Arthur D Little

Healthcare Report

Healthcare Innovation

Value Creation in a Patient-Centric Healthcare Ecosystem

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Executive summary

The pharmaceutical industry is undergoing a profound transition – the long-established business model, in which pharmaceutical companies' primary focus was on prescribers, is giving way to a new paradigm targeted towards patients. This shift to a "patient-centric" model is most evident in the growing market for specialty pharmaceuticals.

The rapid growth of specialty pharmaceuticals is creating structural changes across the entire healthcare landscape. Substantial differences between specialty and traditional pharmaceuticals – not only structurally and chemically but often in terms of distribution, marketing, and regulation – are creating new market opportunities while simultaneously challenging the current healthcare ecosystem. The discovery, development, manufacturing, delivery, and sales of specialty pharmaceuticals require new and advanced tools, technologies, and expertise. The growth of specialty pharmaceuticals is therefore not only driving significant changes along the entire pharmaceutical value chain, but has important implications in terms of value creation for traditional players and new entrants alike.

Traditionally, pharmaceutical companies focused their discovery and development efforts on chemically synthetized molecules designed to treat large patient populations, with an ambition to commercialize pharmacotherapies capable of generating annual sales of over a billion dollars – "blockbusters". The sequencing of the human genome combined with advances in molecular biology and information technologies have facilitated the development of novel therapies, including treatments for previously intractable diseases. Consequently, the pharmaceutical industry is transitioning away from a "mass market" approach to a "specialty" model. Patient populations are becoming smaller as therapies are targeted to those with specific "biomarkers," the presence or absence of a certain gene, metabolite, or other biologic characteristic.

This shift is having a profound effect across the entire healthcare ecosystem, with implications not only within drug discovery and clinical development but also for commercialization, distribution, reimbursement, marketing, and drug delivery. While these structural changes present significant challenges to traditional pharmaceutical manufacturers to comply with new health regulations, they also present opportunities for a variety of stakeholders from biotechnology and diagnostics companies to new entrants, such as third party logistic providers, packaging manufacturers, health economics, information technology, and telecommunications firms.

Introduction

Over the last thirty years the pharmaceutical industry has essentially followed a "mass market" approach, a business model that focused on developing treatments for prevalent diseases or common conditions that emphasize broad efficacy. With the release of the competing ulcer medications Tagamet and Zantac in the early 1980s, this era produced a period of rapid growth across the industry with numerous therapies achieving "blockbuster" status. According to the Centers for Medicare and Medicaid Services (CMS), between 1980 and 2012, the total US prescription drug market increased from approximately $12 billion to $250 billion respectively, with much of this growth driven by blockbuster products.[1] (Figure 1)

However, multiple factors have coalesced to reduce the efficiency, effectiveness, and relevance of this model today. Patents on many current blockbuster drugs, including GlaxoSmithKline's Advair Diskus®, Pfizer's Lipitor®, Eli Lilly's Cymbalta®, Merck's Singulair®, and Bristol-Myers Squibb's Plaxvix®, are expiring or have expired (the "pharmaceutical patent cliff"). Notably, each of these therapies individually accounted for annual peak sales ranging between $5 billion and $11 billion.

Simultaneously, the replacement pipeline for next generation blockbuster candidates is constrained. Despite substantial increases in R&D investments, fewer blockbusters have been successfully launched, part of an overall trend of declining FDA approvals. For example, only 27 "new molecular entities" (NMEs) were approved in 2013 versus 39 in 2012. As a result, although an increase in the overall number of blockbusters is projected, the rate of growth itself will contract moving forward (Figure 2).

The reasons underlying the decline in blockbuster drugs are varied. Often cited is the fact that much of the "low hanging fruit" has been harvested, making it difficult to identify new blockbuster targets – a single, defective biological pathway responsible for a prevalent disease or condition, easily controlled with a relatively non-toxic, small molecule chemical compound. Also, some traditional life cycle management strategies are losing their effectiveness: one common tactic typically used to produce follow-up compounds involved making minor structural changes to current blockbusters, often referred to as the "me too" approach. However, under the Patient Protection and Affordable Care Act ("Affordable Care Act" or "PPACA") of 2010, new treatments that fail to perform measurably better than current therapies will no longer be eligible for reimbursement.

Figure 1. Growth of the US Pharmaceutical Market

Source: Centers for Medicare & Medicaid Services

1 Current dollars

Other studies have indicated that pipeline productivity and success rates have decreased across the entire spectrum (i.e., Phases I, II, and III) while the costs of bringing a new drug to market have increased, forcing many companies to reduce the number of compounds under development. Altogether, the lack of viable replacement therapies to blockbuster products presents significant challenges for the major pharmaceutical companies in terms of revenue growth and shareholder value; many have experienced profit declines over the past few years, resulting in significant restructuring and other cost-cutting measures.

Furthermore, increasing controls on healthcare costs are pressuring providers to prescribe lower cost, generic alternatives to blockbuster brand name products, accelerating an already growing trend (Figure 3). The Affordable Care Act defines prescription drugs as an essential health benefit; as millions of previously uninsured and underinsured individuals gain access to these benefits, insurers will be under even greater pressure to provide less costly generic alternatives to ethical, brand name drugs. One compelling example of this substitution trend includes the increasing use of generic statins to replace branded products such as Lipitor which lost nearly 81% of its US sales in 2012 vs. the previous year after patent expiry in November 2011 (Figure 4).

