Balancing Innovation and Risk Management in Biopharma Commercialization

March 2020

A striking dichotomy exists between how biopharma companies and healthcare stakeholders perceive the value of biomedical innovation and novel drugs. Biopharma companies must work with key stakeholders to ensure that, upon approval, patients who would benefit from these novel treatments have timely access to them. Additionally, both innovation and risk management are important in commercializing these novel treatments. In this article, the RxC team profiles five key trends that are profoundly impacting the commercialization of novel treatments and their implications for biopharma companies.

1) Value-based healthcare is transforming the delivery of care
2) Consumerism in healthcare is a positive driving force
3) Personalized solutions are producing quality health outcomes
4) New technologies are enabling digital healthcare transformation
5) Supply chain networks are facilitating direct distribution models

INTRODUCTION

The United States healthcare system is one of the most advanced systems in the world; however, it is fraught with inefficiencies. Unlike any other sector of the economy, the healthcare sector impacts each of us directly or indirectly—hence we all have a vested interest in shaping the market to assure that quality healthcare is both accessible and affordable. Within the healthcare ecosystem, the life sciences sector has been flourishing. New developments in science and technology are allowing biopharma companies to develop novel therapies at a breakneck pace. These therapies offer hope and despair at the same time—those that have access to these expensive novel therapies are benefiting while others are unable to take advantage of them. The uphill battle that some patients go through to gain access to proper care has been well documented. There's a clear disconnect between healthcare public policy and health economics—both of which are ripe for transformation. The demand for healthcare services is steadily increasing; however, supply challenges continue to pose risks across the delivery spectrum. The current path that we are on, especially rising healthcare costs, is unsustainable and warrants fundamental rethinking of healthcare delivery and associated economics.

Innovation Driving Novel Therapies

The biopharma sector is one of the most innovative sectors in the US economy. There are two types of innovation commonly seen in our sector: a) radical innovation leading to new therapies (e.g., gene therapies offering "curative" treatments) and b) incremental innovation leading to new applications and enhancements of existing drugs (e.g., new indications, formulations, delivery mechanisms). Both types of innovation have allowed biopharma companies to develop treatments to address unmet medical needs across a wide range of diseases. As the sector enters a new era with the launch of gene therapies at $2M plus price points, it's clear that gaining access to these treatments will be a challenge for most patients.

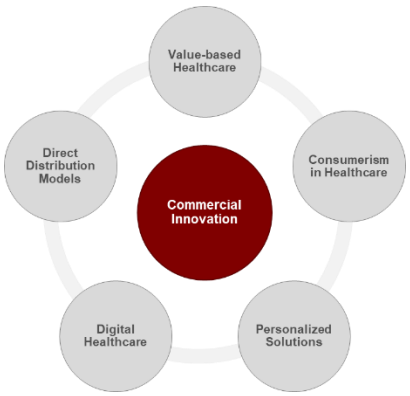
A variety of stakeholders (providers, public & private payers, policy makers, advocacy groups) participate in our healthcare system. The behaviors of these stakeholder groups and their actions are driven by competing incentives that often create conflicts. Healthcare spending is steadily increasing across the board and stakeholders are trying to figure out ways to provide affordable quality care. According to the U.S. Census Bureau, in 2018, approximately 91.5% of Americans had health insurance coverage, two-thirds of which were covered by private insurances. Those that have employer-sponsored insurances and Medicare are content with the system, while others who are paying directly (small business owners, individuals) are not. People who are paying directly often find it challenging to understand the insurance system and the reasons for annual increases in both insurance costs and out-of-pocket costs. The role of intermediaries such as pharmacy benefit managers and specialty pharmacies is not well understood by the general public and in

many cases doesn't translate into direct benefits to patients. Various pricing dynamics in the markets are opaque with low prices for Medicaid and 340(b) programs seemingly invisible to the public. Biopharma commercial organizations must actively engage public and private payers as well as policy makers in order to ensure optimal market access to their novel treatments.

