. In most cases the investigators do not have to return to CHOP again. Occasionally, PDPH investigations stall and investigators need to request guidance from CHOP staff. Since the investigators are under pressure to get things done because of the urgency associated with infection periods, there is tension created. To further exacerbate the situation, it was common practice for there to be different investigators who cover different parts of the city. From CHOP's employee's point of view, this situation becomes confusing as they did not understand who is coming when. CHOP's priority is to make it safe for the patient and let them know their rights. For the Department of Public Health, they need to talk to the patient about the public health concerns of having HIV, but if the patient thinks the conversation is optional, the type of information given by the patient is not the same quality.

By first mapping out each stakeholder's process in a collaborative environment with the stakeholders, the designers set about figuring where the workflow of each stakeholder overlapped. This allowed them to understand more about the other person's priorities and what their job entailed. The overlapping processes on top of the patient journey showed 5 touchpoints where an intervention could have an effect.

For example, one of the touchpoints was to come up with a script on with both parties could agree. Social Innovation Associates co-created a list of talking points for CHOP personnel to use when speaking to the patient prior to the patient talking to the Department of Public Health.

Designing the script for the conversation allows for the priorities of all stakeholders to be met. If a doctor or investigator doesn't understand the patient's life and their priorities in relation to the progression of the patient's disease, they cannot help the patient have their best outcome relative to their priorities. The conversation checklist prompts some sharing of information and helps remind the professionals what information the other professionals need. The checklist also provides some reminders about the aspirations of each organization and reminds both CHOP and PDPH about the shared goals both organizations have. This leads to a better working relationship and hopefully improves the patient experience. Service design is about designing the conditions necessary for the desired action to take place and that includes keeping in mind the type of mindset needed for these types of conversations.

#4 Fitwits[31]

A "B-corp" is a legal framework for a company that provides value to the customer or user while also providing social benefit to the broader community. Fitwits™, is a B-corp spinoff from the Carnegie Mellon University, School of Design to focus on educational programs surrounding childhood obesity in socioeconomically challenged areas. Fitwits formed out of a request for designers to come into a medical office and listen to conversations doctors were having with their young patients about weight management and obesity prevention. The designers noticed the opportunity for better communication around obesity as the physicians struggled to explain what "good nutrition" was and that the physician's office didn't have effective tools to engage children in the learning process and/or discussion. What was observed was that the attempt to explain a Body Mass Index (BMI) card was generally received with blank stares from the child, and downcast eyes from parents. It was further heard that "you cover all the factors that play into childhood obesity in an annual 15 minute well-child visit".

The designers took the physicians through the design process. In the first diamond, the research phase, the designers looked at how nutrition was taught to children and their families, and how to improve health literacy for children. Together with physicians, they started identifying barriers and challenges, and the language used around obesity. Through various design exercises, the group came to an agreement of what the underlying problem was. Participatory design workshops, as shown in Figure 2, allowed the designers to trial and error concepts with stakeholders in the community. These workshops allowed the designers to understand what made sense to the children and their care givers, how these stakeholders related to obesity and what types of steps an individual was comfortable taking. Participatory design sessions are beneficial from both sides, the participant can start to understand what good nutrition entailed, and the designers could see what works and what doesn't as well as gaining insights on how to shift the concept for the next time. Through creating cartoon characters to allow children to tell stories through, they found through these workshops that children could recall information back in the form of a story associated with Fitwits characters with funny sounding names (memorable to the children), such as Elvis Pretzley, Chunky Hunky, Barfenstein, Monty and Jack.

It was important for the Fitwits solution to engage all stakeholders. And an understanding of the child's, doctor's, parent's, and teacher's experience was paramount to their success. Since the goal was to raise awareness in a community about healthy eating, it was

Figure 2: Participatory design workshops fitwits held with the community

important to Fitwits to empower parents. Fitwits tried to instill a sense of responsibility in the parents and community to own the messaging and take over the development of subsequent programs. By empowering parents, this eventually led to parents influencing health policy in schools.

Fitwits developed a train-the-trainer model, and everyone involved in the Fitwits program became agents of change. As Fitwits grew, the additional services came out of engaging with a community in the process. Kristin Hughes, founder of Fitwits, and a professor at Carnegie Mellon University's School of Design states, "We learned that the co-design process inspires motivation and helps build a culture of trust, respect, and dignity. Eventually, communities moved from co-designing to designing on their own. The community began to tell us what they needed."

Hughes continues, "At the start, the physicians were already going into schools. We designed something specifically to help these physician's go into schools to teach children about the effects of obesity and preventative measures to help combat obesity. It was a set of co-designed games and a curriculum for physicians to use for this purpose. As Fitwits grew, the core games and curriculum never changed. Overtime, additional games and wrap around services were added–designed and managed by community members (otherwise known as community champions)" [32]. The bulk of the work was connecting people to make sure all the actors were in place so the community had the confidence to deliver Fitwits. It was about all the touchpoints the community members identified on their own and then fixed.

Fitwits™ has evolved into a system of games, educational materials and services that enable individuals, families, and communities customized opportunities to adopt and maintain healthier lifestyles. The novelty of Fitwits makes learning about health fun and is designed to create interesting hybrid experiences merging technology with hands-on learning by allowing people of all ages the opportunity to interact with each other, ask questions, and contribute their own ideas. The program has been in development at Carnegie Mellon University since 2008 under the leadership of Kristin Hughes. All components have been deployed in schools, physicians' offices, community organizations, and homes with positive results.

Supporting the public to make healthier and more informed choices in regard to their health is an important outcome, and also makes economic sense, because preventing childhood obesity is less expensive than spending money on chronic health problems such as Type 2 diabetes, cancer, heart disease, and high blood pressure.

CONCLUSION

These case studies demonstrated the breadth to what is considered Service Design. Service Design starts first with the experience and then designs the conditions necessary for the experience to come into fruition with a successful outcome. The problem frame comes from the qualitative research done (observing and questioning). The design comes from interacting and understanding the stakeholders, co-designing, testing and learning through small design experiments to then implement a finalized solution.

Service Design in healthcare can build relationships across silos, can improve patient experiences, can reduce medical errors due to misinformation and miscommunication. It aims to build positive working relationships that in turn allow individuals to perform their jobs more

effectively. As there is a direct tie to patient experiences and hospital reimbursement, Service Designers aim to balance the needs of stakeholders while enhancing their experiences.

Service Design works to build relationships over time, it focuses on creating relationships with the customer and participants in the care ecosystem in a way that facilitates non-tangible outcomes or emotions, such as trust, fun, comfort etc. It can also serve as a differentiator of products and services from competitive solutions.[33] Service Design analyzes the process over time and hypothesizes and validates the effectiveness of various possible approaches/solutions as applied to the problem. As with all design, the process is iterative. Four case studies are explored in this paper to demonstrate different examples of service design and the different type of outcomes it can produce.

To summarize the process, Service Design looks at the problem holistically to find leverage points where an intervention/solution can fit. Once leverage points are found, the designer zooms out to then design the conditions necessary for the solution to work. By looking at the entire journey from multiple perspectives, the designer can propose different touchpoints that attempt to connect experiences together. A Service Designer is not just designing the experience when they are interacting with the designed solution, but the before and after the experience as well. The idea is that services are systems that interact with users and provide value over time.

The process a service designer goes through delivers an experience that balances the needs of each stakeholder, keeps their interests at heart, engages them at a deeper level, providing them value over time, and doing so in an intriguing novel way. The end result is not only a better patient experience, but also allowing staff to do their job better, reducing error and miscommunications thereby, leading to lowering costs and increasing the standard of care.

The methods Service Designers utilize are beneficial because they look at the problem and the system the problem sits in and address both in tandem. In an innovation setting these methods and approaches provide value and differentiation. The healthcare ecosystem in recent years has evolved, and technology and innovation are becoming more important players in this system. This leads to Service Designers becoming integral members of the diverse teams developing medical solutions and services.

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Article

Innovation and Commercialization Strategies for Three-Dimensional-Bioprinting Technology: a Lean Business Model Perspective

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ABSTRACT

We examine and analyze the elements important for developing a commercialization strategy for an emerging technology of great relevance to biopharma: three-dimensional bio-printing (3DBP). We begin with a technology overview, identification of multiple, potential end-user market segments, then examine the key forces driving the competitive landscape of the emerging industry. The ability to print engineered 3D tissues advances innovations for human health and 3DBP is a transformative and disruptive technological breakthrough with high commercial potential for both short-term and long-term market applications. The near-term research markets include drug discovery research and development and the long-term markets focused on printing of organs and organoids for regenerative medicine. We include a mini-case study on the emergence of one potential innovation, the FRESH printing technology being developed at Carnegie Mellon University. The case study includes extensive market research made possible by published data, and our customer surveys. The commercialization pathway to innovation is framed in terms of combining two popular innovation frameworks: The Disruptive Innovation and the Blue Ocean strategic frameworks for market entry, growth, and expansion spanning from early adopters to mainstream market segments. We also advocate open innovation as an approach to building the "lean" business model and collaborative ecosystems through strategic alliances with non-competing firms having overlapping interests in 3DBP. This collaboration in parallel enables faster and more capital efficient validation of the process: product development, market development, validation of product/market fit, and market /customer development across the product life cycle spanning short, medium, and long-term visions for the technology. A platform strategy is framed to maximize the power of the technology and development of a sustained competitive advantage through complementary products, services, and partners in the emerging ecosystem.

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EXECUTIVE SUMMARY AND INTRODUCTION

Three-dimensional printing is an emerging and potentially disruptive technology that has made significant inroads within advanced manufacturing across various sectors outside of the biopharmaceutical industry. While bioprinting is still at the earliest stage of the Gartner Hype Cycle, it is apparent that new business models must be developed and implemented for successful commercialization of this radical technology in the biopharma industry. Nevertheless, several innovations are emerging to signal the early stages of evolution and technology adoption. The most notable are commercially available bioprinters, associated control software, and biomaterials specifically for the 3DBP research community. In biopharma, bioprinting has numerous applications that have been identified, ranging from preclinical research for drug screening, to clinical areas including patient-specific medical devices and organ transplantations. In recent years, the pharmaceutical industry has shown keen interest in bioprinting for use in toxicology assays and drug discovery models.

However, skepticism remains until the efficacy of using 'humanized' tissue for screening can be demonstrated to save time and money in the drug development process. In parallel, we note that the cosmetic industry has begun forming strategic alliances with new entrants at the research stage to develop bioprinting technologies for cosmetic development. The global bioprinting market is valued at an estimated $295 million as of 2016 and is growing rapidly at an annual rate of 43.9% to reach a forecasted value of $1.8 billion by 2021 (*BCC Research Reports, 2016*). Therefore, new entrants as well as large incumbents should make appropriate business decisions to extract maximum value from their IP portfolio by matching their product/service differentiations to the defined unmet needs in the market. Accordingly, they also need to develop their innovation, commercialization, and go-to-market strategies to sustain and develop their businesses quickly and with managed risk reduction strategies.

Here, we present various strategies using case studies from our own experience in setting the stage for novel 3DBP technologies. In our pursuit to identify and formulate commercialization strategies for novel 3DBP technologies developed at Carnegie Mellon University, we performed customer discoveries through numerous interviews with scientists, clinicians, surgeons, industry professionals, and investors. Our market study reveals that there is already a substantial market for the offering of a technology platform that will hasten the drug discovery process thereby reducing rate of costly late clinical phase failures during the drug development process. There is also significant value in terms of providing bioprinted tissue scaffolds without cells or for various external non-living tissue implants. As promising as it is for such in vitro applications, there is greater need and potential for 3DBP in clinical, in vivo regenerative medicine and organ transplantation sector as a long-term goal – albeit with substantially higher risk, capital expenditure to market, and longer development life cycle. The potential rewards to the success of this technology could prove massive, not only for the future of public health, but also to create new economic opportunities in accelerating drug development and generating replacement organs.

