PERSONALIZED MEDICINE IN 2019:

THE CHALLENGES AND OPPORTUNITIES AHEAD

CLARKSTON CONSULTING

The advent of personalized medicine is a result of countless innovations in an array of fields, including genomic sequencing, big data and analytics, bioinformatics, bioengineering, etc. Realizing personalized medicine commercially will require the same innovative approach and mindset to execute effectively for long-term, sustainable growth and development.

Though challenging, the benefits to adopting a precision therapy model are readily clear. Personalized medicine has the ability to more accurately diagnose disease states, detect the onset of diseases earlier, target treatments, and increase the overall efficiency and effectiveness of the healthcare system. Apart from these direct benefits, personalized medicine will have ancillary value by reducing R&D expense, decreasing costs related to ineffective treatment, and enhancing focus on previously unmet disease states.

The vein-to-vein nature of personalized medicine will force business leaders to reconceptualize every aspect of traditional operational and commercial models. Soon, if not already, life sciences companies will be forced to address challenges with new distribution channels, more stringent product controls, crunched production and delivery times, pricing complexities, and more.

This eBook evaluates some of the most promising cell therapy companies and summarizes those critical challenges facing these companies as they continue to scale. Opportunities for these companies are virtually endless, with the ability to drive significant value and change throughout the healthcare value chain, ultimately enabling better outcomes for patients, physicians, and the business.

While each of these companies will have their own list of unique challenges based on their particular therapies, there are macro issues consistent across all. We've outlined some of the biggest hurdles for these companies to overcome post-FDA approval. As in all business, some of these challenges will be easier to overcome than others, but everything we highlight will be a new challenge for the pharmaceutical industry to address.

SALES + MARKETING

Determining the best approach to pricing is a well-documented issue in personalized medicine. Cell therapies are costly as a result of small patient populations, narrow treatment windows, and high up-front costs. The lack of available long-term efficacy and safety data also precludes cell therapy companies from establishing pricing models based on historical information. Both the personalized nature of cell and gene therapies and the overall shift to patient-centricity inherently support a value-based approach.

While value-based care models are recognized as the future of pharmaceuticals, there are substantive obstacles slowing the transition from volume selling to value selling. More and more, companies in this space are realizing that a traditional "pharma-first" approach is no longer enough for organizations exploring personalized medicine. Instead, they must evolve to adopt a more patient-centric approach designed around building trust with partners in the value chain.

In lieu of traditional pricing models, companies will need to explore alternative pricing models, such as annuity payment models or pay-for-performance based models, in order to absolve concerns about costs and uncertainty of outcomes. A deep understanding of these pricing models and how to integrate them into the business' long-term financial and revenue objectives will be critical for cell and gene therapy companies.

The drug development industry is betting heavily on personalized medicine, as leading life sciences companies have nearly doubled their investment in personalized medicines in the last five years, and expect an additional 33% increase over the next five years.

Even with the substantial investments being made into personalized medicine, the road to commercialization is still relatively uncharted for companies trying to drive cell therapy treatments to market. A commercialization roadmap will be critical to outline a multi-year deployment plan that ensures sustainable and future-oriented growth and expansion. The complex nature of these differentiated

processes and science in cell therapy require a different go-to-market approach. Additionally, adoption of personalized medicine is different than anything that has been done before and despite the speed at which the science has progressed, adoption is reliant on many external factors. In the journey to commercialization, companies must still first navigate regulatory approval, reimbursement, patient understanding, ethical concerns around patient data and information. These industry-wide factors may not progress as quickly as the life sciences company would like, causing impacts to effective adoption.

Physician education and collaboration is an important part of adoption of personalized medicine. While some physicians are equipped to interpret genetic reports, evidence indicates that the majority of physicians are poorly prepared to deal with issues related to genetics and genomics, and that such patients are likely to be misinformed. More formal and fundamental training is required to enhance physicians' knowledge about personalized medicine therapies.

With both traditional and personalized medicines, there is a clear correlation between patient outcomes and the physician-patient relationship – clear and open communication has been shown to improve adherence, pharmacovigilance, and ultimately, overall outcomes.

The complex scheduling and administration requirements will necessitate personalized care for personalized medicine – that is, patients and caregivers must be adequately engaged for the treatments to be most effective. Coordination at this level requires careful strategic communication planning, resources to engage patients in a timely manner, and the platforms and tools to communicate, store, and share information between patients, caregivers, physicians, clinics, and other stakeholders.

SUPPLY CHAIN

Pharmaceutical manufacturing historically consisted of large batch production with large volume production. As manufacturing personalized medicine requires live cells and are generally produced for a relatively small and dispersed population of patients in most disease states, it is difficult to produce this treatment in a cost-effective manner. Careful analysis of production capacity, patient population density, and physician availability is table stakes for quality

and production needs. Pharmaceutical companies also need to consider facility proximity and travel time as new components into supply chain planning activities.

Personalized therapies are often exponentially more complex than more traditional medicines and simply cannot be made on the scale and with the speed, reliability, and traceability required for the efficacy and safety of the treatment.