Transitioning Care Delivery Models

Hospitals are consolidating and independent clinics are either being acquired by or are becoming affiliated with these hospitals. This affiliation allows independent clinics to function as part of integrated systems. These large integrated delivery systems have enormous leverage and can drive efficiencies through institutionalization of protocols and processes. These integrated systems are able to secure a significant "patient-market-share" in key geographic areas. Closed loop networks such as Kaiser Permanente have shown how institutionalization of care delivery with proper incentives bring efficiencies to the delivery system. At Kaiser Permanente, most patients with acute gastric conditions are exposed to gastroenterologists and advanced diagnostic testing a lot sooner than patients in regular primary care models. As such, the closed loop model provides patients with a chance to benefit from early interventions. At the same time, accountable care organizations (ACOs), which resulted from the Affordable Care Act, have mixed results. In most cases, these mixed results are due to a) stakeholders' incentives not being fully aligned across the value chain, and b) ineffective patient information management systems.

New point-of-care facilities, such as urgent care centers, are emerging across the nation. These facilities provide basic services to reduce emergency room and hospital demand. Some of these point-of-care centers are part of large pharmacy chain operations that provide basic services to patients at retail locations. Virtual services are also being introduced and insurers are supporting telehealth programs and remote monitoring of patients. Additionally, insurers like UnitedHealth continue to purchase physician clinics as part of vertical integration strategy to effectively manage costs. Another example is Amazon's purchase of Pill Pack to deliver drugs directly to patients. Furthermore, soon a large percentage of the population will require long-term care, which is expensive. A solution to this issue may come from new technologies. Artificial Intelligence and Machine Learning are allowing companies to develop better decision-support systems while increasing efficiency and minimizing errors.



1. VALUE-BASED HEALTHCARE IS TRANSFORMING THE DELIVERY OF CARE

Biopharma companies are under siege to justify the value of novel treatments and their cost-effectiveness to the reimbursement system. Furthermore, drug pricing is under enormous government and public scrutiny and it must be reformed. Some states have implemented pharmaceutical price controls (beyond the current "best price" controls) or patient access constraints under the Medicaid program. Other states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid eligible. There have also been recent state legislative efforts focused on increasing transparency or limiting drug prices. Furthermore, there is considerable national debate around universal healthcare.

Given the environmental challenges, biopharma companies must a) acknowledge that the system needs radical transformation, otherwise, novel therapies at the current price points will not be accessible to most patients, b) help stakeholders understand the value of these novel treatments using clinical and economic outcomes data, c) work with stakeholders to develop integrated care models to deliver quality care at a reasonable cost (as the traditional fee-for-service or capitation models are ineffective), and d) show social responsibility around value-based pricing decisions while balancing shareholder expectations. This approach will allow companies to soften stakeholder concerns in the evolving value-based healthcare system.

Value-based Healthcare Models
The value-based healthcare model, by design, focuses on patient outcomes. If effective, this model could conceivably drive down the costs of many chronic conditions. Real-time data collection systems are enabling stakeholders to administer disease management programs more effectively. And there is increasing interest among stakeholders to leverage value-based healthcare delivery supported by outcomes-based risk-sharing reimbursement models.

For example, curative gene therapies often require a large payment, typically paid in installments that are directly linked to health outcomes. When Spark Therapeutics (now part of Roche) gained approval for Luxturna® (for individuals with an inherited retinal disease caused by mutations in both copies of the RPE65 gene and who have enough remaining cells in the retina), the company successfully negotiated tiered outcomes-based payments from insurers. However, if more of these novel gene therapies are approved, they will put an undue burden on the current reimbursement system. This burden may be avoided if costs decrease significantly, or alternate innovative payment models are introduced. The short-term vs long-term tradeoffs associated with these pricing and coverage decisions must be evaluated from a public policy perspective.

Value Assessments and Their Impact
Third-party organizations such as the ICER are attempting to value medicines and treatments based on comparative clinical effectiveness, cost effectiveness, and budget impact. Their recommendations are having a profound impact on payers' and PBMs' decision-making processes about formularies and coverage. Payers have been instituting a variety of effective utilization management controls (prior authorizations, rebates/discounts, higher co-pays), and using formularies to control costs. Some payers have implemented "co-pay accumulator" policies which are shifting the cost burden to patients and manufacturers.

Biopharma companies strive to show the value of novel treatments to stakeholders to gain market access. One argument is when a drug cures a disease, it eliminates all healthcare costs related to that disease—this argument is beginning to play a central role in diseases for which curative treatments are being introduced. Biopharma commercialization efforts must focus on value-based patient-centric reimbursement models. Early stakeholder engagement is required to get buy-in on the value story and to lay the foundation for effective drug launches. For continued differentiation of marketed products, Biopharma companies must leverage RWE to continuously enhance the value story.