As the relevance of the "mass market" approach wanes, a new business model has emerged, centered on another innovation in drug therapy, specialty products, which include a broad range of pharmaceuticals that share many characteristics. Specialty pharmaceuticals are usually complex, fragile compounds discovered through an advanced understanding of genomics and manufactured or isolated using novel and typically highly

Figure 3. The Growing Market for Generics, US

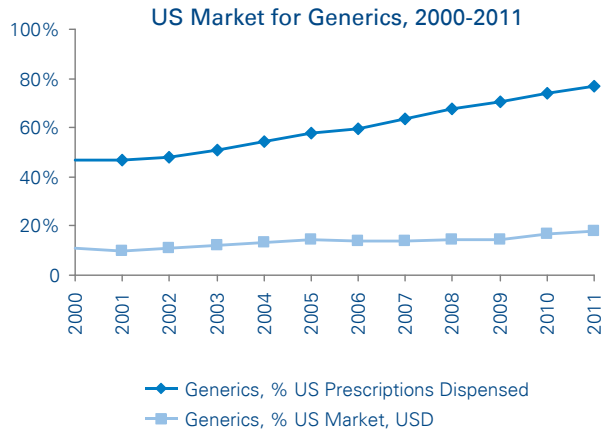
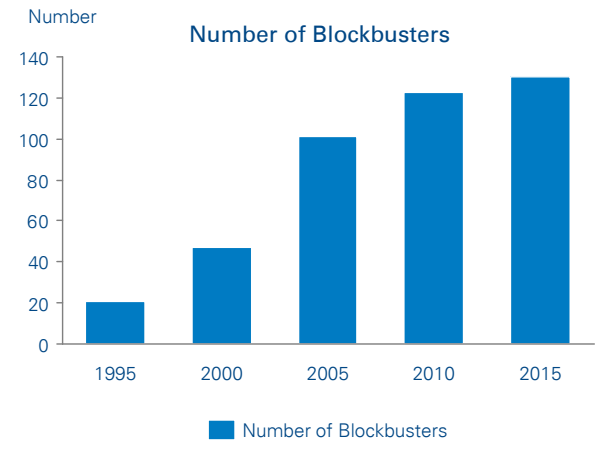
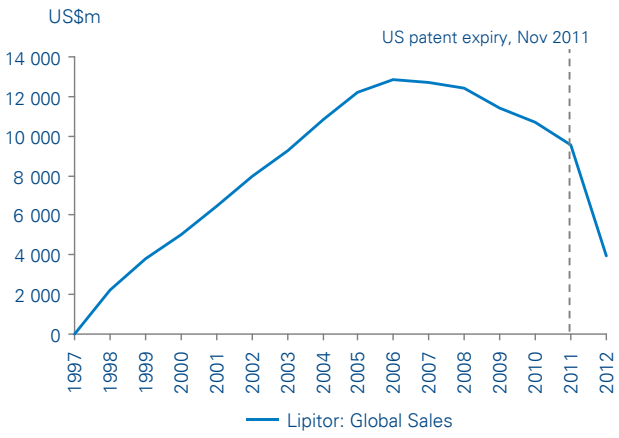


Figure 2. The Declining Growth in Blockbusters



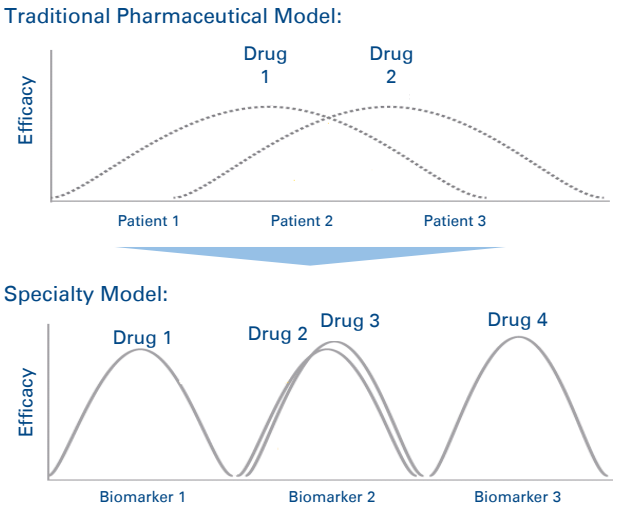
Source: ADL Analysis

Figure 4. Lipitor® Global Sales



Source: Pfizer SEC Filings

Figure 5. Evolution of Therapies



proprietary technologies. Often the diseases or conditions targeted with specialty pharmaceuticals, such as multiple sclerosis, HIV, Crohn's Disease, and rare genetic diseases (e.g., lysosomal storage diseases) are not as prevalent as those conditions addressed with traditional pharmaceutical blockbusters like high cholesterol (hypercholesterolemia), asthma, and atherosclerosis. Many specialty targets also include "orphan diseases," a designation applied to rare conditions (currently defined in the US as affecting less than 1 in 1,500 individuals) by the Orphan Drug Act of 1983, legislation designed to encourage the development of treatments for these diseases through the use of specific incentives, such as tax exemptions, additional patent protections, etc.