While it is both difficult and ambitious for a NewCo to develop both bioprinters and complementary materials, there are several entities that are entering the market with specialized and co-specialized products and services that are signaling holistic growth of the industry. Therefore, it is apparent that a strategic and collaborative innovation is imminent and needed to effectively meet the unmet market needs in both preclinical research and clinical market segments. Our hypothesis is that innovation, adoption, and commercialization of such disruptive technologies can be augmented through open collaborative innovation and developing strategic partnerships for co-sharing the value from IP portfolios, thus co-creating a business ecosystem that will maximize offerings to the customers and growth for the 3DBP market segments within healthcare sector. As noted, given that the expected market will be highly competitive, creation of a platform embedded into a collaborative ecosystem of complementary products and services would be recommended for sustained competitive advantage. If a dominant method emerges, there is potential for near horizontal integration of bioprinting under a dominant company that acquires or incorporates all new bioprinter, bioink and software advancements. A modern example is Google's dominance in online search allowing for a snowball effect of tech acquisitions to the point of restructuring into Google-Alphabet. Other examples of platform dominance might include Facebook, AirBnB, Salesforce, Apple, Amazon, etc. Similarly, a dominant bioprinting company could integrate an entire suite of complementary products and services, e. g. bioprinters, bioinks, software, therapies and researchers under one platform to provide a superior, streamlined bioprinting system.

3D BIOPRINTING: TECHNOLOGY OVERVIEW AND SCOPE OF APPLICATIONS

Evolution of new technologies that are compact and inexpensive, yet powerful and effective, has empowered

researchers to develop novel technology platforms and products that can bring enormous value for various applications within the healthcare sector. Such advancements have the potential for the healthcare sector to meet unmet market needs, potentially causing a disruptive market expansion through agile innovation, commercialization, and adoption strategies. Some of the major transformative innovations in the healthcare sector have been developing from the convergence of different technologies in robotics, software, material sciences, life sciences, and medicine. One such technology that has benefited immensely in recent years is 3D printing, which is expanding its application into areas such as medical/dental applications, customized consumer products and custom parts replacement. More specifically, 3D printing in the form of 3DBP has shown the potential to make different structures, such as, creating replacement tissues, organ parts or potentially whole organ replacement for regenerative and transplantation therapies.[1,2]

Bioprinting is generally described as a combination of engineering with biology to create human tissues that replicate native tissue and can achieve unique tissue-specific metabolic functions.[1] Despite being at an early stage, 3DBP innovation and adoption is now rapidly increasing due to the co-evolution and sharing of technologies such as robotics, high-resolution 3D imaging and printing software, 3D printers, bioprinting support systems, and a growing list of bioprintable materials. Biopharmaceutical and medical device companies, research institutions, and universities around the world are working on developing this novel technology through open sourcing and knowledge sharing. Several funding options ranging from accelerators, angel investments, corporate partnerships, and venture capital funding are available for start-up and early stage companies in the 3DBP technology sector. Accordingly, there is an opportunity and a major driving factor for academia to develop spin-off companies to expand research and provide real-world applications of 3DBP to meet the challenges of the healthcare sector.

The main applications of bioprinting arranged according to their evolution and validation across the product life cycle include the following:

1. Tissue modeling for drug discovery and development
2. Toxicology testing for drug screening and cosmetics
3. Engineering tissues for regenerative medicine, prosthetics and dental applications
4. Transplantations of full organ or organ parts in regenerative medicine and invasive surgeries

3DBP applications in preclinical drug discovery, toxicology assays, and tissue modeling are rapidly expanding in adoption and currently predominates the 3DBP market value. These sectors are attempting to "cross the chasm" of the adoption cycle and entering the early growth phase. While *in vivo* applications of 3DBP in regenerative medicine are still in the embryonic stage and are viewed as mid-term goals of businesses, 3D bioprinting of full organ transplants presents a scope for the long-term vision of the industry, owing to the technological limitation and regulatory barriers.

TECHNOLOGICAL CHALLENGES AND INNOVATION OPPORTUNITIES WITHIN 3DBP

Generally, 3DBP technologies utilizes the layer-by-layer deposition of biomaterials to create tissue-like structures that can subsequently be used in medical and tissue engineering fields.[3] Although 3D-printing itself has been quite successful in prototyping and in the consumer manufacturing sectors, there are major technological challenges to directly translate those advances into the biological/medical domain. 3DBP generally follows three steps: pre, mid, and post-bioprinting.[2,3] Pre-bioprinting involves creating a model through computer aided design (CAD) that the 3D printer will create from appropriate biomaterials of choice. Typically, computed tomography (CT) or magnetic resonance imaging (MRI) of tissues or biopsies are used as the source of the model. The bioprinting step involves placing a liquid mixture of cells, matrix and nutrients, collectively known as "bio inks", in a printer cartridge and fabricating a tissue scaffold by dispensing the bio-ink mixture using a successive layer-by-layer approach to generate tissue-like 3D structures using methods such as photolithography, magnetic bioprinting, stereolithography, thermal inkjet printing and direct cell extrusion.[1] Although, many of these methods are often used to print biomaterials, they can sometime be detrimental to living cells limiting their viability. Once this immature bioprinted tissue is transferred to an incubator and provided with appropriate physiological conditions, it matures into a more cohesive, functional tissue. The post-bioprinting process is necessary to create and maintain stable, viable structures of printed biological material. This is usually done by means of mechanical and chemical stimulations to send signals to the cells to control the remodeling and growth of the tissues.[3] Bioreactor technologies have allowed the rapid maturation of tissues and vascularization of printed constructs.[1]

Products generated by 3DBP primarily require 3D printing hardware systems, imaging and printing

software and tools, and various kinds of biomaterials. The hardware system must ensure that the bioprinting is carried out accurately to mimic the finer details of the 3D tissue structures. Speed is very important since cells do not survive outside of the cell culture incubation system for prolonged period. Hence, the printing and fabrication speed must be fast enough so that the cells of the bioprinted tissue is not adversely impacted and are returned to the culture and incubation system quickly. For example, a low-shear deposition mechanism is essential for maintaining the growth and function of living cells.

The support system for 3DBP also has tremendous scope for innovation, as printing soft tissue at high resolution requires a non-destructive and flexible support bath that not only allows for free-form printing of soft biomaterials, but also maintains the structural integrity during the printing process. The recent development of a novel 3DBP technique from Carnegie Mellon University (CMU), termed Freeform Reversible Embedding of Suspended Hydrogels (FRESH), has enabled additive manufacturing of 3D biological structures using soft protein and tissue materials, which comprise most of the organ system.[4] Another important consideration for healthcare applications is that all components that are part of the bioprinting process that comes in physical contact with the printed tissues must be non-toxic, biocompatible, and sterile to prevent any microbial contamination or cell death.

Given the broad array of steps and requirements for 3DBP, there are many areas for innovation. Hence, there is tremendous opportunities for start-up companies that specialize and co-specialize within each of these areas of bioprinters, imaging and 3DP software tools, novel biofabrication technologies, biomaterials, and reagents to address the needs of the market. Significant progress is being achieved in cost effectiveness of biomaterials and printers, in addition to the ability to print both hard and complex soft tissues – with or without cells.

3DBP CAN POTENTIALLY TRANSFORM THE FUTURE OF THE HEALTHCARE SECTOR

Currently, the early-market applications of 3DBP are mostly focused on the biomedical research, and non-clinical applied sciences areas of the biopharma value chain, e. g. research labs and university markets. Key factors driving growth for instruments and reagents used in these applications are: improvements in bioprinting instrument capabilities; printing speed and precision; better preservation of living cells pre- and post-printing; printing multiple bioinks together; and innovations in bioink and support material formulations allowing printing of soft flexible tissue materials. In this direction, there is also push for innovations to create bio-inks with high usability that are closer and closer to lifelike matrix materials. Rapid innovations in these areas have produced bioprinted 3D constructs with remarkable potential for *in vitro* tissue models that closely mimic the true *in vivo* state and mechanics, thus proving to be a robust tool for the pharmaceutical industry for these applications. For instance, the FRESH method has shown that 3D imaging data of soft tissues as complex as branched coronary arteries, embryonic hearts, and human brain tissue can be printed at micrometer level resolution while retaining the complex internal and external architecture at a reasonably low cost.[4]

Bioprinting for applied industries is estimated at $237.8 million as of 2016, and is growing at 15.5% CAGR to reach $489.8 million by 2021.[5] The two main industries supporting this growth are drug discovery and cosmetics, propelled by the need for better *in vitro* tissue models. In the cosmetics and pharmaceutical industries, bioprinting tools to produce 3D tissue culture and organoid models for toxicity testing are gaining momentum. This is partly also due to the bioethical considerations that push away from traditional animal testing and the associated costs of maintaining and developing preclinical animal disease models.

The basic and translational research market is estimated at $57.2 million in 2016, with a projected CAGR of 20.5% to reach $145.4 million by 2021.[5] Significant federal funding support for 3D model approaches for studying diseases and the growing number of high impact research publications in this field is driving this market. For example, the Human Cancer Models Initiative began in July, 2016, as a research collaboration, which plans to complete an initial 3-year goal of developing 1,000 cancer tissue models for research using the next generation cell culture methods.[6] The Human Cancer Models Initiative includes a consortium of leading cancer research institutions in the U.S. and Europe, including the National Cancer Institute (Bethesda, Maryland), Cancer Research of UK (London, UK), The Wellcome Trust Sanger Institute (UK), and Hubrecht Organoid Technology (Utrecht, the Netherlands). This initiative has emphasized the need to develop 3D cultures and organoids to better reflect human cancers, such as the tumor's natural microenvironment containing a rudimentary vascular system. As part of this initiative, a 3D Cancer Cells Library has been launched recently.[7] Therefore, 3DBP technology platform such as the FRESH method that allows printing of soft tissues with complex architecture including intra-organ vasculature will reap enormous benefits in this market segment.

Although most of the current $295 million market valuation of 3DBP is estimated from its preclinical usage in the pharmaceutical and cosmetic industries, we believe that the clinical market will soon surpass the preclinical market in terms of its economic impact because of its higher price-point and more significant market demand. The clinical regenerative medicine market segment will drive overall 3DBP market growth during the next 5 years from a negligible revenue during 2016 to a forecasted $1.2 billion by the year 2021 (of the total value of 3DBP estimated at $1.8 billion).[5] Major applications include cosmetic surgeries, cardiovascular, orthopedics, wound care, and craniofacial repair. In addition, the aging population of the developed economies has higher incidence of heart disease and diabetes-associated organ failures, which could be treated with 3DBP tissues. Further, accidents and birth defects also drive demand for organ transplantations and other clinical needs. A report in 2009 suggested that only 18% of the US patients awaiting organ donations received an organ transplant and as many as 25 per day died while on the waiting list. There are as many as 120,000 patients in the US waiting for a donor organ and the organ transplant surgery and follow-up clinical visits, with costs as high as $300 billion.[8] Emerging bioprinting techniques allow living cells to be placed alongside scaffolds materials such as collagen hydrogel in a predetermined 3D architecture, which provides the cells an environment to communicate with other cells and to grow. We believe these innovations may help the growing demand-supply deficit and healthcare cost burden in the organ transplantation sector in the longer term. A major concern for the future of organ transplantation is the effect autonomous vehicles will have on the supply of healthy donor organs. As automobile accidents represent a large source of donor organs from otherwise healthy individuals, lower traffic fatalities in the future will subsequently lower the supply of donor organs, furthering the gap between the supply of organs and the growing list of patients requiring transplantation.

Bioprinted tissue constructs have significant clinical benefits in that once available and validated has the potential to drive their adoption going forward. For example in regenerative medicine, the development and use of artificial skin is of strong interest for treating wounds such as burns or surgical cuts. Often, large format constructs are needed for these applications and the current practice of removing a layer of skin from another site for autologous transplantation through simple sutures provide inadequate healing, donor site morbidity, and are painful. 3DBP can meet these clinical needs because it can make large prints of living cells and scaffolds while at the same time producing high quality skin grafts. As a result, there is a strong focus on translational development of bioprinted tissues for these medical applications. Therefore, the startup companies should not limit their innovation and commercialization to only non-clinical usage but also pursue technologies and products with clinical applicability in their strategic vision as well.