2. CONSUMERISM IN HEALTHCARE IS A POSITIVE DRIVING FORCE

Today, patients are putting themselves in the driver's seat as they make healthcare decisions. Widespread access to information enables patients to educate themselves on diseases and treatment options, as well as to gain a better understanding of the complexity of the healthcare system. This is a step in the right direction; however, most patients still struggle to navigate through the healthcare system due to its complexity and lack of transparency. Case in point, Medicare-Advantage plans are a source of major confusion for most seniors. A large insurance provider offers more than a dozen versions of the same plan with different combinations of Medicare benefits. To identify the differences in each of these options, patients often require support from a family member or healthcare advisor.

Patients taking control of their healthcare decisions
Patients are increasingly paying attention to the value of drugs and healthcare services. This is indicated by the fact that more and more patients are signing up for plans that require high deductibles and co-insurances/co-pays. However, while consumers' appetite for information is increasing, the reliability of the information that's available online is often questionable. Patients and caregivers are ultimately responsible for making difficult decisions around care management and associated costs.

Patients are being empowered to self-manage their disease
Today, motivated patients with chronic diseases take advantage of information, programs, and tools offered by insurance companies and third parties. Patient self-management tools backed by clinical evidence, are

being provided to patients. For example, Kaia's chronic obstructive pulmonary disease management tool has digitized pulmonary rehabilitation; making it possible for patients to access this information at home on their smartphones. Employers are also offering programs focusing on prevention, disease management, and health and wellness management. Furthermore, many large healthcare insurance providers have begun including local fitness gym memberships in their standard packages. These memberships are meant to encourage patients to maintain a healthy lifestyle. These programs could have a positive impact on systemwide costs; however, they are difficult to track without prospective controls and often are "self-reinforcing" to healthier sub-sets of patients.

Biopharma companies should support this positive trend of consumerism by offering reliable information and tools for patients to effectively manage their diseases. This requires partnerships with payers, healthcare systems, and advocacy groups, to ensure that reliable health information and tools are made available to patients. These partnerships are essential to garner real-time insights into patient experiences and to offer timely interventions.

3. PERSONALIZED SOLUTIONS ARE PRODUCING QUALITY HEALTH OUTCOMES

It's widely acknowledged that a personalized healthcare approach is key to producing the best outcomes. This approach requires proper diagnosis using biomarkers and optimizing treatments, as well as monitoring disease progression. However, while innovation in personalized solutions is accelerating, regulatory and reimbursement pathways are only slowly evolving.

Personalized Treatments
Today, the ability to offer personalized treatments is much higher than in the past, as patients are better stratified using biomarkers and genetic profiling. New technologies allow providers to optimize treatments, dosing, responses, and minimize side effects with personalized treatments. For example, immune-oncology drugs, which use the body's own defenses to fight cancer, are profoundly impacting how various cancers are being treated using molecular profiling (PD1 biomarkers). Cell and gene therapies are taking us into the next frontier of personalized medicine and there's hope that many monogenic diseases will soon have potential cures.

Chronic Disease Management
Chronic conditions such as cardiovascular, metabolic, respiratory, and neurological conditions are difficult to manage for most patients and the burden of these diseases on the healthcare system is high. Hospital systems and ACOs have been rolling out programs and incentives to manage chronic conditions better, with mixed success. Technology platforms are allowing us to process vast amounts of information (e.g., medication use, hospitalizations) which is useful in identifying appropriate interventions for patients. For example, diabetics must continually monitor their glucose levels; this process can be made easier with the use of continuous glucose monitoring devices which are integrated with automated insulin delivery systems. These devices allow patients and caregivers to stay on top of the diabetic's information and the performance of their medications.

Real-World Evidence
The data generated during clinical trials is required for regulatory approval and marketing of new drugs. However, it's equally important for companies to harness real-world data using registries and other mechanisms. Such data should be used to confirm the effectiveness of drugs in real-world settings and to better understand long-term outcomes. This data is critical for healthcare providers/payers to make better treatment decisions and develop personalized solutions. This is commonly seen in rare diseases but has widespread applications in all diseases.

Biopharma commercial organizations require partnerships to develop and deploy these personalized solutions. These personalized solutions must be integrated into treatment protocols and disease management programs to attain optimal health outcomes. To drive commercial success, personalized solutions must be supported by policy and advocacy efforts to overcome reimbursement and clinical adoption hurdles. Successful personalized medicine solutions should not only deliver value but also command premium pricing by offering differentiation.