Included within specialty pharmaceuticals are "biologics," products derived from either biological processes or living organisms such as cell cultures, bacteria, or yeast. Examples of biologics include antibodies (such as several new cancer and multiple sclerosis treatments), hormones (such as insulin), etc. Arthur D. Little, in conjunction with The Center for Healthcare Supply Chain Research, defines a specialty pharmaceutical as any agent possessing four or more of seven common attributes (Table 1). Figure 5 characterizes the differences between traditional and specialty pharmaceutical models, which is further highlighted in Table 2.

Table 1: Attributes of Specialty Pharmaceuticals (considered to have four or more)

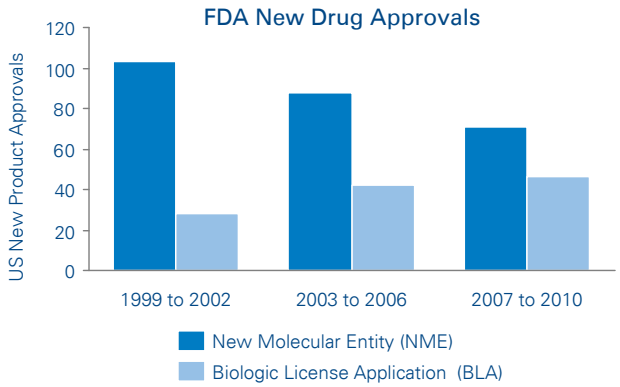
- A typically high cost ($600 or more per month, although annual prescription costs can range from $5,000 to more than $300,000);
- The need for complex treatment regimens that require ongoing clinical monitoring and patient education;
- Have special handling, storage, and delivery requirements;
- Generally biologically-derived products, available in injectable, infused, and occasionally oral forms (when encapsulated so as to survive the digestive tract);
- Dispensed to treat individuals with chronic or rare diseases;
- Frequently have limited or exclusive product availability and distribution; and
- Used to treat therapeutic areas including oncology, hematology, rheumatoid arthritis, autoimmune / immune, inflammation, etc.

Table 2. Traditional and Specialty Pharmaceutical Models

Traditional Pharmaceutical Model: Drugs were designed to be efficacious across a broad range of the population, a one-size-fits-all approach. Although each individual patient's response to a given drug differs based on a number of factors (genetic background, size, weight, age, etc.), most will receive some degree of clinical benefit.

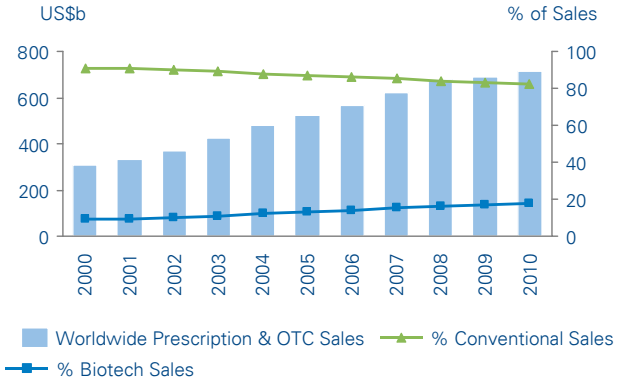
Specialty Pharmaceutical Mdoel: Drugs are engineered to target specific patient populations or even sub-populations. Often these populations are identified by the presence or absence of specific biomarkers, which can be genes / gene products or the output of some biological process (e.g., metabolite, electrical activity).

Figure 6. The Declining No. of Traditional Therapeutics vs. the Growing Number of Biologics



Source: Centers for Medicare & Medicaid Services; EvaluatePharma

Figure 7. Worldwide Total Pharmaceutical Market by Technology



Source: EvaluatePharma; NB: Conventional Sales includes "Unclassifed" products

Driven by advances in biotechnology and disease research, along with incentives provided through legislation like the Orphan Drug Act in the US, the number of specialty products on the market has grown from approximately 10 in 1990 to over 500 in 2012 (Figure 6), with thousands more in various stages of clinical development. ADL estimates that, between 2007 and 2009, nearly one-third of new drug approvals in the US were for specialty pharmaceuticals. This growth is not unique to the US market – IMS Health estimates that the global market for specialty products will exceed $160 billion by the end of 2013, driven by similar orphan laws enacted in Europe and Japan (Figure 7). Many of the trends driving the shift towards the specialty pharmaceutical model are detailed in Figure 8.

Figure 8. Trends Driving the Shift Away From the Traditional Pharmaceutical Model towards Specialty

Shift away from Traditional Model…	… towards Specialty Pharmaceuticals.
■ Diminishing returns from traditional chemical screening and synthesis	■ Legislation incentivizing development of certain drugs, including reduced fees / taxes, faster approval times, regulatory assistance, and longer patent protections
■ Less low hanging fruit for broad-acting, novel, small molecule drugs	■ Increasing understanding of disease etiology due to advances in genomics, new fields (e.g. metabolomics / other "omics," epigenetics), etc.
■ Limited efficacy in certain patient populations due to genetic variation between individuals	■ Advances in technologies facilitating development, production, and administration of novel, often complex therapies
■ Increased competition from "me too" therapeutics and less unmet need within established / known therapeutic classes	■ Conditions targeted, while often small in terms of patient base, are also often chronic, requiring continuing lifetime therapy
■ Increasing time and cost for clinical development and approval	■ Smaller volume specialty products (due to smaller patient populations) require smaller sales forces
■ Patent expiry for many current blockbusters has led to increased competition from generics	

Manufacturing of Specialty Products / Biologics

Specialty products have unique manufacturing and production challenges. Unlike traditional pharmaceuticals, which are chemically synthesized, many specialty pharmaceuticals, including most biologics, are produced by living organisms like bacteria, yeast, etc., requiring novel drug discovery tools and techniques integral to genetic engineering (e.g., high throughput screening, genomic sequencing). The use of these tools and techniques is highly regulated, as the manufacturing process itself can have a profound impact on the quality and efficacy of the final product. In fact, changes in manufacturing facilities, equipment, and processes often alter the biological end product such that new clinical studies are often required for regulatory approval to demonstrate a product's identity, potency, purity, and safety (e.g., immunogenicity).