3DBP INNOVATION AND COMMERCIALIZATION ECOSYSTEM

The key driving forces for 3DBP commercialization and industry growth are: aging populations increasing unmet demand for organ donors; trends towards non-animal testing on therapeutics using 3-D cell culture platforms; clinical needs in wound care; and joint repair and replacement surgeries. These needs can potentially be met with ongoing developments of high performance bioprinting platforms and biomaterials.

Owing to several successes of 3DBP start-up and development stage companies, such as, Biobots, Cellinks, Helisys and Organovo, more university-based novel inventions are spinning off into the start-up ecosystem. The innovation culture and technology transfer offices within the universities are providing an enormous helping hand in terms of technology transfer, business strategies, incubation funding, licensing agreements, IP creation and patent filing and supporting the team to start-up the business. Community support ecosystems in the US and elsewhere, and international conferences and knowledgebase consortia also provide enormous support. Emerging clusters of academia, biotech, and pharma hubs in the US include Boston, San Francisco, and San Diego. These clusters play a key role at the delicate early stage of the company through open sourcing of ideas, and enabling both seed funding and business support infrastructure. Various biopharmaceutical corporations also have new venture funding initiatives and are willing to participate in the early stage of such companies, as they see the potential of reducing the enormous failure costs of the drug discovery process. *In vivo* animal models are often non-predictive of drug failure in later clinical trials, and pharmaceutical industry bears the high cost burden for failure at the late clinical trial phases. We envision that such private industries, academic institutions and startup business partnerships will be crucial to drive faster innovation of 3DBP and bring the technologies and products to the market in the most efficient manner. As it stands currently for drug discovery, the transitions from 2D human cell culture, to animal

models, back to humans represents drastic environmental changes in which drugs can falsely fail. Drugs that fail in animal trials may have potentially worked in humans, but failed due to differences between species. As a result, 3DBP may provide the ability to simplify or replace the first two stages of drug discovery by creating 3D human tissues to replace 2D cell culture models or 3D animal models.

Although technologies in each component within 3D printing are evolving, the excitement and hype about 3DBP has often outpaced actual innovation and development in the field. In fact, many of the technologies that make up the entire 3DBP industry are often well-studied, with scientists "siloed" in individual disciplines for decades such as material sciences, life sciences, engineering or software tools. However, the innovation can be accelerated towards actual products if we think about each of these technologies as elements of the entire system rather than separate pieces. By embracing the system's multidisciplinary nature and complementary tools, we can connect domains to each other in the pathway to designs of 3DBP. Once we can design these elements to interface with each other and corresponding complementary technologies, true manufacturing solutions can be achieved for bioprinted products. We believe the following aspects are essential to foster 3DBP innovation:

1. **Open sourcing**: Accessibility is crucial for enabling 3DBP innovation as it encompasses multidisciplinary technologies. For instance, if development of a fully equipped 3D printer or advanced material are barriers to develop new products, then it can only be overcome with open sourcing of domain expertise necessary, similar to Google and its Android OS. From our study on commercializing the FRESH bioprinting technology from CMU, we surmise that the open sourcing platform has not only enabled rapid printer adoption, but has also helped in advancing various forms of biomaterials that can be used and provide a faster dissemination of new technologies.
2. **Open innovation (OI)**: Due to the interdisciplinary nature of 3DBP, we believe it is essential to imbed open innovation approaches into the business models of both new entrants and large incumbents who are entering 3DBP market. OI approach will not only accelerate technological development, it also will bring benefits to product design, new market insights, customer intimacy, and business model innovation.[9-11] Modes of OI, including licensing, joint ventures, strategic alliances, contract research organizations, university collaborations, equity in university spin-offs and venture capital investments at very early stage of the NewCo or university research are particularly useful in both innovation and quicker adoption of emerging 3DBP technologies. Companies must choose different modes of OI, depending on the available resources, strength of their IP, strategic directions in their autonomy and time horizon of entering and expanding their niche market. For example, the recent collaboration of L'Oreal and Organovo is helping both innovation and adoption of 3DBP in skin and cosmetic industries.
3. **Modular designs**: 3DBP poses a potential for disruptive innovation in healthcare sector and hence business models need to become modular and adaptable. Companies can decide to adopt a narrow (niche market focused) or wider (design, manufacturing and distribution) or shorter (only design) business models.[11] Owing to its disruptive nature, 3DBP will likely serve new sub-sectors within healthcare industry, new markets, and even entirely new consumer segments. Therefore, the business models must become adaptable to changing market conditions, as well as move within its own market segment.
4. **Informed understanding of customer need and market segments**: The technology should be applied in customer segments where it makes the biggest impact, and is applicable to jobs to be done that are not well done with current solutions. For instance, if new alternative and cost effective solutions are developed for certain unmet needs, then merely using 3DBP in those areas may be difficult. This approach would be illustrative of the technology-push approach. It is common to develop a niche technology and then search for customers – a hammer looking for a nail – instead of assessing customer needs and building technology to address those concerns. Therefore, extensive customer discovery and intimacy with lead customers (or users) is critically necessary in identifying key areas of innovation. Identification of receptive markets is a worthwhile investment to identify opportunities for products/services

that provide differentiated values to the customers. For example, we suggest using a combined disruptive innovation/Blue Ocean strategy approach informed by user/customer immersion to understand customer needs and their current options. Figure 1 illustrates this model using the blue ocean framework (*adapted from blue ocean strategy tool, originally described by Kim & Mauborgne*).[12] We suggest that the earliest stage of market entry would be the Innovators who serve as reference customers for the first market entry stage. These innovators could develop partners who might serve as Beta Testers, or possibly non-paying thought leaders in the scientific community. Once established, it is possible to proceed to Tier 1 which would represent the earliest adopter segment to demonstrate the efficacy of the technology/solution and to gain initial early adopters- and perhaps demonstrate a profitable business model in the entry market. Once the technology is advanced and credibility established, the innovation team could then move onto Tier 2 (a scaling stage) where further development and validation would provide additional elements to the value curve. Then, finally to Tier 3 which is the largest mainstream market segment (again with further developments). To further illustrate, we might consider the following potential strategy for 3D Bioprinting (more detail to follow in the case study presented in next section):

Tier One Markets to demonstrate validity of the technology and develop entry market foothold - *Biomaterials for research and drug discovery application perhaps in academia and startup companies, partnered with bioprinters and software organizations. Initiates formation of an ecosystem needed to go beyond a single product.*

Tier Two Markets for growth – *Commercial market expansions. Drug discovery and development in partnership with selected organizations in biopharma and CROs.*

Tier Three Markets for expansion and long-term potential – *Regenerative medicine for selected tissues and disease states.*

While we have used Blue Ocean Strategy and Crossing the Chasm concepts here, it is also useful to utilize disruptive innovation concepts to illustrate the market entry and growth strategies. In any event keep in mind that the initial offerings are low cost solutions that require acceptable performance and low cost business models, e. g. channels and partnerships to market.

CUSTOMER DISCOVERY AND GO-TO-MARKET STRATEGIES: A MINI-CASE ON COMMERCIALIZING FRESH BIOPRINTING TECHNOLOGY

While academic institutions are very good at invention, more successful innovations emerge when a combination of technology, business, and design thinking are employed to inform appropriate commercialization and innovation strategies. For 3DBP we would also need to include: bioengineering and tissue engineering, in collaboration with larger incumbents of 3D printing industries such as HP and 3D systems. Here, we sought to perform extensive customer discovery to gain market insights while formulating commercialization and business development strategies for a unique 3DBP technology, called the FRESH method, developed by CMU scientists and engineers.

One of the major limitations of traditional biofabrication technologies is ability to print high resolution soft tissue materials, such as extracellular matrix (ECM) of organs and vasculature. Commercial bioprinters available from BioBots and EnvisionTEC have expanded the accessibility of bioprinters beyond the groups that custom build their own systems.[13-15] Recent approaches for 3DBP of biological hydrogels use syringe-based extrusions of organic (alginate), semi-organic (gelatin methacrylate), or synthetic (polycaprolactone) inks. Fibrins and gelatin materials have allowed the ability to print ECM. However, the complexity of microstructures and 3D anisotropy that can be created are highly limited as there has not been a way to prevent these printed soft gel structures from deforming when stacked in layers in open air.

Significance and Impact of Fresh Technology Innovation

FRESH uses a thermo-reversible support bath to enable deposition of hydrogels in complex, 3D biological structures and is implemented using open-source tools, serving as a highly adaptable and cost-effective 3DBP platform.[4] FRESH overcomes major limitations of 3DBP such as the ability to print high resolution soft tissues while maintaining complex internal and external geometries found *in vivo* in a cell-friendly, non-toxic and sterile manner. The key evolution of this technology that is expected to positively impact commercialization success is the deposition and embedding of hydrogel materials within a second hydrogel support bath (composed of gelatin micro-particles) that maintains the soft structure during the bioprinting process, significantly improving print fidelity. The support

bath behaves as a rigid body under low shear stresses, but flows locally as a viscous fluid at higher shear stresses. This breakthrough results in very little resistance when a needle-like nozzle moves through the bath, but allows the extruded hydrogel deposited within the bath to be held in place. Thus, soft materials and liquids are easily maintained in the intended 3D geometry during the bioprinting process, which otherwise would collapse on its own weight if printed in air. Moreover, this can be achieved in a sterile, aqueous, buffered environment compatible with cells, as the cells together with hydrogel extrusion can maintain viability. In the post-bioprinting process, the entire bioprinted 3D structure can be recovered by simply raising the temperature to a cell-friendly 37°C, causing the support bath to melt in a nondestructive manner. FRESH printed scaffolds retained the integrity of complex internal and external architecture of a coronary artery vascular tree, whole organs such as embryonic chicken heart, and a human brain structure with major anatomical features down to a resolution below 200 μM.[4]

Opportunity Landscape of 3DBP for Soft Tissue Printing

As the global 3DBP market is expected to reach $1.82 billion in the next 5 years, more preclinical and clinical applications such as toxicity testing, drug discovery, engineering functional tissue, ECM scaffolds and organ implantations of 3DBP are being investigated. The broader, global soft tissue repair market itself is estimated to reach $14.7 billion by 2019.[16] The significance and market impact of soft tissue printing is particularly increasing due to burgeoning incidences of soft tissue injuries amongst the aging population, increasing sports injuries, obesity rate and healthcare expenses due to lack of substitutes for soft tissue repair surgery. The global biopharmaceutical market is expected to grow at a CAGR of 9.4% through next 5 years, reaching $278 billion, and the cell analysis, improved accuracy of drug screening assays which in turn reduce time and cost of drug discovery process will be pivotal driving force in this market, where 3DBP can bring enormous value.[17-18]

Strategic Initiatives and Alliances: Building Differentiation and Sustained Competitive Advantage by Blue Ocean Strategy with an Open Innovation Approach

As this FRESH technology meets some significant unmet needs and circumvents major limitations of soft tissue bioprinting. Since FRESH can be used on an FFF 3D printer of any cost, we envision a business that can be built around FRESH as a technology platform company, rather than a hardware-focused start-up. By strategic alliances with other leading firms in the complementary tools and services of the 3DBP technology, an effective innovation and commercialization ecosystem should be built to augment the market further.

Among the various printer technologies, syringe-based printers dominate this technology segment, as these printers allow working in sterile environment, have wider applications including fabrication of scaffolds, cell strips and tissue printing. Current key players operating in 3DBP are: Organovo Holding Inc., Cyfuse Biomedical, BioBots, CellInk, 3Dynamics Systems, Stratasys Ltd., Voxeljet, EnvisionTEC, Bio3D Technologies, TeVido BioDevices, and Solidscape and this list is increasing as novel technologies are emerging and new patents being filed in various components of 3DBP process. These players are involved in various strategic initiatives for new product launches, including strategic alliances and M&A, to gain competitive advantage over peers within the same niche. The recent collaboration of L'Oreal and Organovo to develop skin tissue using NovoGen Bioprinting platform has inspired more such open innovation through alliances in the 3DBP sector.

