From the Board Room

Emerging Business Models and Strategies to Accelerate Innovation in the Biopharmaceutical Industry

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ABSTRACT

We focus on assessing and addressing the current challenges faced by the companies that comprise the biopharmaceutical industry. These include: improving productivity in the drug development process while managing many issues arising from partnering across the value chain more effectively; pricing of its products in the face of long, risky, and expensive development cycles; and, regaining the public trust as an industry that reliably and repeatedly delivers value to its constituencies at an affordable cost. The motivation for this paper is derived from a panel organized for BIO 2016 in San Francisco, organized by the author and the leadership team of the 12th annual entrepreneurship Boot camp held there. The panel discussed "Emerging Issues and Trends in the Business of Biotechnology Entrepreneurship". Discussion was held around three topics that are pertinent to accelerating innovation in the industry: emerging business models; applicability of the lean startup model to biopharma; and pricing. The panel was led and moderated by the author, with participation of Steven Sammut, James Jordan, and Dennis Gross. Their specific contributions are noted in the text, and their overall contributions to the panel and to this article are gratefully acknowledged.

Journal of Commercial Biotechnology (2016) 22(3), 53–59. doi: 10.5912/jcb753

INTRODUCTION

Innovation and change in the biopharmaceutical industry has never been more needed as the industry is faced with numerous challenges including: R&D productivity; patent cliffs; changing patient demographics; healthcare reform; and, pricing/reimbursement. Additionally, patients are faced with an increased burden to afford the cost of the innovative drugs that the biopharma companies (pharmaceutical and biotechnology) strive to develop at increasingly high costs and lengthy, regulatory-burdened clinical trials. The industry argues that the high drug costs are required to provide sufficient return on investment for the high capital cost/long life cycle of drug development with a success rate of less than 1% from lab to market. While sustaining innovation at the company level is certainly a challenge, the negative public perception of the industry severely constrains the companies individually and the industry collectively. For example, we cite Jennifer Miller who in a recent paper claims that the trust in the pharmaceutical industry has ebbed significantly; Miller (2015). (Ref. http://www.brinknews.com/lost-in-translation-restoring-trust-mission-and-ethics-in-the-pharma-industry/). From studies conducted at the Langone Medical Center at NYU, and Bioethics International, Miller states that only 12% of Americans trust pharmaceutical companies as being honest and ethical; and, 70% think that companies put profits before people. Further, it is noteworthy that as she points out, until about 17 years ago pharmaceutical companies still ranked among the top ten most admired companies! The urgency to change could not be higher for the industry and for the companies that comprise the industry! An effective solution certainly requires better "messaging" to the public and government, but change is also needed by the industry to support that message.

We recognize the continuing evolution of the biopharma business models using the terminology from Ernst & Young's annual state of the industry report, Beyond Borders (available from their website, www.ey.com). The industry has evolved thru at least three

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generations: Pharma 1.0 (blockbuster drugs); to Pharma 2.0 (balanced portfolio development); to Pharma 3.0 (healthy outcomes and patient centricity) which is the current model. While Pharma 3.0 is still underway, we suggest that it is time to start framing Pharma 4.0, which we suggest should not only deal with healthy outcomes and patient centricity, but also restoration of public trust, and providing solutions at an affordable cost and high value to the industry constituents and end users - the patients, payers, physician, and providers. Key here will be patient advocacy and balancing the interest of the constituents comprising the industry innovation ecosystem: the 4Ps (patients, payers, physicians, and providers), and the industry partners across the value chain (the 5th P). Of course we also need to incorporate the role of the government, e.g. funding early stage R&D, regulating the industry, and an essential component of the payment system. Framing the solution thru adoption of open innovation, and inclusion of all parties "at the table" at a much more rapid pace should be the highest priority for all parties concerned.

In this paper we advocate user-centricity with a focus on wellness and prevention, improved industry/company efficiency thru open innovation (collaborative partnering across the value chain), private/public partnerships, cross-disciplinary, collaborative teams working across the product life cycle with organizational structures to "translate research and technology from laboratory to market" more efficiently.

In the latter regard, there are certain principles borrowed from the lean startup approach taken from the tech industry that could be and should be applied selectively to the pursuit of innovation in the life sciences. We would advocate cross industry benchmarking to observe how best practices might be applied to accelerate innovation in life sciences, e.g. open innovation and lean methodologies. Similarly, we also advocate creation of public-private coalitions to lead the change process required to reestablish the credibility and public reputation of the biopharma industry.