The rise of the specialty pharmaceutical industry has created another multi-billion dollar, adjacent industry consisting of companies that design and develop innovative laboratory equipment and technologies (e.g., drug discovery, clinical development, quality assurance, etc.) as well as consumables. Notable examples include 3M, which has a dedicated line of filtration solutions for the production of biologics, and Praxair, which provides cryogenic equipment. Honeywell, ABB, and Siemens manufacture control systems as well as automation and measuring equipment that meet stringent regulatory requirements of biologic manufacturing.

In addition, specialized knowledge focused on the manufacturing and regulatory aspects of specialty pharmaceutical development has fueled increasing demand for outsource service providers. Such companies provide manufacturing and / or clinical and regulatory services in order to enhance the probability of success for companies designing and developing innovative specialty therapeutics. These include firms offering contract manufacturing services, such as Fujifilm Diosynth Biotechnologies, Althea Technologies, and Laureate Biopharma, as well as companies that have capabilities to address the manufacturing needs of biopharmaceutical firms like Lonza, Royal DSM, Wacker Chemie AG, and electronics giant Samsung. Even established biopharmaceutical manufacturers are investing in advanced manufacturing technologies – Amgen and Genzyme (Sanofi) are actively developing "continuous production" (also called continuous flow) methodologies meant to replace the current "batch" protocols in order to increase efficiencies, decrease production costs, and meet increasing demand.

ADL Case Study 1 – Specialty Products Joint Venture

Operating in a market that had fluctuated widely in recent years, an industrial machinery and engineering company was looking to expand into new markets with more stable earnings, away from the bigger-is-better machine sales industry. With the healthcare industry offering attractive profit margins, the client turned to ADL to assess the business case of establishing a joint venture ("JV") in vaccine contract drug manufacturing as a next generation business platform.

ADL assessed the prospects for this JV by evaluating pipeline products from a commercial and scientific point of view to understand the true market opportunity they represented. ADL also examined the legal / regulatory risks on the specialty pharmaceuticals side as well as those associated with the proposed joint venture. Finally, ADL identified specific opportunities projected to offer the client the highest probability of success, formulating concrete business models for the segments the company needed to tackle for a successful market entry.

ADL identified the strongest market opportunities in the target field, as well as the specific risks that needed to be addressed. After presenting the findings to the client's CEO and head of their new business planning division, the client confirmed their commitment to forming an alliance with their partner to establish the JV. ADL provided additional guidance necessary to set up and launch the JV.

HCIT, Telecommunications, and Mobile-Technologies

Several technology companies have sought to capitalize on market opportunities driven by the growth potential of specialty pharmaceuticals. Semiconductor manufacturers Atmel, IBM, and NXP Semiconductors have announced or are producing radio-frequency identification (RFID) chips designed to track high value pharmaceuticals in order to provide a digital pedigree as a means of thwarting counterfeiting. Also, to ensure proper cold chain management, companies such as American Thermal Instruments and VeriTeQ offer both active systems, RFID monitors that can record (or even transmit) environmental conditions like temperature throughout the entire channel (from transit to warehouse), as well as passive systems such as stickers that change color if certain temperature thresholds are exceeded. Even packaging companies Cold Ice, Polar Tech, and NanoPore, have contributed, supplying components such as advanced containers with better insulators to help protect sensitive pharmaceuticals while reducing shipping weight.

ADL Case Study 2 –Tracking Specialty Products with RFID

ADL was retained by the US National Association that represents healthcare distributors, the vital link between the nation's pharmaceutical manufacturers and healthcare providers. ADL was commissioned to conduct an independent analysis of the distribution of specialty pharmaceutical products including assessing the role of the specialty distributor in the specialty pharmaceutical supply chain segment. Through its work, ADL explored the roles of the specialty pharmaceutical distributor, from both qualitative and quantitative perspectives, and assessed their economic impact.

ADL interviewed a wide variety of stakeholders and experts including specialty distributors, specialty pharmacies, and specialty pharmaceutical manufacturers. Based upon these interviews, ADL identified a number of key findings which served to underscore that the growth of specialty drugs presents significant opportunities for specialty distributors. In particular, it was revealed that because each specialty pharmaceutical product has its own unique characteristics, specialty distributors are well-positioned to provide value-added services to ensure the safe and cost-effective delivery of these medications, including cold chain handling and pedigree tracking. ADL found that in response to growing concerns regarding tampered and / or adulterated products entering the healthcare supply chain, specialty pharmaceutical manufacturers and distributors increasingly would need to offer RFID technology to meet new regulatory pedigree requirements for specialty drugs throughout the supply chain.