4. NEW TECHNOLOGIES ARE DRIVING DIGITAL HEALTHCARE TRANSFORMATION

Technology is an integral part of healthcare delivery and is pushing the boundaries of innovation. Leading technology platforms are allowing companies to develop innovative solutions for care management. These platforms are also allowing companies to support patients throughout their journey. However, the frameworks for direct to patient contact and patient access to these technologies vary widely. Some of these devices and technologies are not regulated tools and don't require FDA approval. The complexity of managing regulated healthcare information has resulted in these technologies being implemented slowly.

Diagnosing Diseases
Many rare diseases are difficult to diagnose due to the lack of appropriate biomarkers or diagnostic tools. Today, digital technologies are empowering providers, patients, and payers to better understand disease pathways using sophisticated data management tools and predictive analytics. For example, artificial intelligence and machine learning solutions that can diagnose certain cancers more accurately than experts are becoming mainstream. These diagnostic solutions are key to practicing evidence-based medicine.

Optimizing Treatments
Treatment optimization requires using proper medication, monitoring its effectiveness/side effects, evaluating potential poly-pharmacy implications and ensuring compliance to produce good overall health outcomes. Digital technologies are allowing physicians and patients to closely monitor outcomes. For example, Voluntis has an FDA approved medical device Insulia® which provides automated basal insulin dose recommendations and coaching messages for people with type 2 diabetes while enabling the health care team to remotely monitor progress. These treatment optimization and monitoring solutions are essential to effectively manage chronic diseases.

Increasing Adherence
Most patients with chronic diseases tend to be noncompliant with their prescribed medications. According to the CDC, one in five new prescriptions are never filled and half of them are taken incorrectly. But digital technologies (wearable/mobile solutions) are providing a solution to this challenge by providing companies with real-time data and notifications. For example, MedTech's *Leap* is a wearable medication alert and inventory tracking device. *Leap* tracks prescription use and alerts patients when they need to take their medication. *Leap* also alerts caregivers and others if a patient does not take their prescription. Additionally, *Leap* sends auto-refill requests to pharmacies.

Improving Patient Connectivity
Holistic care management requires patient connectivity with their healthcare providers, caregivers, and others. New remote monitoring technologies such as biosensors and wearables, are allowing companies to create eco-systems in which this connectivity becomes seamless and allows providers to monitor patients remotely. Social media and gaming systems are also increasingly being leveraged by the healthcare community. That being said, it can be difficult to collect longitudinal data due to changes in technology and societal trends (e.g., brand selection). This lack of longitudinal data makes it difficult to collect hard evidence of course-correction in disease treatments.

In the past, biopharma companies have successfully marketed products with wrap-around services such as patient education and support programs. However, now biopharma companies must evolve, and this evolution should involve a) providing integrated solutions, b) optimizing treatments, and c) engaging patients. This approach would allow biopharma companies to further differentiate the value of their products and services.

5. SUPPLY CHAIN NETWORKS ARE FACILITATING DIRECT DISTRIBUTION MODELS

Today, biopharma companies manage global supply chain systems that procure raw materials, manufacture and package products, and distribute them to the end consumer. The advent of serialization has allowed companies to closely manage the supply chain network. Such management is vital to avoid counterfeiting and to provide timely interventions (e.g., if a product needs to be withdrawn for safety or other reasons). These supply chain systems

must be efficient to assure quality and to garner public trust. Increasing focus on biologics, cell therapies and gene therapies forces commercial organizations to rethink their global supply chain networks.

Centers of Excellence Models
Special expertise and infrastructure are required to administer new gene and cell therapies to patients. Biopharma companies are developing Centers of Excellence (CoE) in collaboration with leading institutions where multi-disciplinary teams are training providers to administer these novel therapies. New supply chain networks must be fostered to bring patients to these CoEs. Biopharma companies must also develop capabilities to oversee patient support solutions, REMS programs and registries as required.

Direct Distribution Models
Biopharma companies are deploying direct distribution models in rare diseases to effectively support patients scattered across the country. In addition to delivering products directly to patients, biopharma companies support patients with a variety of outreach programs. These outreach programs connect patients and caregivers with providers and healthcare institutions. These programs also allow companies to take control of patient data in order to develop new value-add services.