INDUSTRY AND COMPANY PERSPECTIVE ON PRICING

This "From the Boardroom" article is intended to provide some key highlights relevant to the need for incorporation of pricing into the business model and to guide companies as they rationalize their pricing consistent with the value created by the products and to reward risk taking with appropriate financial return. Given the current importance of this topic, the author, along with Steve Sammut and Himanshu Singh is developing a subsequent paper on pricing of biopharma products that will provide a literature survey and more details on pricing models for branded pharmaceuticals, targeted therapeutics, and for orphan drugs. The author acknowledges the contributions of both Sammut and Singh to the abridged material that follows.

It goes without saying that the biopharmaceutical industry operates in a complex market with continuously shifting power balances. We could utilize the 5-force model developed and popularized by Michael Porter (1979) as a framework where the five industry forces include: (1) rivalry among existing competitors: (2) the threat of new entrants (from other pharmaceutical companies or from emerging and larger biotechnology firms; (3) the threat of substitute products (e. g. generics and biosimilars); (4) the bargaining power of suppliers; and, (5) the power of the buyers. In the biopharmaceutical industry we would expand "buyers" to include the more complex set of forces that act – patients, physicians, providers and payers: the 4Ps. We also note that the 5th P, partners, certainly must be included (especially in the open innovation paradigm where potential competitors could become suppliers and/or partners).

We note that in the Pharma 3.0 business model the power has shifted to payers, and patients while certainly the physicians (and more recently nurse practitioners) still retain the ultimate power to prescribe (albeit somewhat moderated due the ability of companies to advertise direct to consumers since the mid-1990's), and of course to the emergence of search engines as a source of intelligence.

There are three frameworks of pricing to consider:

- **Value-based pricing**; see Brennan and Wilson (2014), Caifee and DuPre (2006), Edelman, (2004), and, Gregorson, Sparrowhawk, Mauskopf, and Paul (2005).
  - Based on what the "market" is willing to pay for the value created by the product (with the value to be determined by the payers – patient and payer/insurer)
  - Note here the importance of creating and articulating a target product profile (TPP) to differentiate the product and identify its target market segment
  - Perhaps a subcategory here might be the recently emerging "pay for performance" model where the producer and the payer agree on performance criteria that specifically defines the value created and delivered to the end user, e.g. life extension, remission, cure, etc.,

or, to costs saved by the "system" in reducing it's overall cost of care.

- **Reference pricing**; see Lee, Fisher, Shrank, Polinski, and Choudhry (2012)
  - Most often used outside of the United States, this is a system in which similar bioactive ingredients and therapeutically interchangeable drugs are grouped into a reference drug group. One or more drugs are then chosen as the reference for that group. The cost for the reference drugs, or perhaps the lowest priced drug, is the amount that will be reimbursed by the health insurer.

- **Competitive pricing**
  - Most often used for generics, the price tends to fall with the increase in the number of other generic competitors, leveling off after several entrants have entered the market. Most likely a cost plus fixed fee methodology would be employed.

We argue that value-based pricing is appropriate for differentiated products such as targeted therapeutics, and branded, patented drugs including orphan products. This may eventually include biosimilars, now emerging as a separate category that may retain some aspects to the patented brand. See, Brennan and Wilson (2014), Caifee and DuPre (2006), and Edelman (2004). However, generics are more amenable to more traditional competitive or reference pricing.

Given the above discussion, the challenge for companies and for the industry at large can be simply stated. How do you establish "value" and articulate that value proposition for a life saving or life extending drug, while also articulating the level of a justifiable ROI needed to sustain the company and the industry in both public and private markets? Certainly there is a role here for patient advocacy, and also government involvement since at least in the US, the cost of healthcare is approaching 20% of GDP and costs must be contained (while improving quality and offering higher value).

Pricing drugs is currently one of the most controversial issues in the industry for two reasons

- Largely, but not exclusively as a result of a "few mavericks" that have recently introduced excessive price increases in drugs already on the market regardless of public sentiment "because they could due to scarcity of competitive products and severe need".
- Out of pocket expenses for drugs has continued to escalate at excessive rates – this affects individual users and payers adversely.

The industry would argue that the several billion dollar cost of development for a single drug, and the 13+ years to bring the product to market as a basis for the cost of drug thru development. Others outside of the industry may point to the inefficiencies (high failure rates) in the discovery and clinical phases, and the need for improvement. Or, is it a regulatory problem that adversely affects the low rate of drug approval by the FDA? Nevertheless the message to the public is that the industry expects the public and payers to pay for "our" inefficiencies.

Isn't this really a shareholder & company/industry issue? Perhaps the industry would be better served by communicating ongoing efforts to become more capital-efficient and productive, and that it's return on investment goals are reasonable for sustainability. Demonstrated value-based pricing and pay-for-performance for differentiated products/solution should be expected to emerge, c. f. Brennan and Wilson (2014), as should transparency to all parties, especially the public and government.