The flexibility in materials used and architectures printed by FRESH method defines a new level of 3DBP capability of soft materials. Higher resolution is possible using higher-precision printers, smaller-diameter needles, and gelatin slurries with a smaller particle diameter. Hence, partnering with BioBots, who provide high precision bioprinters can be mutually helpful in market penetration. Cost is an important consideration for the future expansion of 3DBP, as the commercially available custom-built tissue biofabrication platform currently cost more than $100,000 and require specialized expertise to operate. In contrast, FRESH is built on open-source hardware and software and the gelatin slurry is low-cost and readily processed using consumer blenders. To emphasize the accessibility of the technology, the inventors at CMU could implement the patent-pending FRESH method on a $400 3D printer. The open-source STL files to 3D print the custom syringe-based extruder can be downloaded from NIH website (3dprint.nih.gov). Thus, we anticipate that the affordability and ability to print a range of hydrogels using FRESH will enable the expansion of bioprinting into many academic and commercial laboratories who are currently priced out of the market by the $100,000 custom bioprinting systems. In academic settings, the NIH grants usually stipulate a limit of $5,000 for expenses in purchasing equipment. Hence, providing a

bioprinter for less than $5,000 can lead to rapid adoption and dissemination of this 3DBP platform across laboratories and core facilities of biomedical research divisions within academic institutions.

In addition to the bioprinters, the quality of bioink is also essential in achieving high print quality. Currently, CellInk AB is a leading innovator in this area and have established a market providing excellent quality living bioinks. Cellink AB itself grew by forming strategic alliances with RoosterBio. Thus, partnering with CellInk and BioBots, the FRESH technology platform can establish a strategic ecosystem to provide high quality and cost-effective bioprinters, bioinks, support bath system and services to bioprint high resolution soft tissue materials, thus providing a complete offering and solutions to the end user customers.

Entering any new market in a technology focused arena requires intimate customer contacts and elaborate customer discovery process. This can be augmented through social media and open-source platforms, attending conferences, and technology exhibition events. It also requires high flexibility to add new products, complementary goods and services to the offerings to meet customer needs in the research-intensive biomedical sector. The time window for entering the market in knowledge-intensive industries is extremely short and if a NewCo waits too long to develop all capabilities before entering the market, it may entirely miss the opportunity as technology changes rapidly. A shorter development process for each product can only be achieved through access to skilled personnel, strategic marketing, alliances and partnerships to achieve synergy among various complementary entities. For instance, CellInk AB entered the 3DBP market by first offering a universal bioink; however, its success came through the introduction of the complete package consisting of bioprinters, reagents, bioinks and application knowledge through partnering with a matured stem cell company and launching the BioVerse community.

Patents should be carefully drafted as broad as possible for the application and usage of the technology of a NewCo. Multiple partnerships with various non-competing entities through licensing for specific usages can be useful in capturing maximum value from IP portfolio, widespread dissemination of the technology, and further innovations. For instance, such strategic deal making was pivotal for the success of the technology platform developed by Millennium Pharmaceuticals.[19]

Developing visibility of any new technology is highly important. It's part of the customer communications piece of the business model canvas starting with awareness, followed by consideration, choice and retention. For a new, disruptive technology, engagement starts with the scientific community that is a potential user and customer of the emerging technology. Engagement should start very early, possibly even before the formation of the NewCo. Inventors publishing their findings in peer-reviewed research journals provides solid scientific credibility and a strong foundation to begin a marketing campaign for the potential of the technology. Research and investor communities, both local and national can be identified and reached via short videos, publications, and pitches. Customer discovery is extremely essential where face-to-face or video conferences with the subject matter experts should be established to identify pain points and illuminate potential products or services based on customer-driven need. This not only provides a better understanding of the market, but also builds relationships and visibility to those who may become early trial customers. Popular articles, magazines, visiting technology trade shows and conferences will help in furthering visibility and establishing strategic partnerships. For example, CellInk formed a relationship with RoosterBio through a trade conference. A material transfer agreement with potential alliance partners can allow for the testing of products and complementary technologies prior to a full-scale release.

Similarly, education and training of customers are an essential part of the business and provide market advantage. In our customer discovery process, we learned that most laboratories focus on a highly-specialized area of biomedical research, and that they would most likely benefit from an offering that provides cost-effective bioprinters, bioinks, reagents and most importantly knowledge and training services. Thus, we surmise that utilizing the open-source platform that the inventors of FRESH technology have developed and by forming strategic partnerships with lead entrants in complementary goods/services of 3DBP, a sustainable business ecosystem can be developed quickly through further IP portfolio development to capture this growing market.

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Article

MEDRAD Innovation Journey - from start-up to Industry Standard: Mountain Climbing, Spelunking, Over the Horizon Home Runs, and creating a "DC-3 Effect"

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ABSTRACT

Medrad was a pioneer and is now a current leader in the medical imaging industry; which, after acquisition is now part of Bayer Radiology. In this case study, we describe the customer, user, and ecosystem centric processes employed by the company to identify underserved, unserved, and as yet unimagined markets to commercialize its technology. The evolution begins at the start-up stage, follows the development and growth stages, and includes the history, philosophy, and principles that created a global leader in med tech innovation. You will see the journey described through several metaphors - "mountain climbing, spelunking, and over the horizon home runs". We also describe the importance of the "DC-3 effect" which has been used in the aerospace industry to describe the importance of assembling all the right elements, similar to an ecosystem, to build an industry standard platform. Many of the processes employed by Medrad utilized innovation principles before they became well developed and popularized; they sought "blue oceans", understood disruption, and utilized design thinking principles. The company also adopted the balanced scorecard approach to align corporate vision and goals before the methodology became common in many industries.

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INTRODUCTION

After a start-up, development, and market launch stage, MEDRAD grew the sales of its products and services at a compounded rate of 16.0% per year for the 25 years from 1982 to 2007. MEDRAD's products are primarily electromechanical injectors and associated disposables used to deliver fluids in imaging procedures. These products are used by doctors and medical professionals worldwide in a number of medical imaging and treatment modalities. MEDRAD grew as a privately held and then public company, and after an M&A exit, it became part of Schering AG and is now an integral part of Bayer Radiology, a global healthcare organization. The journey started with two doctors seeking solutions for problems that they and other doctors were encountering in performing a new medical procedure (an unmet need in an imagined market). The introduced and perfected some innovative products, and leveraged professional management to create an industry standard organization that was recognized, not once, but twice with the Malcolm Baldridge National Quality Award.

MEDRAD was started in the Pittsburgh, PA area in 1964 by two doctors, Dr. Steve Heilman[1] and Dr. Mark Wholey. In early 1964, Mark had just returned from 2 years in Sweden where he learned angiography. Angiography is a medical procedure for assessing the condition of blood vessels in the body by inserting catheters into and through the vessels, injecting liquid X-ray contrast, and then imaging the vessels with an X-ray system to look for blockages, narrowing, bleeding, or other problems related to the vessels. At that time angiography, was difficult. It was very hard to inject the viscous X-ray contrast agent through the long, thin catheters to get good images every time. There needed to be a better way to inject the contrast in angiography.

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Steve Heilman agreed to work on this contrast agent injection challenge with Mark. The name chosen for the company to pursue commercialization was MEDRAD (**MED**ical **R**esearch **A**nd **D**evelopment). While Steve Heilman worked as an emergency room physician, he and a team developed the world's first flow controlled injector. There were two powered injectors on the market at the time, but both set the pressure of the injection, which meant that the flow was not well controlled. Steve's key innovation was a flow controlled injector. A doctor could select the desired flow rate and the injector would develop whatever pressure was necessary, up to 1200psi, to deliver the contrast at that programmed flow rate. This was a technology breakthrough, although the whole procedure of angiography was still in its infancy. As with any innovation in an emerging market that is being created, growth was slow as innovators and early adopters provided the early market and the technology advanced. By 1974 MEDRAD had developed the Mark IV which became a worldwide leader for angiography injectors. One of MEDRAD's associated innovations was the use of a relatively transparent disposable plastic syringe inside a strong, transparent reusable pressure jacket. This allowed the doctor to visually inspect the syringe to confirm that no air would be injected into the patient. Air injections could be fatal. MEDRAD sold a new, sterile, single-use syringe for each imaging procedure.

In the late 1960's Drs. Michel Mirowski, Morton Mower and William S. Staewen invented and worked on the world's first implantable cardioverter defibrillator (ICD). They eventually obtained support from a major pacemaker company in 1970 to further develop the ICD. But after 2 years the company decided there was no market for the device. In 1972 Mirowski was introduced to Stephen Heilman. Heilman was excited by the concept of the ICD and immediately put some of MEDRAD's engineers at Mirowski's disposal.[2] A sister company, INTEC Systems, was formed to develop and commercialize the technology. It took until 1980 before the first human implant took place. FDA approval came in 1985 and the technology was sold to a pacemaker company, Cardiac Pacemakers, Inc., in 1986 (quoted from Wikipedia) [1.]

During the 1970's MEDRAD patented and commercialized a flat-profile guidewire and worked on catheter improvements, both of which could be of use in their mainline business, the angiography procedure.

With the invention of CT in 1972, there was some concern that angiography would become obsolete, so MEDRAD launched an effort to develop an ophthalmic ultrasound imaging unit.

After a period of "mountain climbing and spelunking", MEDRAD in 1981 brought in a professional manager, Tom Witmer, to be the CEO and focus on growing MEDRAD's business. Tom was instrumental in the development of The MEDRAD Philosophy in 1983, stating that

"MEDRAD exists to
Improve the quality of healthcare
Ensure continued growth and profit, and
Provide an enjoyable and rewarding place to work".

This vision is consistent with a balanced scorecard philosophy and pointed the way to the creation of industry leading products, national recognition and ultimately acquisition. MEDRAD was a private company at that point, and this philosophy and metrics were used to assess the organization's success going forward. This leads to our reference to the "DC3 effect" term, coined by Peter Senge[3], and described more fully below –basically, the term refers to where one organization's innovation is happening in an ecosystem of innovations. Changes being made by many other, non-competing organizations, leverage "the dance of innovations" to create new, industry leading platforms or procedures.

One of the first product moves the new management team made was to adapt MEDRAD's injector from angiography to CT. At that time, it took 1 to 2 minutes to do a CT scan of a patient's head or liver. To assess the presence of cancer in the liver, a patient would receive a gravity-driven intravenous infusion (IV) of X-ray contrast while lying on a gurney in a waiting area. After 2-3 hours, their liver would be scanned. Many cancerous tissues would appear brighter or darker because cancer has a different uptake of the X-ray contrast than the normal liver tissue. Similarly, to assess a stroke, the patient was given gravity infused IV contrast. After a very short time, though, the patient was brought into the CT scanner and a scan taken, with the area of the brain affected by the stroke appearing whiter. A challenge was that if there was a delay in imaging the patient, the contrast continued to diffuse in the brain and caused an incorrect estimate of stroke size and location. MEDRAD believed that if an injector was used to inject the patient while they were on the CT scanner, just the stroke region would be seen and the inaccuracies from diffusion would be minimized.

MEDRAD's CT injector was a relatively simple adaption of the angiography injector. The only change was to the controls, to limit the flow rate to 10ml/S and the pressure to 300psi so the device didn't seem as intimidating to the doctors and hospital imaging technicians. Sales were expect to go well, but didn't. The doctors and technologists believed that they didn't have frequent enough problems with delay imaging after gravity infusions to make it worth buying a power injector. MEDRAD's warehouse had a very significant supply of CT injectors at one point. About a year after the CT injector was introduced,

an unknown researcher figured out that by giving a slow, but steady IV injection over 1.5 minutes while the patient was being imaged, it was possible to look for cancer in the liver without the 3 hour delay. This became the "over the horizon home run" that caused a CT injector to be sold with every CT scanner. Each scanner needed an injector to perform this procedure, and once there was an injector on the scanner, it was much more efficient and effective to use it for every injection. This discovery of a new, faster, and better way to do the liver cancer procedure also significantly increased the number of these procedures performed, increasing the market for injectors and CT scanners. This discovery would not have been possible without an injector to try it. This is an example of the DC-3 effect, as imager improvements came together with injector improvements to make a new procedure possible.