Product Manufacturing

Single-use technologies, for instance, are already enabling flexible, multi-product, small batch production, a crucial component for personalized medicine. Modular construction lowers plant capital costs dramatically while enabling the ultimate in manufacturing flexibility. With these innovations, costs can come in as low as one-fifth of building a permanent stainless steel vessel batch facility. For continuous manufacturing, the challenges involve sophisticated process controls. Decision makers must be able to review all production variables as an integrated, interdependent system so that a change in one is met with the right response – all while the system continues to operate. This will also revolutionize the quality assurance functions in your organization.

Time and Temperature

The time and temperature sensitivities inherent to personalized medicine will also require companies to ensure that every node of a product's cold chain is virtually error-free. For example, with a CAR-T autologous therapy product that is classified as gene-modified cell therapy and is designed or "trained" to attack cancer cells. This therapy requires T cells that are extracted from a patient's blood, re-engineered in a lab to recognize and kill cancer cells, and then re-infused back into the patient, a process that may require 5 different shipments of 3 different materials at 4 different sub-zero temperatures. The shipping process would require strict quality control and safety requirements, and be completed in less than 3 weeks – all for one batch for one patient. The structure of this complex and intricate supply chain will present new challenges for both emerging biotech companies and for big pharma.

Cold Chain

The existing cold chain capabilities of most pharmaceutical companies is likely adequate for the transport of personalized medication, but the necessary error rates of nearly 0% will pose a big challenge. Improving your cold chain capabilities for transportation and storage (usually 2–8°C) requires a huge network of time and temperature sensors in factories, warehouses, trucks, labs, and pharmacies that can monitor and send this information for both clinical trial supplies and approved products.

IoT tracking sensors and networks help life sciences companies ensure the safety and efficacy of their products in transit and in storage. The need for complete chain of custody capabilities and chain of identity will also have an enormous impact on the current supply chain model. This involves individual tracking from manufacture to patient delivery and sometimes from patient to manufacturer. This exacerbates the need for individual packaging, increased temperature monitoring, aid in customs clearance, GPS-based alerts for potential delays, and other regulatory hurdles.

Demand Planning

Personalized medicine will also shift the way manufacturers manage demand. Capacity planning, equipment maintenance, and production scheduling will be significantly more complex with personalized medicine. Companies focused on understanding all of these supply chain challenges at a detailed level for a small population set will set them up for success when they need to put the technology and processes in place to manage demand for larger patient populations.

With 25% of pharmaceutical costs tied to the supply chain, improving to a 0% error rate will be expensive. Very few pharmaceutical companies would call supply chain management as a core competency of their business and building out a flawless process would be extremely challenging even for the most advanced. However, initiatives underway at most pharmaceutical companies around serialization and theft reduction are a good prelude to preparing your supply chain for the era of personalized medicine.

QUALITY

From the first mention of personalized medicine, the industry's well-documented focus on quality controls, metrics, and processes was highlighted as a major hurdle to approval. How can precise standards and controls be set for a drug that is variable from patient to patient? Setting and demonstrating quality control around the factors that are not variable will be even more important with personalized medicine.

Quality Standards

While the practice of medicine has always been personalized—individual patients treated based on their health profiles and disease markers—the evolving field of personalized and precision medicine involves more refined diagnostic testing than traditional medicine. And treatment is tailored to the patient after accounting for the patient's unique biological, physiological, and environmental profiles.

But given the departure from one-size-fits-all or trial and error diagnostic and treatment models, unique quality assurance challenges arise. For instance, there is a significant burden on clinicians and pathologists to ensure that specimens remain valid and reliable throughout processing.

Adverse Event Tracking & Pharmacovigilance

With such a high degree of specificity, processes like adverse event tracking are even more complex. When each treatment is unique to each patient, how do we truly define what is a side effect for one vs. a side effect for many? Ironically, though the prevalence of adverse events theoretically decreases with the targeted provision of personalized medicine, a new problem of tracking adverse events emerges. While adverse event tracking in traditional medicine involves large sets of variable data, in personalized medicine, the number of variables is vastly increased.

Sophisticated big data analytics will continue to play an important role in adverse event detection, developing efficient flows of information and complex algorithmic solutions to assist pharmaceutical and biotech companies as well as regulators in successfully interacting with adverse event data.

Pharmacovigilance, an already intricate practice, will require a concentrated focus on the pieces you actually can control, i.e. the processes behind the drug development and production. Root-cause analysis as a part of pharmacovigilance will need to go much deeper to account for the individualized nature of each drug and partnering with the providers will be critical to understanding root-cause.

Data Integrity and Privacy

In an industry that already manages a tsunami of data, personalized medicine will add more data to manage. The privacy and safety of protected health information is even more critical as pharmaceutical companies will require information down to the individual genetic code. Establishing a baseline operational structure of managing data effectively will mitigate the risk of potential breaches.