Cross Industry Benchmarking - Applicability of Lean Startup and Open Innovation Principles to Biopharma

The key elements of the lean startup model as described by Erik Reis (2011), and Steve Blank (2013) include the following essential components:

- **Mantra** is to apply a hypothesis driven approach to product development and to customer (market) development
- Use an **iterative**, hypothesis-driven approach to product development and to product fit into the target market fit until product-market fit is validated.
- **"Get out of the building"** – in this case the lab – to engage all constituencies in the product/market fit validation and in the business model validation (use the Osterwalder business model canvas to make and validate hypotheses for all 9 elements of the business model; offering/value proposition, target market, customer

relations, channel, revenue model of the customer facing side; and resources, processes, partners and costs on the company facing side); c. f. Osterwalder and Pigneur (2010)
- **Pivot** as market feedback is gathered and the viability of the entry market and product market fit is established

The scientific method is certainly known to all scientists, both physical and biological, and hypothesis-driven discovery is expected for technological and scientific advancement. The lean startup methodology effectively "borrows" this methodology, but applies it to both product development and to business model development, e.g. in the lab and in the market. We advocate that hypothesis - driven business model development should be an important part of the life science innovation playbook – bring in all of the 4Ps plus partners early and often thru iterative cycles identify the target (entry) market, and then to validate product/market fit. This should be the underpinning of bringing the lab and the market together for a more effective approach to translational medicine.

Open Innovation Principles to Improve Efficiency thru Partnering Across the Value Chain

Open innovation (OI) has been promoted and developed by Chesbrough (2003) starting with work at Harvard in the 1990's and then extending to his work at the University of California, Berkeley.

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, c. f. Chesbrough and Garman (2009) to provide an augmentation of the resources and processes (and culture) 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 (or renting) 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 the firm.

As discussed in more detail by Boni and Moehle (2014), the best cross - industry practices include the following:

1. Focus on creative value sharing across the value chain
2. Create stage-appropriate financing vehicles (to cross "valley, or valleys of death") – leverage private/public partnerships
3. Develop and grow "seasoned" management teams through collaborations, accelerators, and other such vehicles. Collaborative interdisciplinary teams evolve thru commercialization phase. But, some of the creative "DNA" embedded at the earliest stages must persist to sustain further innovations.
4. Incorporate Agile and Lean Development Teams where business and technology expertise work collaboratively to advance the science while adapting solutions to market and user expectations and norms (see more below).

Selected Discussion Points Provided from the Panel Discussion

In addition to the material discussed above, we highlight two additional pertinent factors that are noteworthy. James Jordan provided the following:

"The context of this entire discussion can be framed within national priorities as it relates to the continuous growth of gross domestic product. GDP is calculated by adding total consumption, investment, government spending, changes in inventories, and net exports. GDP is the only measure to compare worldwide economies and its analysis echoes national priorities, opportunities and constraints".

"Healthcare will consume up to 20% of the US economy in the coming decade. In terms of measuring the quality of the investment into healthcare, the United States spends materially more dollars than other economies, yet on many measures has equal to or worse outcomes. Other leading nations spend between 8% and 12% of their economies on healthcare".

"Although one can argue that there is national investment and return on the "product side" of healthcare, in general, health care is theoretically the nation's "consumption" to sustain the population's health - it is not perceived as an investment in future profit. In that spirit, the United States needs to dramatically improve their "percent of spend" on healthcare while simultaneously maintaining or improving the Quality of Care at an affordable price to all parties".

"In the context of this national priority, The Patient Protection and Affordable **Care** Act (PPACA), commonly called the Affordable **Care** Act (ACA) or, colloquially

"Obama Care" has set forth measures in both quality and cost to pursue this national goal. Given the complex nature of the US healthcare system, and its lack of closed - loop information systems, tactical behaviors to improve both quality and cost is more intuitively applied then mathematically conceived. Unfortunately, this frequently results in unintended consequences, and the biotechnology and pharmaceutical industries are receivers of unintended consequences as it relates to funding innovation".

One component of these consequences is the political one, drug pricing is perceived as high, and drug companies are perceived as garnering unfair profits. There are two sub-situations that the drug companies have not managed well. Drug pricing is high due to the nature of long clinical trials and material investment in assets. This is not witnessed by "the public" since they just look at the percent of net income to revenue when compared to other industries. Additionally, utilizing financial rationale to maximize firm profit by pricing overseas products to maximize volume, result in radically different pricing, contributing further to the perception of price gouging".