In early 1980's MEDRAD applied for patents on a new injector and an improved way to connect and disconnect an angiography syringe plunger to an injector for use in their next generation injector, the Mark V. The Mark V was introduced in 1985 and became the market leader. It included a number of additional user and technical improvements. It became the basis for MEDRAD's next generation CT injector, the MCT. This for the first time provided patent protection on the disposable syringes that were used with MEDRAD's injectors.

With CT growing faster and becoming larger than angiography, MEDRAD decided to design an injector just for CT. Feedback from the customer resulted in a product that was much smaller, lighter, and had a newly patented plastic syringe that did not need a pressure jacket, so the syringe could be easily mounted and removed from the front of the injector. The EnVision™ injector was introduced in 1995 and continued MEDRAD's growth in CT.

During the 1970's magnetic resonance imaging (MRI) was being developed. By the mid1980's it was starting to gain traction. MRI uses a very different imaging physics, and so could provide exquisite images of soft tissue, much better than X-ray or CT could do. There was the thought that MRI would replace X-rays, CT, and the need for X-ray contrast. If true, this presented a serious threat to the CT business. Contrary to that, Schering AG, a German manufacture of X-ray contrast saw an opportunity in MRI contrast. Similarly, some at MEDRAD believed that dynamic contrast injections would always play a part in selected diagnoses, so MRI would need an injector. Schering developed the world's first MR contrast agent and MEDRAD set to work to design an injector to work in the MRI suite. This was very difficult because of the high magnetic fields and the need for ultralow electrical noise performance. By electrically and mechanically adapting a Mark V injector, the world's first MRI injector was developed relatively simply and inexpensively. The Spectris® MR Injection System was introduced in 1996.

Over the decades since its discovery, CT systems went through several generations of improvements. This produced improvements in speed and imaging resolution and resulted in an increasing number of scanners each doing an increasing number of procedures daily. MEDRAD found that the revenue from the syringes grew much faster than the revenue from injector sales. In comparison, even though an MR injector is sold with every MR scanner, the rate of use of MRI injectors has remained significantly lower than for CT for several reasons. MRI systems are much more expensive, the imaging procedures are much longer than CT, and hand injections are practical for many MR procedures because timing is not as critical.

The Stellant CT injector was MEDRAD's first formal ethnographic effort. Table AA shows a partial list of multiple feature improvements based on and **understanding of customer need**. One of the improvements was a new, patented front load syringe which was even easier to install than the EnVision's bayonet mount. Another improvement was the option to have a second syringe for a saline flush. This was included because during the ethnography, a few users were seen to be reducing contrast cost by putting 100ml of contrast and then 50ml of saline into the single injector syringe rather than using 150ml of contrast. It was thought that the dual syringe might appeal to only 5% of the purchasers because the injector head was more expensive as were the two syringes used per patient (as compared to a single syringe per patient).

When the Stellant debuted in 2003, after initially brisk sales, there had to be a slowdown in sales because MEDRAD could not keep with the demand for syringes. Contrary to expectations, most sites were purchasing the dual injectors. This happened because between Stellant's concept definition and the product launch, additional improvements had been made to CT

Table AA: Ethnography Prompted Innovations Designed into Stellant

Saline Flush	Auto Docking
"Prime tube"	Profile Review
Pressure Monitor	Remote "check for air"
Remote "Arming"	"Swab able" Valve Transfer Set
Bottle Holder	Multiple disposable kits
Robust System Configuration	Color Touch Screen
Integral Auto load	Four different models, one with dual syringed
Orientation Independent Syringe	

scanners, specifically faster rotation times and wide beam CT. These additional improvements enabled CT angiography (CTA), which is the imaging of the coronary arteries via the IV injection of X-ray contrast rather than the more invasive angiography. To accomplish this, the IV contrast injection must be followed by a saline flush. Thus every new wide beam CT needed a new dual syringe injector, and once a dual injector was sold, two syringes and saline flush were usually used for all the imaging procedures, effectively doubling the syringe use. This is a second instance of the DC-3 effect in which MEDRAD's innovation of a dual syringe injector coincided with the imagers improvements to enable CTA.

MEDRAD continued using ethnography to understand customer/user need as they designed and launched the MEDRAD Avanta® Fluid Management Injection System for cardiovascular procedures in 2005 and the Intego™, the first automated FDG delivery system for use in PET imaging in the U.S in 2008. And, the efforts are continuing.

In addition to the innovation progression described above, MEDRAD went to great lengths to build and maintain an excellent company culture. MEDRAD made use of Design Thinking and the Balanced Scorecard before they had been formally named as such.

DISCUSSION

From the beginning, MEDRAD was going after blue oceans, or at least "blue puddles" or lakes (Blue Ocean Strategy had also not yet been developed formally). Angiography started as a small opportunity, but Drs. Wholey and Heilman believed that it would grow. MEDRAD found a key way to improve it, by adding flow control, were awarded a patent and developed the product. MEDRAD grew with the imaging modality. The implantable defibrillator was a very large, difficult opportunity. This was more an effort in mountain climbing than in blue ocean finding. Everyone could see the tremendous market need. It's just that the climb to success was so very daunting that no one else was trying. When you reflect back on the decisions of the pacemaker company to stop the project and of MEDRAD to pick it up, from their individual perspectives, both were right. It was a long time and a significant investment before the ICD would become practical and become a significant business compared to the existing pacemaker business. And as a small, private company dedicated to MEDical Research And Development, MEDRAD was doing what it was founded to do.

In the 1980s MEDRAD employed around 200 people. The key engineers had firsthand knowledge of the medical procedures in which the products were being used and connecting with the customers was relatively easy. MEDRAD worked with key customer sites to develop next generation CT and MR injectors as well as catheters, guidewires, and other potential or actual products. Design thinking just happened. No one knew it as anything different than good engineering practice at that time. It was how the company was started, working with doctors who needed better equipment - although we didn't use them as much at this stage of evolution.

As MEDRAD grew, the Stellant injector was the first product to use a formalized ethnography process. Ethnography gave insights leading to the creation of quite a few improvements to better satisfy explicit and implicit (unarticulated) unmet needs. But as described earlier, the Stellant was an "over the horizon home run", a beneficiary of the DC-3 effect because it was the first injector with dual syringes at the time when improvement in CT scanners made CTA possible. The dual syringe was included as a response to a customer need to save contrast, but it turned out to be an enabler to a whole new procedure, CTA, that made it a market winner.

The publication of *The Innovator's Dilemma* [4,5] and the concept of disruptive innovation to compete "under the radar screen" to disrupt successful companies using these principles led us to think about why MEDRAD had not been disrupted. If MEDRAD didn't understand its reasons for being successful, how could success be sustained? As you read this story, you'll realize that MEDRAD has grown by moving to "blue ocean" adjacencies or "competing with non-consumption" and then growing due to finding a few "over the horizon home runs".

While this narrative discusses the very successful moves that MEDRAD made, many others were only moderately successful. A number of them are listed in Table BB. In many ways, the process MEDRAD was going through was closer to spelunking than mountain climbing. Find a "tunnel" that looks promising, that has a visible "business excuse" to justify entering it, and then go down it. Sometimes the tunnel opens into a cavern of breathtaking size and beauty. Other times it is a modest success. The rest of the time it breaks even or is a loss.

We believe that this apparent randomness is the result of the "DC-3 effect" and the fact that one organization's innovation is happening in an ecosystem of innovations and changes by many. Peter Senge in *The Fifth Discipline* coined the term the "DC-3 effect"[3]. He uses the following example to explain the synergy that can happen in a system where the capabilities or

benefits of the whole can be greater than the sum of the parts:

> On a cold, clear morning in December 1903, at Kitty Hawk, North Carolina, the fragile aircraft of Wilbur and Orville Wright proved that powered flight was possible. Thus was the airplane invented; but it would take more than thirty years before commercial aviation could serve the general public.
>
> Engineers say that a new idea has been "invented" when it is proven to work in the laboratory. The idea becomes an "innovation" only when it can be commercialized and replicated reliably on a meaningful scale at practical costs. If the idea or invention is sufficiently important (and provides significant user value), such as the telephone, the digital computer, or commercial aircraft, it is called a "basic innovation, or platform," used to create a new industry or transform an existing industry. …
>
> In engineering, when an idea moves from an invention to an innovation accepted by the market, diverse "component technologies" come together. Emerging from isolation, developments in separate fields of research, these components gradually form an "ensemble of technologies that are critical to each other's success. Until this ensemble forms, the idea, though possible in the laboratory, does not achieve its potential in practice.
>
> The Wright Brothers proved that powered flight was possible, but the McDonnell Douglas DC-3, introduced in 1935, ushered in the era of commercial air travel. The DC-3 was the first plane that supported itself economically as well as aerodynamically. During those intervening thirty years (a typical period for incubating basic innovations in this field), myriad experiments with commercial flight had failed. … the early planes were not reliable or cost effective on an appropriate scale.
>
> The DC-3, for the first time, brought together five critical component technologies that formed a successful ensemble (in today's language they created a platform). They were: the variable-pitch propeller, retractable landing gear, a type of lightweight molded body construction called "monocoque", radial air-cooled engine, and wing flaps. To succeed, the DC-3 needed all five; four were not enough. One year earlier, the Boeing 247 was introduced with all of them except wing flaps. Lacking wing flaps, Boeing's engineers found that the plane was unstable on take-off and landing and had to downsize the engine.

After sharing the 5 critical component technologies part of this story for a decade to help people understand MEDRAD's success, a gentleman who heard the above narrative explained the economic side of the story. Tom Petzinger, the author of *Hard Landings* [6] explained that it was the fact that the DC-3 carried 7 rows of 3 people whereas the Boeing 247 had 7 rows of 2 people that made it a success, a commercial success that is. This choice to carry 21 people was made in close consultation with C. R. Smith, the CEO of American Airlines, and is an example of Design Thinking. Before the DC-3, carrying air mail, not passengers, is what had made the airlines economical in the much larger market of transporting people.

While discussing this new perspective with Robert Uber, a private pilot, he explained that all planes of that time could achieve the effect of flaps by lowering both of their ailerons at the same time. The difference was that when the DC-3 added the 50% more passenger capacity, Douglas did not increase the wing size proportionally. Thus they had to use flaps for take-off and landings and needed the larger engines to fly faster and create the extra lift when cruising. This had the added benefit of decreased flight time, further increasing both customer satisfaction and airplane economics.

Reading further on the Boeing 247 in Wikipedia, the 247 didn't need flaps, or to use the ailerons as flaps, because it could fly at the very low speed of 62mph and the engines were downsized at the insistence of United Airlines pilots who were not used to the power.

This expanded "DC-3 effect" illustrates many important thoughts that are necessary for understanding innovation. The first is how hard it is to get the real, complete picture of any situation, and the number of perspectives that are necessary to approximate that. The second is that innovation takes place as part of an innovation ecosystem. The third is that what appears to be randomness to one participant is actually a "dance of innovation" among all the participants in an ecosystem, with each providing key parts of breakthroughs that only can be recognized as such in hindsight. MEDRAD's innovation ecosystem consists of imager manufactures, contrast suppliers, doctors, imaging equipment operators, and healthcare payers. With the first CT injector, MEDRAD provided the tool that enabled the discovery of a new way to assess liver cancer. Similarly, if MEDRAD had not had a dual injector when CTA became possible, the procedure probably would have had limited use until someone

understood the need for saline flush and developed a dual injector to meet that need.

There are additional perspectives around MEDRAD's injector success, too. The head of marketing in the 1980's has commented that one of the things that increased injector sales was the reduction in the image reconstruction time. When the image could be produced within minutes of the scan, the doctors and technologists could see for themselves the benefits of injector use. Another perspective is that injector sales benefited from the CT scanner "slice wars", meaning the continual technical progress in scan speed and additionally the number of simultaneous slices that a CT scanner could do.