ADL uncovered that RFID technology – which has, to date, focused mainly on physical asset management, patient identification and tracking across inpatient settings and inventory management – is expected to have a substantive impact on the pharmaceutical industry and, most notably, on specialty pharmaceuticals. Given the $1 billion plus costs associated with developing and commercializing each new specialty drug discovery combined with the high cost of specialty pharmaceutical treatment regimens (which can total tens of thousands of dollars per month per patient), ADL's work revealed that RFID technology would be a key technology to counter specialty drug counterfeiting, estimated at 5% to 8% of global pharmaceutical sales, improve the reliability and speed of the specialty drug approval process, and enhance the tracking of drug usage throughout clinical testing protocols.

Design and Manufacture of Drug Delivery Systems

The rapid rise of specialty pharmaceuticals is also having a profound effect downstream of research, development, and production – particularly with regards to product administration (i.e., drug delivery). The physical and chemical distinctions between traditional and specialty drugs necessitate unique formulations and delivery systems. Rather than stable chemical structures, many specialty products are comprised of proteins, such as monoclonal antibodies or insulin. Proteins primarily function as a result of their three-dimensional structure and the stability of this shape is dependent upon a number of factors, including temperature and the solution in which the compound is dissolved. Many of the types of proteins that make up specialty products are sensitive to even minute environmental changes, making them highly unstable.

In order to be successfully administered to a patient, most specialty pharmaceuticals are either injected or infused (slowly introduced into the body intravenously). Unlike traditional pharmaceuticals, which are primarily small molecules (chemically synthesized compounds), oral formulations of specialty pharmaceuticals are uncommon since many biologics are fragile and unable to withstand the process of digestion. Consequently, specialty products often require extensive formulation development to ensure their preservation and stability. Treatments may require complex preparations such as specific mixing or compounding by an appropriately trained healthcare professional. Whereas most biologic specialty pharmaceuticals have been traditionally shipped in glass vials and injected via syringes or infused at a doctor's office or in a hospital setting, more advanced delivery systems are being developed to allow patients to self-administer these medications at home (e.g. Alkermes' Medisorb microsphere technology enables the once-weekly self-injectable formulation of Byetta® / Bydureon®). The PPACA will further incentivize the development of novel delivery systems that enable patients to self-administer and allow caregivers to monitor compliance.

As the specialty pharmaceutical market continues to mature, delivery systems such as pre-filled syringes, auto-injectors, pen systems, and inhalers are becoming a threshold requirement versus a requirement for success. As health costs continue to increase, pressure is mounting for patients to self-administer their own treatments especially for those suffering from chronic conditions like Type 1 diabetes, who require daily injections of insulin.

Furthermore, as first-generation biologics face patent expiries, novel self-administration delivery systems are becoming critically important to extend patent protections through product differentiation and life cycle management. This strategy not only benefits the specialty pharmaceutical manufacturers and the companies designing such delivery systems but other participants across the healthcare landscape as well: patients, who are able to maintain more active life-styles; physicians, who can better assess treatment response and monitor compliance; and payors, who can better prevent potential downstream complications arising from poor compliance or adverse responses. Whether the device increases ease of use, improves compliance and / or efficacy, or simply extends the product's life cycle, novel drug delivery systems are playing an increasingly important role further driving innovation and creating new market growth opportunities across the entire healthcare ecosystem.

Non-pharmaceutical companies – particularly those adept at manufacturing packaging, materials, or plastics outside of healthcare – have been leveraging their expertise to take advantage of the growth of injectable products such as biologics. The SHL Group, which began as a manufacturer of rehabilitation equipment before producing auto-injectors for Upjohn in 1994, is now one of the leading manufacturers of advanced drug delivery devices with the dominant market share of auto-injectors. Similarly, precision plastics manufacturer Nypro, which was acquired by electronics manufacturer Jabil Circuit, Inc. in 2013, was originally founded in 1955 as a nylon manufacturer but entered the healthcare market and currently produces devices such as inhalers, auto-injectors, and pen-injectors. Germany's Gerresheimer, founded in 1864 to manufacture glass containers for the food & beverage industry, expanded significantly into healthcare in 2004; the company currently produces insulin pens, advanced inhalers, and needle-free injection systems. These injection systems have become increasingly more complex – Nypro's Memoir Insulin Pen manufactured for Eli Lilly & Co. has a digital display that integrates a patient's dosing history (including time and date). Next generation systems are expected to include internet

connectivity as well as reporting usage activity to physicians for enhanced patient monitoring and compliance.

Specialty packaging may extend more broadly than drug delivery. Many specialty products are highly specific, benefitting only certain sub-patient populations with many treatments often accompanied by companion diagnostics. For example, in one of the first major successes of genome-based, personalized medicine, Genentech's monoclonal antibody Trastuzumab, marketed under the brand name Herceptin®, is effective only against a certain type of breast cancer in which malignant cells are overexpressing the receptor HER2. Patients must first be screened for HER2 before the drug can be administered – one of the major diagnostics used to conduct such screening is developed and sold by Genentech's parent company, Roche (Figure 6).

ADL Case Study 3 – Drug Delivery for Specialty Pharmaceuticals

A leading global packaging company was looking to accelerate organic growth by expanding into adjacent industries – specifically the healthcare space. ADL was retained to identify value-maximizing opportunities in key market segments within the medical / pharmaceutical industry that offered the best opportunity for the client to succeed.