"The second contributing component is the time and nature of market forces. Let's take the category of aspirin which was developed in the 1890s for pain, acetaminophen followed aspirin around 1946, followed by ibuprofen in the 1960s. What are these market-moves? They are simply the natural progression of market categories developing and splitting. Market categories will always develop, markets will be grown, competitive entries segment the markets into smaller pie slices and, as with aspirin today, the original developer ends up with a relatively small portion of the market".

"The implication of the above is a perception of the drug industry being receivers of unfair profits. Nevertheless, industry investment in a new drug will be applied to smaller and smaller market segments. This is not a sustainable combination of events".

Dennis Gross then provided the following:

"As we have heard for the past years it is not enough to have a regulatory strategy, and an intellectual property strategy, but now a reimbursement strategy is critical to a drug's success in the marketplace. The problem, however is that the 'customers' are so different. In the US we always think of the physicians and now the nurse practitioners (since they can write Rx) as the customer, but it is also the HMO and PBMs in the US. Complicate that with the VA as a single drug formulary purchaser. Now go overseas and you have the foreign governments of each country as a purchasing agent and in China and Canada each province has its own formulary; this paradigm fragments the purchasing picture".

"The concern is how do you change the R&D model with those external pressures and constraints? Do you develop for fragmented regional markets? How do you manage the change that this will require? How do we educate our esteemed legislators who think part of the solution is to reduce patents for drugs to force them into being generic sooner, not realizing that the average patent life post-FDA approval is actually only 6.8 years? Do you plan the game that Merck and BMS are now doing with the PD-1 inhibitors in layering use patents for the boutique indications for cancer? One claim after another and see how the chips lay. Interestingly Optivo was not approved by National Institute for Health and Care Excellence (NICE) as a cancer monotherapy as being too expensive for the short life extension it provides, but it was recently recommended by NICE in combination therapy. How do you plan for that and how can that mix color your research approaches? It could be combinatorial explosion and really change the model of who become your partners even in research let alone development. It is really going to be hard to differentiate between the business of science and doing science in a business-like manner".

"Personally I think there are very few academic institutions agile enough to participate in the pivoting needed to address being a partner in future drug R&D needs and the changing marketplace. Those that can will be very successful partners with biopharma, and be those windows on new technology that biopharma needs as they increasingly move into new hot areas".

Conclusion – Establish a Sense of Urgency and Collaborative Solution to Mobilize and Renew Public Trust in the Industry

When addressing the need for change, we'd suggest reference to a classic and well-cited source, John Kotter, now retired Harvard Business School professor who has developed and validated an 8-step process for leading change; Kotter (1996). More recently Peter Boni has

developed a similar approach from his extensive experience in the private equity industry; Boni (2015). Both start with the same theme – establish a real, sense of urgency. Kotter's 8 steps that are to be followed sequentially are summarized below:

- Establish a sense of urgency
  - The sense of urgency in the pharmaceutical has already been established as a result of the negative press coverage recently regarding poorly justified price increases (even for older drugs), and the continued escalation of prices for new approved drugs for chronic diseases, including orphan products. The industry is now voicing concern, and a sense of urgency as evidenced by the comments of Jim Greenwood during a speech at the 2016 BIO International Convention
  - "The threat we face is real. We've come too far to let bad policy unravel a system that has made our biotech industry the gold standard of the world"…

- Create the guiding coalition
  - In this situation, who needs to be involved here? We would suggest a coalition of private and pubic sector leaders from BIO (Biotechnology Innovation Organization), PhRMA (Pharmaceutical Research and Manufacturers of America), along with leaders from government, academia, and perhaps some members of the press. The key would be to engage thought leaders who can develop and articulate the vision and strategy.
- Develop a vision and strategy
- Communicate the change vision
- Empower broad-based action

Following these first 5 steps Kotter's next three steps include:

- Generate short-term wins
- Consolidate gains and produce more change
- Anchor new approaches in the culture

Peter Boni (2015) has developed a similar model and approach to leading change that he refers to as "The ABCs to Advance". This is a three-stage approach to follow after establishing the sense of urgency. It consists of 1) hatching the plan, 2) kicking off the plan, and 3) executing the plan.

Stage 1 – Ask questions and listen, and ask for help; Base the plan on what you hear, see, or don't see; Challenge the sacred cows or status quo; and, Share the vision to create a collective strategy.

Stage 2 – Act boldly; Build on strengths; Control through active and visible management; and, Streamline the activity schedule.

Stage 3 – Assert yourself at the focal point; Borrow from alliances and partnerships; Communicate progress and results to stay on track; and, Share the rewards of wealth and recognition when things go your way.

Now is the time for a proactive and collaborative approach to move the industry forward to Pharma 4.0.

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