This recognition of a "dance of innovations" by different stakeholders and different companies in an innovation ecosystem is one thing that seems to be missing in the initial Clayton Christensen book, The *Innovator's Dilemma*[4]. The hard drives that Christensen initially studied do not have much utility by themselves. They were generally part of computer systems. The other members of that innovation ecosystem were companies who made computers, integrated circuits (ICs), displays, and software to name some. The hard- drive innovations that ultimately became disruptive innovations were those that combined with equally "disruptive" innovations in the other aspects of the ecosystem to move the whole industry from mainframe to mini to desktop to laptop computers and on to handhelds. The losing disk drive manufactures and their customers, the computer manufacturers, were disrupted together.

As Christensen has described, only IBM was able to successfully thrive in the mainframe, mini, desktop, and laptop computer markets[4]. They did that by starting fully separate divisions for each of these transitions. This separation was needed to allow for the very different business models, with different cost, product, and service structures, which enable success in the new business. This change in business model is what makes the transition so difficult within a single business. (Christensen's Innovators Dilemma led to the Innovators Solution thru a separate but related business unit with a different business model and approach to innovation)[5].

The DC-3 effect does for business what chaos theory does for physical systems. James Gleick published "Chaos: Making a New Science"[7] which became a best-seller and introduced the general principles of chaos theory as well as history to the general public. The DC-3 effect explains the apparent sudden emergence of a breakthrough innovation from a number of seeming small innovations. Chaos explains how small changes in initial conditions can create tremendous and apparently random changes in macroscopic system behavior.[7] There are chaotic systems that are perfectly deterministic mathematically, if we knew all the initial conditions with sufficient detail. But in the real world, this can never be known, ultimately because of the Heisenberg uncertainty principle that limits what can be known; the position and the velocity of an object cannot both be measured exactly, at the same time, even in theory[8]. The existence of an ecosystem of innovators creating innovations somewhat independently, unknown and unknowable to the others, may be the business equivalent of the Heisenberg Uncertainty Principle. Perhaps it could be termed the "Business Innovation Unknowability Principle". The interested reader is referred to a previous article in this volume authored by the Special Edition Editor and contributor. Boni discussed the inability to achieve algorithms to predict business outcomes, and instead the need to rely on patterns, screens or heuristics. He stated that, "the last stage (or predictability, which is) seldom achieved in business, is the desired end point, or the ability to predict the outcome precisely.

Clayton Christensen, the authors of this paper, and many others decry the apparent randomness to new product success. Given better theories and the execution of the right actions, we all want to believe that randomness can be reduced, if not eliminated. And it is a goal of this paper to help you reduce the downsides of relying on chance and increase your rate of success. But, there will always be a measure of indeterminism in new product success. This is due to the DC-3 effect amplifying the variability from the "Business Innovation Unknowability Principle".

One final note: MEDRAD's successful, enduring products are the injectors for angiography, CT, MR, and most recently nuclear medicine, all of which have a razor-razorblade business model. MEDRAD has stopped making several products that it created and/or brought to the market that did not involve a razor-razorblade business model. So while MEDRAD has successfully innovated products many times over the decades, they all have operated according to that same general business model.

CAVEATS AND POST SCRIPT

As with all case studies or exercises in looking back, there is a risk of hindsight bias.[9] Patterns can be seen that were not actually there or could not be known as time unfolded. Similarly, as is heard on many investment advertisements, past performance is no guarantee of future performance. What worked in the past will not necessarily work in the future. The innovator's dilemma

Table BB: History of MEDRAD Innovations

1964	Doc Heilman created the first angiographic injector in the kitchen of his home. In 1967, it would become the Heilman-Wholey Injection System.
1969	The Heilman-Wholey became MEDRAD's first commercial product.
1970	Mark™ II Injection System launched.
1972	Mark™ III Injection System launched.
1974	Mark™ IV Pedestal Injection System launched.
1976	Angiographic Guidewires introduced.
1978	Mark™ IV Rack Mount Injection System launched.
1980	MEDRAD® (Intec) brings to market the first commercial ICD
1985	Mark™ V Injection System launched.
1985	CT202 Injection System launched.
1986	Omniplane™ Film Changer launched.
1988	MEDRAD® enters MR market by designing an MR-compatible TMJ device
1988	Angiography presence expanded with introduction of the Omniplane Film Changer product.
1988	MCT™ Injection System launched.
1989	MRInnervu® endorectal coil introduced.
1991	Introduction of Mark V Plus™.
1991	MEDRAD revolutionizes vascular injection by introducing the first-ever Front Load Syringe (FLS), marketed as Qwik-Fit Syringe® Disposable.
1991	FluoroVision/Pathfinder products introduced.
1991	MCT Plus™ launched.
1995	Introduction of EnVision CT™ Injection System.
1996	Introduction of Spectris® MR Injection System.
2000	MEDRAD acquires MR monitoring products from MRE Corporation.
2001	MEDRAD Pulsar™ Ultrasound Injection System is introduced.
2002	MEDRAD introduces Continuum, the first MR-compatible infusion pump.
2003	Spectris Solaris® MR Injection System introduced.
2003	Stellant® CT Injection System introduced.
2005	MEDRAD Avanta® Fluid Management Injection System launched for cardiovascular procedures.
2005	Veris® MR Monitoring System launched in the U.S.
2006	Stellant DualFlow introduced.
2006	MEDRAD launches first prostate eCoil™ for 3.0T MR magnets.
2006	MEDRAD installs 5,000th Stellant® and 5,000th MEDRAD Vistron CT® Injection Systems.
2007	MEDRAD launches XDS® Extravasation Detector for Stellant.
2008	MEDRAD introduces its first application for P3T® (Personalized Patient Protocol) for Cardiac.
2008	MEDRAD® and Possis® Medical sign definitive merger agreement.
2008	MEDRAD launches and installs Intego™, the first automated FDG delivery system for use in PET imaging in the U.S.
2008	MEDRAD introduces Continuum Wireless MR Infusion System.
2009	MEDRAD launches the Certegra™ Informatics Platform.

is actually an example of that. The rules of "normal" project choice work most of the time, but "normal" investment prioritization fails when a business is faced with a disruptive innovation, although this happens very seldom and may only be visible in hindsight.

The principles of design thinking, customer/user centricity, a balanced scorecard, and the others discussed here are useful guides or models, but do not guarantee success.

If a blue ocean, *i.e.* an opportunity is easy to reach, it would quickly become red because others would be there, too – building a sustainable competitive advantage is necessary. Our view is that blue oceans come in two varieties. The first are those that you can reach by mountain climbing – moving

successively from Tier 1 to Tier 2, to Tier 3 markets with their attendant challenging product improvements demanded by downstream market segments (as described elsewhere by Boni in this monograph). The results of success are relatively knowable, but the path to success (the climb) is very difficult and has many unknowns to be resolved. Often times this is an iterative path guided by the convergence of customer/user input and observation, technology advancement, and product/market fit validation. This path was illustrated by MEDRAD's implantable defibrillator. Most biopharma/medtech development projects are "mountain climbing projects". The second variety are those that come through spelunking, exploring blue puddles and lakes to see if any of them have tunnels that lead to blue oceans, to mix the metaphors. In this latter case, the oceans are still blue because they were previously unknowable.

In closing, there are a number of lessons learned, and key takeaways that are worthy of inclusion in this paper focused on medtech innovation.

Patents are a key part of growth and success in any biopharma/medtech business. Aggressively filed and defended patents on innovations with broad claims are needed in this field. They provide one important form of competitive advantage. If you're going to be successful, plan on your patents being challenged by incumbents and prepare for legal remedies albeit expensive. Some sage once said that "patents are only as good as the money that you have to defend them".

Cook Medical: Bill Cook founded Cook Medical in 1963 https://www.cookmedical.com/about/history/). Cook Medical along with Medrad are good examples of long-term innovators. Cook Medical made guidewires and catheters while MEDRAD made the injectors and syringes. (parenthetically, Schering AG and others made the X-ray contrast, and Siemens, General Electric and others made the imaging equipment). Cook would build what a doctor sketched on a napkin, and then when it worked the way that he wanted, Cook would commercialize it with that doctor's name (brand) on the product. So, both are customer centric innovators.

MEDRAD has brought to market many new and innovative products over the decades. They have all been focused around medical imaging and image based therapies. Some have not been successful, such as an injector for ultrasound contrast. Looking with a DC-3 and innovation ecosystem lenses, one thing that is missing in ultrasound imaging is operator independent imaging. The author believes that this dependency on the skill of the operator is one of the limit's to ultrasound's success. A second innovation that ultrasound needs is standardization and improvement in the speed of the examination. Perhaps some of today's portable ultrasound imaging innovations will recognize this missing element.

The lessons of *Built to Last* were commonly known and applied by MEDRAD senior management, especially the "Genius of the AND". Jim Collins[10], the author of *Built To Last* and *Good To Great,* has a powerful tenet in his thinking. It's called "the genius of the 'and'". Collins states that the truly visionary companies of the 21st century are able to embrace both ends of a continuum: continuity *and* change, stability *and* revolution, predictability *and* chaos, heritage *and* renewal, etc. Pursue productivity and sustaining innovations along with disruptive innovations. MEDRAD pursued all of innovation frameworks described by Christensen, and as he predicted, very few of the innovations were truly disruptive innovations (most were sustaining). See Table BB for reference.

In 1990 MEDRAD started using Total Quality Management in the organization to help a now much larger organization maintain or refocus on our customers, process improvements, and an explicit balanced scorecard. Winning the Malcolm Baldridge National Quality Award[11] twice, and their continued growth demonstrates that this focus on customers, process and improvements was worthwhile. There is nothing wrong with growing at or just a little above the overall market rate when you have a significant market share and are helping the market grow faster than GDP or other, broader growth metrics.

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Article

Moleculera Labs Story: Lessons in a Capital Efficient Start-Up

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ABSTRACT

This case study focuses on Moleculera Labs, an emerging biotechnology R&D company developing clinical diagnostics and identifying novel biomarker targets for neuropsychiatric disorders. This article covers commercialization and innovation strategy applicable to an emerging biotech company that has utilized patient-centric, capital efficient, and lean principles for development, validation, and go-to-market execution. This case study includes key factors that are essential for successful biotechnology companies. These range from management of technology, market, and team/leadership risks to dealing with financing, regulatory, IP, and reimbursement issues.

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INTRODUCTION

It is not uncommon for scientists, physicians and engineers to have an "aha!" moment where they come across a discovery that leads to an inspirational idea for a product that could be a life-changing treatment, test or medical device. These are the inspiring moments that trigger the next thought "should I start my own biotech company?" For those who move forward with a resounding "yes" I would like to briefly share highlights in our story of the startup and development of Moleculera Labs, a clinical diagnostics company with an R&D focus on companion diagnostics and identification of new therapeutic targets. I'll intersperse this story with a bit of practical advice about our journey and how the concepts discussed in Section 1 are played out in real life for the biotech entrepreneur.

All successful biotechnology companies start with an innovative technological discovery that is directed toward a chosen market application with a critical unmet medical need. The larger and more acute the unmet medical need, the more meaningful the solution. It is essential for current and future entrepreneurs to realize the numerous business components that successful biotechnology companies must simultaneously manage. There are eight factors I want to share with entrepreneurs who are interested in starting their own company.

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Eight Business Components Essential to Building a Successful Biotechnology Company

- **Carefully Manage *Timelines*:** Product development encompasses lengthy timeframes that may span decades of work. Timelines need to be carefully managed, and milestones must be reached in a timely manner in order to sustain momentum.
- **Continuously *Raise Capital*, and at the right time:** Massive amounts of capital are required at each development stage. Having continuity of investment capital is a critical requirement in order to have unimpeded development progress.
- **Identify and hire a *diverse Team of Talented Individuals*:** Successful companies demonstrate the ability to recruit and retain a specialized team of individuals with diverse expertise and backgrounds, and motivate them to work collectively as an integrated team.
- **Understand and manage the *Regulatory* risks:** Biotech companies operate in an industry with one of the highest and most stringent regulatory hurdles. These barriers can become roadblocks or they can be stepping stones to success. Having in-depth knowledge of evolving regulatory issues is critical for success.