Organizing the case into three distinct phases, ADL first performed a strategic and financial review of the client's capabilities and R&D / Technology Platforms. Simultaneously, ADL defined the potential Opportunity Space using a key trends and future drivers analysis. This Space was further defined via market segmentation profiling current and future unmet needs. Based on technology scouting and an assessment of the competitive landscape, attractive drug delivery market segments were then selected.

Within each selected drug delivery market ADL then developed a segment-specific value proposition, identifying and prioritizing customers. Further, a go-to-market strategy, complete with technology profiles, was developed, including business cases to assess the financial impact of different strategic options.

Finally, an operational roadmap was assembled, describing the business, technical, and operational requirements as well as the sequencing of options, timing, and "go / no-go" decision points.

As a result of our analysis, a business case for entering the drug delivery healthcare market was developed by ADL and presented to the Executive Committee.

Distribution / Related Services

The same qualities of specialty pharmaceuticals that require enhanced delivery mechanisms – their inherent physical and chemical structures – also require extremely precise and product-specific handling protocols. Cold chain management, keeping the products at specific temperatures throughout their entire distribution, is a vital necessity. Stringent humidity controls are also commonly required, impacting all aspects of specialty distribution. For example, packaging for specialty therapeutics often must take into account the necessary environmental conditions required to maintain the compound's stability. This may involve the inclusion of insulation or refrigerable gels to keep products at a certain temperature for a prolonged period of time. Special handling is required typically during the distribution of these products to ensure precise environmental conditions are maintained and the products remain efficacious.

Benefitting from this growth of specialty products are service providers offering specialized distribution services to specialty pharmaceutical manufacturers. These companies ensure the safe and effective transportation of specialty pharmaceuticals, often directly from manufacturers to healthcare providers and patients, providing invaluable and scalable services to manage regulatory compliance and enhance patient safety.

Market opportunities also extend to product monitoring during their physical distribution to ensure that specialty pharmaceuticals do not exceed certain temperatures nor are exposed to adverse conditions (e.g., sunlight) to maintain product fidelity. One of the hallmarks of specialty products is their high cost, making them susceptible to counterfeiting. Newer technologies are enabling manufacturers and distributors to physically track shipments instantaneously, providing precise data on location as well as local environment. These technologies are likely to become more common as legislation, such as California's E-pedigree / Track and Trace Law, become standard.

Complexity has resulted in significant growth opportunities specifically for specialty pharmaceutical distributors, such as Cardinal Health, McKesson, and AmerisourceBergen, who play an increasingly important and critical role in the healthcare supply chain, safely and reliably ensuring the flow of specialty pharmaceuticals from manufacturers to healthcare providers and patients.[2]

Third party logistics providers like FedEx, UPS, and Geodis offer a range of distribution services to specialty manufacturers, solutions which include warehousing, temperature controlled shipping environments (which are recorded and monitored), and twenty-four hour / seven day a week shipping, including nights and weekends.

In summary additional service requirements of specialty pharmaceutical products are driving the growth of value-added services, which may even be outsourced to additional parties. These services include but are not limited to:

- Physical transport of specialty pharmaceuticals – ensuring the proper (and cost-effective) distribution of the specialty product, ranging from the delivery of a single vial to provider or patient to large shipments from a manufacturer to a major distributor.
- Specialized handling, including cold chain management – as detailed above, services may even include storage capabilities.
- Ensuring product fidelity – the use of advanced software / labeling (usually referred to as Track & Trace) to track products from warehouse to end user to prevent counterfeiting, monitor expiration dates, enable recalls, etc.
- Maintaining and ensuring product authenticity – collecting, monitoring, and maintaining documentation to accounts throughout the entire chain of custody of a drug from manufacturers (and even raw material suppliers) to patients.
- Ensuring Risk Evaluation and Mitigation Strategies (REMS) protocols are followed – described in the section below, this may include services such as educational support for both healthcare provider and the patient.
- Maintaining communications between manufacturer and provider / patient – services can include reimbursement support, patient follow-up, and even the collection of market data.

2 For more, see Specialty Pharmaceuticals and the Role of the Specialty Distributor, a report produced by Arthur D. Little and the Center for Healthcare Supply Chain Research, the research foundation of the Healthcare Distribution Management Association (HDMA).

ADL Case Study 4 – Due Diligence of Specialty Distribution

Arthur D. Little was asked to conduct a commercial vendor due diligence of a global manufacturer of containers for air cargo shipments of biological and other temperature-sensitive drugs. The manufacturer had experienced rapid growth and wanted to better understand potential threats and opportunities, revise strategic directions, and validate top-line forecasts.

ADL began its approach with in-depth analysis of the market for insulated shipping solutions assessing both industry attractiveness (which included a top-down and bottom up market sizing, as well as a detailed analysis of the major growth drivers, such as the biopharmaceutical industry pipeline, to project market growth) and competitive positioning (which included an analysis of competitors, customer satisfaction, trends in major underlying market, and the potential threat of substitutes). ADL then performed an in-depth analysis of the company, which included assessing operational efficiencies, financial forecasts, and sales strategy.

Arthur D. Little delivered an exhaustive vendor due diligence report, which included a detailed description of the market and the company, including its future potential and evidence-based recommendations for how to refine its strategy and focus sales efforts to optimize enterprise value.