Virtual Care Delivery Models
Home-based diagnostics (e.g. AliveCor's KardiaMobile portable EKG cell phone units) virtual health assistants, telemedicine services, urgent care centers, and automated prescription services are all transforming how healthcare is delivered. Recently, Amazon purchased Pill Pak and started offering prescription fulfilment services. Amazon may also expand its services into other areas, thereby implementing a direct distribution model. These models may build patient affinity either directly to a brand or operating ecosystem (like Apple). These transformations require supply chain systems to be flexible to meet customer needs.

Biopharma companies are developing sophisticated supply chain networks to bring patients to healthcare centers and healthcare to patients. Newly emerging healthcare delivery networks require close collaboration with 3rd parties and technology platforms to manage the integrity of supply chain systems. Regulating authorities must also look at reducing hinderances to advancing care while still providing proper oversight and controls to protect patient privacy and rights.

ENSURING COMMERCIALIZATION INNOVATION WHILE MANAGING RISKS

Due to complex regulations, biopharma companies must manage a variety of risk factors during commercialization of novel agents. Some of the most common risk factors are a) competitive risks (product differentiation and market access), b) product experience risks (promotion, persistence and compliance), c) technological risks (new technologies impacting patient journey), and d) supply chain risks (drug shortages, recalls, counterfeiting). The degree of impact of each of these risks varies depending on the product and the environment in which it's being used. Biopharma commercial organizations, in collaboration with other cross-functional legal/compliance teams, must track these risks closely and put appropriate mitigation plans in place to avoid business disruption.

In this fluid and evolving healthcare environment, commercial organizations must be agile and ensure that innovative efforts are balanced with appropriate risk management. Successful organizations foster a culture that encourages teams to collaborate with each other to devise innovative commercialization approaches. In the long run, these commercial efforts will create significant value, if mutual trust is established with external stakeholder groups. The RxC team suggests that companies leverage the framework provided below to uncover potential areas for commercial innovation and risk management.

Framework for Commercial Innovation and Risk Management				
1. Value-based healthcare is transforming the delivery of care	**2. Consumerism in healthcare is a positive driving force**	**3. Personalized solutions are producing quality health outcomes**	**4. New technologies are enabling digital healthcare transformation**	**5. Supply chain networks are facilitating direct distribution models**
Drivers of Innovation to Focus on				
• Is the clinical data supported by HEOR? Does the clinical data show value? • Does clinical data align with the RWE? Does RWE further strengthen the value story? • Are you continuously harnessing RWE to assess value and impact? • Are you engaging stakeholders in value-based conversations?	• What are the unmet needs of consumers (education, access to care, socio-economic support)? • Is your consumer-centric approach showing value and aligning it to cost? • What information and tools are needed to empower consumers?	• What are the unmet needs around diagnosis and treatment optimization? • Are you developing personalized solutions and capturing evidence? • Are you able to enhance patient experience and adherence?	• Are you leveraging new technologies to optimize the patient journey? • Are you able to engage patients and enhance connectivity with providers using new technologies? • Are you able to create patient-centric ecosystems using social-media platforms to exchange information?	• Are you optimizing the supply chain network and direct distribution models (as applicable)? • Which strategic partners are critical to making your supply chain efficient and effective? • What technology platform is needed to effectively monitor supply chain integrity?
Risk Management Areas to Monitor				
• Instituting RWE capture systems • Assessing value with 3rd parties (ICER) • Evolving healthcare delivery networks	• Changing consumer attitudes • Increasing healthcare costs • Adhering to treatments (persistence and compliance)	• Enhancing patient experiences • Dealing with regulatory hurdles • Dealing with Reimbursement hurdles • Ensuring compliance	• Adopting new technologies • Ensuring HIPPA guidelines • Managing information flow and connectivity • Managing cyber security	• Ensuring physical access • Avoiding drug shortages and recalls • Ensuring quality control and assurance

About RxC International

Authors: Subbarao Jayanthi, Managing Partner and Jose DeLeon, Executive Partner.

RxC International is a premier life sciences management consulting firm with a passion for helping clients with growth strategies. Our consulting team has deep expertise in strategic planning, new product planning, and commercial excellence. Our clients include leading pharmaceutical and biotechnology companies around the world. Additional information about RxC International can be found at www.RxCInternational.com.

If you have any questions or need additional information, please contact us at info@RxCinternational.com