- **Strategically build an *Intellectual Property (IP)* portfolio:** Successful companies map out an IP estate that provides them with protection in an chosen area they will be commercializing. IP comprises the rights to the underlying assets that the company will sell or license at an exit.
- **Develop a clear *Insurance Reimbursement strategy*:** Medical and biotechnology products are typically reimbursed by third party or government agencies. Charting a clearly defined and realistic reimbursement pathway is essential.
- **Understand, define and target the needs of the *right Market Segment*:** Although the technology may be stellar, the choice of the first application is critical and can make a difference in the success or failure of the business. Understanding the needs of the target market segment is key to adoption and investor interest.
- ***Persevere in Leadership* throughout the journey:** Investors back seasoned entrepreneurial teams as much as they bet on the product and market. The leader must exhibit passion for their work and be able to communicate a vision that others will follow, even when circumstances look grim.

When entrepreneurs understand these eight critical business factors necessary for building a successful biotechnology company, they have taken the first step toward managing each of these risks. Also, they will encounter fewer surprises arising from "unexpected" problems, or circumstances that were not considered along the way. Most biotech companies do not have the luxury of starting out with a complete and seasoned management team. Nevertheless, it is important that the entire team, however large or small, understand business risks and manage them appropriately, because any one of these issues can be the downfall of an emerging enterprise.

PUSHING THE BOUNDARIES OF MEDICINE

Biotechnology companies are typically considered "first-movers" because they are pioneering development in segments of medicine and biology previously unexplored. With the exception of the emerging sector of biosimilars, the biotechnology industry is predominately a first-mover industry. Biotechnology is also a transformative industry. The scientists, physicians and engineers discover new paradigms that profoundly impact the practice of medicine. Examples of transformation include the paradigm changing premise that Helicobacter Pylori was the underlying cause of peptic ulcers when conventional wisdom said that stress and gastric acid production was the cause. We see transformative discoveries resulting in medical device products such as drug-eluting stents to prevent vascular occlusion. There are now targeted therapeutics in immune-oncology that direct therapy to specific cancer cells and there is the future opportunity for genetic editing and expansive applications of CRISPR Cas-9. This is what makes the biotechnology industry exciting because it produces break-through treatments, diagnostic tests, medical devices, and agricultural products that diagnose, treat or improve the lives of millions of people.

However, what this also means is that the science and biology of a condition or disease may not always be fully understood at the time a particular company is formed. For instance, when HIV infections were reported in increasing frequencies in 1983, the goal of some biotechs was to simply develop a vaccine to stop the spread of this viral disease. However, during the early 1980's very little was understood about how HIV evaded the immune system. Even more critical, the field of immunology was still in the "dark ages," compared to what we know today. Many of the strategies that were used to develop HIV vaccines proved ineffective because at the time it was not fully understood how the immune system operated, consequently, each of these early vaccine strategies failed. We see the same principle occurring in the Alzheimer's field where the biology of how this disorder progresses is not fully understood, neither is it fully understood that causes this disorder. When new discoveries are able to explain the biology, and the mechanism of a particular disease is better understood, effective diagnostics and therapeutics can be developed to identify and treat the underlying root cause.

This brings us to the principle that when starting a biotechnology company there are inherent unknowns about the biology and science of how the human body interacts and progresses to a disease state. Because of this lack of understanding and the unpredictability of the science, the technology risk is high in these circumstances, which adds to the market risk and management risk of virtually all new biotechnology ventures.

A COMMON THREAD LEADS TO COLLABORATION AND TO A COMPANY

The genesis Moleculera Labs is similar in that we were operating in a segment of biology having more unknowns and fewer scientific principles of how infections, the human immune system, and brain interact to produce disease. The science that underlies our company began with an opportunity that arose out of research in seemingly unrelated fields of neuropsychiatry and infectious disease. Dr. Madeleine Cunningham, a tenured and endowed professor of microbiology and immunology at the University of Oklahoma Health Sciences Center had been studying streptococcus and rheumatic fever for over 30 years. Her research led to the identification of a common epitope, or protein antigenic site in strep, that mimicked portions of certain proteins in the brain, particularly lysoganglioside GM1 and certain dopamine receptors. This was discovered by studying the serum of patients with a condition known as Sydenham's Chorea, which is the neurologic manifestation of Rheumatic Fever and triggered by a streptococcal infection. "Molecular mimicry" was a recognized principle that had been described as a possible mechanism in other disorders, but the actual mechanism was not clear how an individual could be infected with strep, contract Rheumatic Fever and then manifest neurologic symptoms of obsessive compulsive disorders (OCD) and involuntary motor movements. However, in medical literature there was a clear and direct clinical connection to neurologic manifestations and streptococcal infection, as the primary treatment for Rheumatic Fever was antibiotics, which also resolved the OCD and motor tics.

Many discoveries arise out of close collaborations with researchers in distinctly different disciplines. Such was the case when Dr. Cunningham was contacted in the 1990's by Dr. Susan Swedo, a pediatrician and Branch Chief of the Pediatrics and Developmental Neuroscience Branch at the National Institutes of Mental Health (NIMH). Swedo made the clinical observation that a population of children presented to her with sudden-onset of OCD and motor tics, were curiously preceded by a recent strep infection. This led to her contacting Dr. Cunningham who was a well-published researcher in the study of Streptococcal infections. Based upon their collaborative work they came up with a clinical model of an infection-triggered autoimmune disorder resulting in neuropsychiatric symptoms that Swedo had previously termed PANDAS "Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection."

Cunningham continued her research with a clinical study at the University of Oklahoma, enrolling over 900 children with sudden onset of neuropsychiatric symptoms that were preceded by a strep infection. In this study, the children testing positive in a research panel for autoimmune antibodies against particular neurological targets, were treated for their infection and immune dysfunction, and remarkably improved. This study supported the scientific premise that in some patients who are exposed to strep and other infections may generate autoimmune antibodies that can interfere with, or interrupt normal functions of brain. As the research study concluded, Cunningham and her laboratory began receiving frequent telephone calls from other parents wanting to have their children enrolled in the concluded study, but there was no avenue to help them. As time passed and the frequency and urgency of the parent calls continued, it was clear that this was an unmet medical need. The question to be answered was, how big and how viable was the unmet need, and whether or not it was sufficient enough to sustain a business, as opposed to becoming an interesting research project. Furthermore, it was unclear whether this patient response was a pent-up demand that would dissipate once the backlog was addressed, or whether the solution developed could become a sustainable business. This acute need was the motivation that led to our founding. Our focus was to become a neurobiology company, developing diagnostics that could uncover how infections trigger the immune system to stimulate neuropsychiatric disorders through "molecular mimicry," hence the name "Moleculera Labs."

On the business side, there was a vast gap between identifying an unmet medical need and being able to raise enough capital to build a successful biotechnology company. As referred to above in the eight factors essential for successful companies, there were financing challenges since we were located in the middle of the country and we were not in a biotechnology hub. Although Oklahoma produces great research and development and a number of successful biotechnology company exits, compared to the Boston and San Francisco ecosystems, there was only a fraction of venture-type capital available in the region. However, one advantage we did have was a pervasive entrepreneurial spirit and a willingness of individuals and organizations to help each other for the greater good of others. Understanding this challenge, I spent a large portion of time creating a business plan with a vision and execution strategy for an organization that could change how medicine would be practiced for neuropsychiatric disorders. Business plans of 25-30 pages in length may not be the first document that any potential investor wants to see or read, but this exercise is essential for the entrepreneur and start-up team in order to map out the plan and strategy for moving forward.

START-UP CHALLENGES- IDENTIFY THE BEST MARKET APPLICATION OF YOUR TECHNOLOGY

Just as in the case of Moleculera Labs, most all biotech companies start with a newly discovered or novel technology that is tied to a specific application that has been directed to a presumed market need. I say "presumed" because without historical evidence of market adoption it is usually an assumption. As a result, all entrepreneurs contemplating starting a biotech company should engage in as much market research as possible prior to selecting an application for their technology. This is because the sustainability and future value of the organization is dependent on a continuous and growing demand for their product or service. In addition, the selection of the optimal disease or market application, and then carefully defining the target market segment of customers, is critical to raising investor interest and finding capital for the company. Getting the application right in the beginning is key, because once the market application is selected, all the company efforts move in that direction, and it requires a large amount of retooling effort to alter that direction. Adding to that complexity, if you have already secured investor capital under a proposed market application, if you change, those investors must accept that your original target market application was a mistake.

A point to remember is that a technology is not beholden to any one specific market application. For example, in the biotechnology industry, a scientific discovery that interrupts cell cycle control could be directed toward the development of a therapeutic for breast cancer, prostate cancer, or brain cancer. Often the choice of application is a result of the entrepreneur's familiarity with a market problem, or more often—convenience. For instance, if down the hall from the entrepreneur is a surgeon or researcher who has breast or prostate tumor tissue available from dozens of cancer patients, the research and presumed market application can easily be directed toward breast or prostate cancer therapy. However, glioblastoma, a type of brain cancer having a more acute market need, has a lower hurdle for effectiveness than a new breast cancer therapeutic. The National Cancer Institute's website lists over 55 drugs used to treat breast cancer. Whereas currently, the FDA has approved only 5 drugs for glioblastoma—none are curative. A technology applied to breast cancer or prostate cancer therapeutic would have higher hurdles of efficacy than for glioblastoma due to the greater number of effective alternatives. Too often market applications for a technology may have been selected because of convenience when that application may not have been the best for business success. There are technical, biological and regulatory issues that also must be factored into the selection of a market application, but at the outset, entrepreneurs must first seek to align their technology with an acute market need in order to be successful.

For Moleculera Labs we determined that the underlying technology and mechanism of molecular mimicry may account for a broader range of chronic and debilitating conditions. Therefore, our focus in the beginning would be PANDAS, then branching to other neuropsychiatric disorders, such ADD/ADHD, Chronic Depressive Disorder, autoimmune epilepsy and others, as long as there was an underlying etiology of autoimmunity triggered by an infection. As we searched the literature there were archives of publications identifying inflammation (a function of the immune system) and immune involvement with neuropsychiatric disorders, as well as many other chronic and debilitating disorders. Research from Cunningham's laboratory identified many specific brain targets of autoimmune antibodies and that these antibodies indeed crossed the blood-brain-barrier and were found to be present in the cerebrospinal fluid of afflicted patients. We realized that this area of immuno-neurology was relatively uncharted territory, yet we found research and literature support for this principle and hypothesis, as well as clinical evidence that supported this as a pathogenesis for a segment of patients with neuropsychiatric disorders. The missing element was laboratory evidence from blood tests to identify the segment of patients who would respond to anti-infective and immune modulation therapy.

RAISING CAPITAL FOR THE START-UP

From past experience I knew that the average start-up diagnostic company consumed between $25MM to $75MM in capital in order to begin generating a significant amount of revenue. I realized that by not being located in one of the large biotech clusters, raising that amount of capital would be challenging and require an inordinate amount of time to complete. In a previous diagnostic company, we did raise over $20MM in equity capital, and in another company that we took public, significantly more was raised. However, the financial markets were not the same as many years prior when this occurred. In order to have the best opportunity to build the market for a diagnostic that would change how neuropsychiatric disorders were treated, we needed to have enough time to grow the market and yet ensure financial sustainability. The conclusion was to start as a very lean organization and enlist the human resources and capital of those who had a vested interest in our mission. The

second objective was to reach break-even as quickly as possible so as to sustain the organization and allow more time for research to be conducted while growing the organization to be positioned for future rounds of institutional or venture capital. Because of the acute medical need and condition that these patients and family members were experiencing, we were backed by strong patient involvement and patient advocacy. I knew that the company would need to operate as virtual as possible until there was enough capital and momentum, and this would greatly reduce the risk of running out of capital before this vision was realized.

A virtual company is simply a company that may not have much brick and mortar and few, if any, full-time employees. However, a virtual company will still function just the same as any other company but it will carry out its business through the outsourcing of non-core activities while retaining the core capabilities in-house. As the organization grows, certain functions are strategically brought back in-house or assigned to someone internal who manages portions of each outsourced activity. Companies will grow in their various business functions but should continue to operate as virtual as possible, with the recognition that core functions are not outsourced. In the beginning it was just myself in a one-room office in the Research Park, followed by the addition of a couple part-time consultants who worked on different functions of the business activities.