Insurance and Reimbursement for Specialty Pharmaceuticals

On March 23, 2010, the Patient Protection and Affordable Care Act (PPACA) was signed into law with the aim of increasing access to affordable health insurance for all Americans. Comprised of numerous provisions – commencing implementation in January of 2014 – the PPACA requires insurance coverage for all US residents, with limited exceptions. The PPACA further mandates that insurance companies offer consistent rates regardless of pre-existing medical conditions or gender.

As a means of controlling costs, insurance benefit plans generally classify prescription drugs by tiers, categories defined by different patient cost-sharing levels (often in the form of copayments or coinsurance) and determined by price negotiations between insurers and drug makers. For example, standard tiers usually include generic, preferred brands, and non-preferred brands. With regard to specialty pharmaceuticals, all health plans offered under the Health Insurance Marketplace of the PPACA will be required to provide specific specialty pharmaceutical drug tiers, a feature already included in Medicare Part D.

The inclusion of these tiers has significant cost implications for both patients and insurers. Specialty pharmaceutical tiers, which often entail higher out-of-pocket costs for consumers, may significantly affect patient outcomes as there is a strong correlation between compliance and overall out-of-pocket expenses. However, the PPACA establishes out-of-pocket maximums, an element that places additional cost pressure on insurers given the more significant costs of specialty products relative to traditional drugs. Given that specialty products are more commonly used for chronic conditions, costs accumulate quickly; for example, AbbVie's antibody-based treatment for rheumatoid arthritis Adalimumab (Humira®) can retail for several thousand dollars per month and may be taken indefinitely. The lower a health plan's monthly premium, the higher the burden on patients to cover these costs; many of the less expensive bronze and silver health plans require patients to pay up to 50% of the total cost for these expensive therapies. Under such scenarios, patients on expensive drug regimens can reach the PPACA out-of-pocket maximum of $6,350 for individuals ($12,700 for families) fairly quickly – leaving insurers to cover the balance.

For these reasons – the ever-growing prevalence of chronic illnesses, the continued expansion of specialty pharmaceuticals, and the economic realities of the PPACA – insurance companies are anticipating increasing cost pressures as the sum of patients in need of expensive care begins to outweigh revenues generated from the plans' healthy customers. Because insurers remain unable to charge chronically ill patients more for their health insurance coverage, they must look towards other options for cost-containment and / or revenue generation if they hope to avoid increasing rates for all patients on a particular plan.

In an attempt to control costs and maintain affordable premiums, insurance companies are facing the option of imposing various restrictions on expensive therapies in hopes of steering patients toward cheaper, more cost-effective generic alternatives – one of the most promising being "biosimilars." Biosimilars, essentially biologics that have lost patent or other regulatory protections, are akin to generics for traditional pharmaceuticals. Unlike small molecules, significant challenges often arise in attempting to replicate a biologic. Variations in the production processes, which often remain undisclosed and may range from specific production cell-line through growth conditions to the purification processes, have significant effects on the efficacy as well as safety of a biologic. For these reasons, no biosimilars have been approved thus far in the US despite the regulatory framework established for biosimilars in 2009 under the Biologics Price Competition and Innovation Act (BPCIA). Although the PPACA and the Biologics Price Competition and Innovation Act have created pathways for biosimilar products to gain regulatory approval within the US, the industry still awaits clear guidance on how these products can more quickly enter the US biopharmaceutical market.

Exacerbating potential cost containment issues for insurers, numerous stakeholders within the industry (e.g., foundations, government programs, drug makers) have discussed efforts to assist patients with chronic illnesses afford their share of drug costs by offering substantial patient discounts. In 2011, healthcare stakeholders distributed more than $4 billion in discount coupons for these high cost specialty medications. In numerous cases, these discounts have helped patients to meet their out-of-pocket maximums – making costly therapies available to more patients at minimal cost – while insurers are left to cover the full price of the therapy.

As the PPACA and the new health insurance exchange programs continue to be implemented, it remains unclear which cost containment strategies insurance companies and other stakeholders will pursue in order to address new cost pressures. Many healthcare stakeholders remain opposed to patient support programs, such as discount coupons, claiming that these programs undermine attempts to steer patients toward less-costly alternatives, such as generics and biosimilars. These sentiments have been supported by the US Department of Health and Human Services (HHS) – including the Centers for Medicare & Medicaid Services (CMS) – which discourages the use of coupons and encourages insurers to reject them.

ADL Case Study 5 – Strategy Development and Implementation for Managed Care Provider

The client, one of the nation's leading managed care companies, derives most of its revenue from Medicaid operations. Based on anticipated market changes as an outcome of national healthcare reform, the space in which the client operates is becoming increasingly competitive with the addition of numerous new market players. Additionally, state governments facing budget reductions comprised much of the client's existing customer base, creating downward pressure on rates. Finally, concerns regarding care providers within the client's networks and their willingness to absorb substantial growth in patient volumes with lowering reimbursement rates posed a significant challenge to the client's future growth.

In order to increase its market share and profitability in this environment, the client sought Arthur D. Little's guidance in the development, evaluation, and prioritization of strategic options which would ensure that the company was optimally-positioned relative to both established and new competitors – while maintaining an efficient, value-added, high quality product offering of managed care services.