Specimen Processing: A Lack of Standardization

A celebrated tenet of personalized medicine is that only treatments likely to benefit the patient are administered. But it was discovered that unreliable specimens led to inaccurate HER2 tests in up to 20 percent of cases, leading to inappropriate breast cancer treatment decisions. As a result, guidelines were established to ensure proper specimen-handling. However, such guidelines are not the norm vis-à-vis specimen processing and there is generally a lack of standardization as specimens travel from patient to pathologist.

No Clear Regulatory Framework

Another challenge for pharmaceutical and other life sciences companies is anticipating the regulations related to personalized healthcare, including gene and cell therapy. As human cell and gene therapy-related research and development rapidly expands, all stakeholders must watch for equally rapid shifts in regulations.

Lately, many international workshops have convened to address the emerging regulatory issues pertaining to cell therapy while regulatory bodies have published guidance for cell therapy products—including several guidance documents added by the FDA in late 2017 and again in July 2018.

The well-known provision for real world evidence (RWE) in the recent 21st Century Cures Act (the "Cures Act") has the potential for a major impact on the approvals of personalized medicine products. Given the non-traditional treatment profile of a gene therapy, RWE is especially helpful in assessing personalized medicines' long-term benefits and risks in clinical practice. Under the sixth

installment of the Prescription Drug User Fee Act (PDUFA VI), the FDA has committed to speeding the drug approval process by hiring more highly qualified experts as well as facilitating a "more well-established use of real-world evidence to support post market drug safety surveillance" by instating a new safety review system.

The Quality and Regulatory Landscapes Will Evolve

As with many emerging technologies, the enthusiasm surrounding personalized medicine is tempered by uncertainties in quality and regulatory schemas. As the shift to personalized medicine is younger than the laws that otherwise regulate the medical and research fields, there are frustrating gaps between technology and oversight. But these gaps should narrow while companies continue to make reasonable assumptions while they wait. As always, all stakeholders must remain vigilantly abreast of quality and regulatory developments as personalized medicine shows promise as the future of healthcare. Vigilance is particularly important to the many smaller developers of personalized medicines that may have limited resources or regulatory support.

Stakeholders must remember that regulatory views differ on a global basis, including between the FDA and the EMA. We expect a common set of principles to emerge as personalized medicine continues to secure its foothold as an accepted field of medical treatment.

TECHNOLOGY + SYSTEMS

To make the promise of personalized treatments a reality, drug makers must build the infrastructure to operationalize the science behind cell therapy and explore the commercial process for personalized medicine. The focus has shifted more heavily to the commercial processes necessary to deliver, administer, and optimize the outcomes of the treatment. One question many are asking is whether SAP, the dominant player in enterprise software in the life sciences industry, can accommodate the unique production, planning, and scheduling aspects of cell therapy treatments.

Driven by the potential and opportunity in these new therapies, pharmaceutical companies are making massive investments to acquire or develop capabilities relative to cell therapy – including multibillion dollar acquisitions, specialized talent, and upending tried-and-true manufacturing processes.

This shift to personalized medicine is making headlines and dominating boardroom discussion today but there are some significant new technical capabilities are required to operationalize the business strategy. Technology is required to:

- Track chain of identity management,
- Coordinate scheduling and planning with clinics and apheresis centers,
- Manage billing, reimbursement, and revenue recognition,
- Encourage patient enrollment,
- Support logistics and materials transportation, and
- Plan manufacturing capacity allocation.

Each of these processes require unique technical enhancements or modifications to support personalized medicine treatments.

COMPETITION AND GROWTH STRATEGIES

Pharmaceutical organizations looking to grow into personalized medicine are leveraging high-dollar acquisitions of cell therapy companies to quickly enter the space and meet the evolving industry trend and patient expectation for tailored, targeted therapy. Just in the past five years, leading life sciences firms have nearly doubled their investment in personalized medicine. On top of that, over the next five years, that investment is estimated to increase by 33 percent.

It's expected that the number of acquisitions of cell therapy and emerging technology companies will continue to grow as the science progresses and FDA approvals are granted. Just in the past year, two large acquisitions have occurred with Gilead Sciences acquiring Kite Pharma and Celgene Corporation purchasing Juno Therapeutics.

In pursuing an acquisition strategy with a cell therapy company, it's becoming clear that traditional strategies for M&A diligence and integration are not going to work. Understanding the differences between cell therapy companies and traditional pharma companies is paramount for businesses looking to add cell therapy to their portfolio.

CONCLUSION

The global life sciences industry is on the verge of a revolution that will change how drugs are developed, marketed, and priced for patients. As this new personalized landscape evolves, collaboration within the healthcare ecosystem will be essential so biopharmaceutical manufacturers should also be considering the portals by which they'll connect with both patients and providers to drive effective and sustainable engagement.

A transformation is underway in patient treatments. The science is moving away from a one-size-fits-all, trial-and-error approach toward a targeted approach that uses patients' molecular information to inform health care decisions. Although many doctors still prescribe therapies based on population averages, it is clear that healthcare professionals are already seeing the potential for personalized medicine to have a measurable impact on their ability to deliver more effective treatment options.

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For more information about how we can help your company with the challenges and opportunities associated with personalized medicine, please contact us.

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