Sometimes a technology discovery or medical condition will require speed in development in order to be competitive, such as with CRISPR Cas-9, or the emergence of Ebola and Zika viruses to name a few. In these cases, it is opportune to raise large amounts of capital and apply sufficient resources to address or solve the urgent need or opportunity. Regardless, entrepreneurs should utilize a capital efficient model to ensure sustainability and to buy time such that incremental development progress will aid in raising more capital at increased valuations. I often liken the building of a biotechnology company to the assembly of an airplane while it is taxiing down the runway, in that you are feverishly working to complete a structure before you exhaust your runway room. The key reason for operating as a virtual company is sustainability. Too many biotech companies fail, not because of inferior technology or poor target applications, but because the overhead was unsustainable and they ran out of capital before reaching a critical milestone that attracted subsequent investor groups.

One may erroneously believe that "capital-efficiency" means lower quality and less proficient in operations and output, but nothing could be further from the truth. A well run-and well-operated virtual company may often be more efficient and more effective than a vertically-integrated organization that performs all the functions required for every facet of business. Virtual companies should accomplish the same set of functions as a larger organization; however, many of the non-core activities are outsourced and you or your team will oversee multiple facets of your business. Having a good working relationship with the licensing university is essential. I was fortunate to be able negotiate a lease on a portion of Cunningham's research laboratory and also lease part-time individuals who were already employees of the university until we could support our own full-time employees. Although the speed of development and commercialization activity is slower than if there were extensive amounts of capital for a fully-staffed team, the science and medical understanding of the autoimmune neuropsychiatric field was not mainstream at the time. Therefore, from a competitive standpoint we could also afford the time to build the company in this capital efficient manner.

After outlining the vision and putting together the plan, the next step was to set up the corporate entity in order to license the technology from the university and also to raise capital. An Oklahoma LLC was established using MyNewCompany's turnkey incorporation tools, and I held our first official company meeting, electing Cunningham and myself directors. Working from a one-room office in the Presbyterian Health Foundation Research Park I set up our "corporate headquarters." The next step was to work with the Technology Transfer Office at the University of Oklahoma on the license. We negotiated an Exclusive Option Agreement that would allow me to raise enough seed capital, and once $100,000 was secured we could negotiate an Exclusive License agreement for the proprietary know-how to the technology. An "Option" agreement is a mechanism that allows the university to delay full-commitment of a license to a licensee until certain milestones are met. I recognized that it was simply an assurance for the University that the company would have finances to develop the technology prior to fully negotiating an Exclusive License Agreement. Although I wanted an Exclusive License Agreement rather than an Exclusive Option Agreement, this still gave me the right to seek investors with the assurance that once seed funds were raised it would trigger the right to secure the Exclusive License for the technology and know-how. I then opened a corporate bank account with some contributed personal finances and not too long afterwards, a parent of a child who was diagnosed during our clinical study, tested, treated, and recovered, agreed to invest the first $100,000 in our company. We structured this seed investment into a Convertible Note that would convert into the Series A Preferred shares during the next financing round. With this investment, I negotiated the Exclusive License, initiated a provisional patent application through

the assistance of a patent attorney whom I previously worked with on another patent matter. Next, I sought the help of technical persons, and who better to help than the individuals who assisted in the development and performing of these specialized tests at the university. I was able to negotiate with the university a lease of key personnel on a part-time basis, in addition to leasing portions of the research laboratory and an allocation of time on some key equipment.

It is critically important for young companies that license university technology, to establish and maintain a close working relationship with the various groups at the university, and especially the Technology Transfer Office. You will need them and their resources to help you as you grow, but they have mandates and responsibilities that don't often include nurturing start-up companies. There are significant advantages to having the university as a partner, which include the ability to modify or renegotiate some of the license terms if there are delays in funding, or if certain milestones are not met in the exact timeframe anticipated. It is also important to realize that a university has legitimate concerns of potential conflicts of interest for their professors and employees, and these must be carefully managed. To help mitigate this concern, you should identify the relevant departments within the university to work with as they typically have procedures and boiler-plate agreements to ensure that a founding professor does not unknowingly create unmanageable conflicts-of-interest with a company. Some assurances include checks and balances on the mechanisms of who makes decisions on agreements when it involves use of a professor's time, resources, their laboratory and students, and assurances that the university will be properly compensated when these agreements are made. These are the steps that allowed us to begin and operate as a virtual company, yet have the resources and knowledge base that was needed to develop and build a commercial entity. Equally important were the large group of parents of patients who had been tested during the research studies, and became our supporters with resources and financial backing. During the clinical study many of these patients received a clarifying diagnosis of an infection-triggered autoimmune neuropsychiatric condition and received proper treatment such that their condition resolved or significantly improved. As I reached out many of them to share our mission for the company, those with the financial ability comprised a good portion of the early stage capital we raised under a convertible note, and some others joined during our Series A Preferred Financing. Not only did these parents support us through their financial investment, but many of the parent advocacy groups learned of our work and began sharing with others on social media about our company and mission.

Fortunately for us, in Oklahoma we have two state-funded agencies created for the purpose of economic development and matching funding for scientific and high-growth endeavors. The Oklahoma Center for the Advancement of Science and Technology (OCAST) is an organization that reviews and awards competitive grants to Oklahoma researchers similar to the federal SBIR program, but competition is limited to researchers and companies within the state. A subsidiary organization managed by Innovation-to-Enterprise (i2E) assists with commercialization efforts and equity funding for high growth technology organizations. We were successful in receiving grant funding from OCAST to help advance the research, as well as negotiating for Series A Funding from i2E. This support allowed us to attract other angel investors to our early stage endeavor, and in total provided enough funding such that we raised $5MM in a few tranches over the course of several years. This continuous source of capital helped to equip the laboratory, hire critical staff and obtain federal and national certifications and accreditations in order to open and operate our clinical laboratory.

UNDERSTANDING THE PLIGHT OF THESE PATIENTS

Often there is a segment of patients that succumb to a complex medical condition that may not have straightforward answers, and a condition that cannot be understood in a typical physician office visit that may only last 15-20 minutes. Such is the case of patients with PANDAS and PANS. In 2013 the New England PANS PANDAS Association conducted a parent survey of about 200 families shortly after their organization was founded and uncovered some distressing statistics common to the families with children afflicted with PANDAS and PANS. The findings revealed that the majority of these families had taken their children to between 5, and as many as 15, doctors before they were able to receive a diagnosis that gave them the right treatment toward recovery. Most of these parents spent an inordinate amount of money on testing, treatments, therapies and medical care that was outside of their medical insurance coverage, or greatly exceeded their savings and financial resources. With this understanding, it was clear that the path to increasing utilization of our test panel would be medical education, research publications and increased awareness.

SELECTING THE RIGHT BUSINESS MODEL

For some products, the appropriate choice of business model is straightforward as in the categories of biologics and small molecule therapeutics. Whereas in the diagnostic and medical device segments there can be some discretion and a couple business model options to consider. For instance, in diagnostics one can choose a business model for developing and manufacturing a diagnostic or in-vitro-diagnostic kit that is approved by the FDA under a 510(k) or Premarket Approval application (PMA). Under this model a company may develop novel biomarkers for disease or a test that directs treatment, and these are translated into kits that are manufactured and sold to clinical laboratories and doctor's offices that operate them on some platform instrument. Alternatively, another business model for diagnostics is known as a Laboratory Developed Test (LDT) which is developed, clinically tested and validated in one single laboratory that is accredited, regulated and inspected under the Clinical Laboratory Improvement Amendment (CLIA) along with other accreditation bodies such as COLA and CAP. Under this model, there is only one laboratory permitted to legally perform the service. The one laboratory is the organization that researches, develops, clinically tests, validates and seeks accreditation for the clinical laboratory service. This organization then performs services, markets, and contracts with insurance in order to grow their testing market. We chose the latter LDT, CLIA Laboratory model for reasons that were strategic to the company and fit with the best way to utilize this high-complexity technology. There are strengths and limitations of this model. The strengths include a shorter to market commercialization strategy, but it only allows one laboratory to perform this as a service. This model also necessitates that in order to be competitive and gain traction the company must have identified Current Procedural Technology (CPT) codes which are reimbursement codes that are accepted by federal and insurance agencies. We hired professionals to assist in the identification of the proper CPT codes and gained confirmation through a reimbursement professional and reimbursement attorney. This allowed us to provide the assistance of billing a patient's insurance carrier on their behalf to help they obtain reimbursement for our test panel. As a virtual company this function was initially outsourced but as we grew it was later brought in-house to improve our time to payment.

PROTECTING THE ASSETS

As with any biotechnology product, be it a therapeutic, diagnostic or medical device, there is a need to protect the intellectual property (IP) and develop a strategy that would allow the company to raise money to continue product development and ensure that all this work is not in vain. There are several ways to protect intellectual property and the most common is securing patents on the product itself and methods for use of the product. Not only are patents one important way of protecting IP, but additional mechanisms include the use of Trade Secrets and Trademarks. Our desire was to utilize all three methods. We leveraged the use of trade secrets because the testing methods were highly complex and involved the use of radioisotopes, and required specialized reagents and specialized technical skills. We also had an inventor, Dr. Cunningham, who had a very good reputation in this field and was well-published, such that we named and trademarked the panel of tests "The Cunningham Panel." The trademark initially helped with recognition, branding, and allowed us to differentiate our product from potential future competitors. While we maintained some trade secrets about how the test was run and certain requirements to achieve the results, it was also important that we were successful in obtaining an issued patent on the test panel. We are actively filing additional patents on various iterations and novel applications of this technology for other indications, and this should be an ongoing and evolving strategy for all entrepreneurs.

WHY DO WE DO THIS?

There are considerably easier things in life that one can choose to make a living, other than starting a biotechnology company. However, the reason we do this is because it is a mission and opportunity to impact and improve the lives of potentially millions of individuals in the future. Often individuals who start and lead biotechnology companies have a bit of an "altruistic" streak, in that they want to make an impact in the field of medicine, biology, science or agriculture and to leave a legacy for others to follow. Such is the case for us at Moleculera Labs. We do this because we want to give hope to those suffering from debilitating neuropsychiatric disorders and to provide them with answers that can change their future. Our desire and vision is to utilize our scientific discoveries and testing services such that individuals suffering from chronic neuropsychiatric disorders will be transformed and live restored lives.

SUMMARY

By working in a capital efficient manner and outsourcing selected functions of the business while maintaining core capabilities, Moleculera Labs achieved break-even status by the end of 2017. Within a few short years, our growth has accelerated and during that time we tested over 6,000 patients in the U.S. and other countries. Our prescribing physician base has grown from 20 prescribers to over 1,000 clinicians with 20-30 more each month placing orders for testing. There are significant growth opportunities for our business in other chronic medical conditions, but the common purpose of our testing is to uncover neurological and psychiatric disorders that are stimulated by an infection that triggers an underlying immune system attack on organs in the body. We are researching immune system involvement in patients with ADD/ADHD, Chronic Fatigue Syndrome (Myalgic Encephalomyelitis), Chronic Depressive Disorder, segments of Autism Spectrum Disorder (ASD), seizures with normal EEGs and several other complex neurologic and neuropsychiatric conditions. The recoveries and significant improvements in the health and well-being of these individuals who were properly diagnosed and treated for the underlying etiology has been nothing short of remarkable.

Had we embarked on first raising large amounts of capital typical of the needs of a diagnostic company prior to growing our company, we may not have been successful and may have missed an opportunity. By utilizing a capital-efficient approach, coupled with a strategy of outsourcing non-core functions, and leveraging outside human resources, we were able to build a business that is making an impact on how medicine is practiced for patients with chronic and complex neuropsychiatric disorders. By supporting the science through clinical testing and unraveling the mechanism of these chronic disorders, we are experiencing a significant increase in the utilization of our testing service with expanded utilization in other disorders. For those contemplating starting a biotechnology company, or those in a development-stage company, making use of capital efficiency and lean startup, open-innovation frameworks can leverage the capital raised, and greatly improve your likelihood of success.

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