Leveraging decades of industry experience in the healthcare sector, as well as a vast network of Experts and Key Opinion Leaders, Arthur D. Little conducted a comprehensive assessment of strategic options – characterizing, profiling, and evaluating each potential opportunity relative to the expected potential impact on the client's business, competitive position, as well as anticipated changes within the dynamics of the US Health Insurance market.

Developing a prioritized list of potential strategic options, ADL created an actionable implementation plan for the client comprised of an optimized list of strategic recommendations based on market, competitive, and financial inputs. This implementation plan was presented to the client's Executive Management Team, and subsequently adopted and implemented by the client.

Marketing / Post-clinical Monitoring Services

Unlike most conventional drugs, the administration of specialty pharmaceutical products is considerably more complex. Patients may need to be clinically followed and monitored much more closely during their treatment, necessitating the performance of routine lab tests throughout the duration of the treatment protocol (which may be long-term vis-à-vis chronic conditions). Monitoring may need to continue for several hours after a treatment is given as well. For these reasons, specialty therapeutics are often known as "high touch" products based upon the multiple handling points that commonly occur during their distribution, dispensing, administration, and follow-up.

For a variety of reasons, the FDA may mandate that a manufacturer include a Risk Evaluation and Mitigation Strategy (REMS) with their pharmaceutical product. REMS are protocols designed to address potential risks associated with a drug, and may range from including a Medication Guide (MG) describing the medication and its potential risks, to a more complex protocol such as a Communication Plan (CP), setting up specific communication channels between healthcare professionals, patients, and regulators. A REMS may even include an ETASU (Elements to Assure Safe Use), which may mandate that the pharmaceutical may only be administered in specific places and that patients be enrolled in a registry. Non-pharmaceutical companies, including the specialty distributors described above, are increasingly providing services that link healthcare providers (including pharmacists) and patients to the manufacturer including ensuring a particular REMS protocol is implemented. Additionally, multiple IT companies have also begun to offer technology solutions to assist specialty manufacturers manage REMS programs as well, including software companies IQware, ParagonRx, and Microsoft (in a joint venture with the contract research organization PPD).

In terms of the overall health information technology (HIT) infrastructure, the rapid growth in specialty pharmaceuticals is having a significant impact on the development and growth of mobile-Health technologies and applications ("m-Health"), the provision of health services utilizing telecommunications / mobile devices. The administration of specialty products is often complex and challenging requiring precise treatment regimens delivered under strict supervision. For example, a specialty drug may require weekly infusions at an outpatient clinic lasting several hours for each administration.

With the increasing adoption of smart devices (smart phones, tablets, smart watches, etc.), m-Health provides an effective means of communication between patients and healthcare providers, from physicians and pharmacies to manufacturers and, in particular, for patients who require specialty products. m-Health applications can be used to send treatment reminders or provide educational materials regarding potential side effects. m-Health technologies can also offer a means for providing feedback to healthcare providers. One example of a company providing this technology is CareSpeak, which supplies its m-Health platform to healthcare providers of patients diagnosed with cancer and hepatitis.

ADL Case Study 6 – m-Health Market Opportunities

A leading mobile provider operated in a promotions-driven, largely prepaid market with a high churn rate. Looking to optimize and redesign their entire non-voice product portfolio as part of their 5 year strategic plan, they retained ADL to review the operator's m-Health potential in order to highlight future business opportunities.

ADL first constructed a detailed market and consumer trends assessment that included evolution scenarios. A detailed value proposition was then developed based on relevant drivers and barriers, including addressable market segments, market share projections, and a go-to-market model. A detailed business case was then developed, including revenue projections, CAPEX estimates, and OPEX estimates. Finally, an implementation roadmap was constructed, defining relevant next steps and milestones.

ADL successfully provided the client with a holistic view of the m-Health market and all relevant drivers as well as currently underserved market needs. The report also included a detailed implementation roadmap necessary to introduce m-Health applications.

Conclusion

With an enhanced ability to treat chronic diseases, the demand for specialty pharmaceuticals will continue to grow as will market opportunities across the broader healthcare ecosystem for products and services that optimize the discovery, development, commercialization, distribution, sales and marketing, and drug delivery administration of these novel therapeutics. ADL's work with leading biotechnology and specialty pharmaceutical manufacturers, outsourced services and third-party logistics providers, innovative packaging and drug delivery companies, as well as health economics, information technology, telecommunications, and wireless technology firms confirms the extraordinary market attractiveness for specialty pharmaceuticals given the accelerating investment and growth of adjacent product and service segments. Furthermore, as nascent markets such as m-Health continue to develop, they in turn will also serve as growth drivers of more advanced specialty pharmaceuticals, operating as a positive feedback loop further enhancing the attractiveness of this market. It is clear that value will accrue to those market players that are able to innovate and capitalize on the vast patient-centric market opportunities that span not only specialty drug discovery and development but equally important and related markets such as diagnostics, drug delivery, packaging, distribution, information and mobile communication technologies.

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As the world's first consultancy, Arthur D. Little has been at the forefront of innovation for more than 125 years. We are acknowledged as a thought leader in linking strategy, technology and innovation. Our consultants consistently develop enduring next generation solutions to master our clients' business complexity and to deliver sustainable results suited to the economic reality of each of our clients.

Arthur D. Little has offices in the most important business cities around the world. We are proud to serve many of the Fortune 500 companies globally, in addition to other leading firms and public sector organizations.

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