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# Medicines as a Service

## A New Commercial Model for Big Pharma in the Postblockbuster World

*Soeren Mattke, Lisa Klautzer, and Tewodaj Mengistu*

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The past decade has not been kind to large pharmaceutical companies. Their share prices have been lagging the market after many years of outperforming it (Paul et al., 2010). Many had to undergo painful restructuring and workforce reductions because their traditional blockbuster model, i.e., finding effective medicines for common conditions and selling them in large volumes with substantial margins, is becoming extinct. More and more top-selling drugs are being replaced by cheap generics, and developing new drugs is more difficult and more costly because fewer opportunities exist and research and development (R&D) productivity has declined. Although this diagnosis is not disputed, the best course of treatment is not clear. Companies have tried to stop the bleeding with the help of mergers and reorganizations and infused new blood by acquiring biotech companies or their innovative products or by diversifying into products other than prescription drugs.

In this paper, we propose that the pharmaceutical industry can reconfigure its considerable resources to develop innovative and meaningful business models that are based on services related to prescription drugs for chronic conditions. We argue that such innovation beyond the pill is consistent with the core capabilities of large pharmaceutical companies and has the potential to achieve profit levels similar to those of its traditional models. Our argument is based on the fact that, although effective medicines for most chronic conditions exist, access and adherence to medicines

are far from what would be needed to achieve full treatment efficacy. Therefore, value can be created by getting and keeping more patients on their drugs, and innovative business models would allow pharmaceutical companies to capture that value.

### The Swan Song for the Blockbuster Model

More and more so-called originator drugs are facing competition from generics (Hunt, Manson, and Morgan, 2011). All of the top ten prescription drugs by volume sold in the United States in 2010 were generics (IMS Institute for Healthcare Informatics, 2011). Generic market share by volume sold stood at 78 percent, up from 63 percent in 2006 (IMS Institute for Healthcare Informatics, 2011), even though this translated into only 13 percent of sales because of the higher prices of originator drugs. The year 2011 witnessed generic entry of competitors to several multibillion-dollar drugs, such as Lipitor® and Actos®, and more will follow in 2012, such as Seroquel®, Plavix®, and Singulair®. Goldman Sachs estimated that up to 14 percent of, or just over \$50 billion in, pharmaceutical sales will be wiped out because of generic entry. Even when exact generic equivalents are not yet on the market, there is often at least one generic alternative for the first-line treatment of the most-common chronic conditions, and makers of originator drugs are increasingly challenged to demonstrate value against these inexpensive alternatives. Finding new medicines to replace lost revenues is becoming increasingly dif-

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difficult for two reasons: declining opportunities and decreasing R&D productivity.

### **Declining Opportunities**

Many low-hanging fruits for drug development have been harvested as researchers translated the growing knowledge of the physiologic mechanisms behind common diseases into drugs that alter these mechanisms. Such drugs typically focus on ubiquitous receptors and enzymes that they inhibit or stimulate. Current drug development, however, aims at the genetic or molecular dependencies of disease physiology—processes that are much harder to understand and influence and that vary a lot more by patient. Thus, the probability of a compound becoming a marketable drug declines. According to a Bain and Company study, in 2003, only one compound in 13 discovered reached the market, compared with one in eight discovered between 1995 and 2000 (Bain and Company, 2003). In spite of the rapid growth in investment in R&D, from \$2 billion in 1980 to \$43 billion in 2006 nominally, the number of drugs approved remained roughly the same (Garnier, 2008).

### **Increasing Development Cost**

Drug development cost has increased, partly because of the growing complexity of preclinical research and partly because of more-stringent requirements during the clinical development phase, such as larger clinical trials. Together, those two effects have increased the average estimated cost per approved drug from \$318 million in 1987 to \$802 million in 2000 and to \$1.2 billion in 2007 (Rasmussen, 2007; DiMasi, Hansen, and Grabowski, 2003). This trend has hit the major pharmaceutical companies (“big pharma”) particularly hard. Large, global companies can be at a disadvantage to smaller biotech in terms of cost relative to revenue because they tend to have higher overhead and higher fixed costs. And the more planned and bureaucratic approach to development in large companies proves to be less productive than the hit-or-miss one of the biotech world. In 2007, the biotech industry had more compounds in phase II and III trials than the pharmaceutical industry had in most therapeutic classes (except for respiratory agents),<sup>1</sup> and, by the same token, biotech firms outperformed

large pharmaceutical firms on earnings growth (28 percent versus 13 percent) (Ling et al., 2007).

### **Specialty Drugs May Not Be the Answer**

Although their traditional success model seems broken, it is less clear what path large pharmaceutical companies should take to replace dwindling sources of revenues and profits. At the moment, most bets are on what we call, for the purposes of this paper, targeted treatments, which are biologics or small-molecule drugs that specifically target the genetic and molecular dependencies of a disease in a given patient subset or are tailored to the susceptibility of a patient subset to side effects. Thus, at least in theory, they can be highly effective with limited side effects. Such drugs, which are sometimes referred to as personalized medicines, have been developed for cancer, immunologic disorders, and other conditions. Given their specificity, those drugs reach much smaller populations than the conventional blockbusters, but they can achieve similar sales because of their high prices. In 2010, Lipitor was ranked the 12th-most-prescribed medicine in the United States (45.3 million prescriptions), with a total spending of \$7.2 billion, but none of the top three selling biologics (Epogen®, Remicade®, and Enbrel®), each with annual sales of \$3.3 billion, made it into the list of the top 25 most-prescribed medicines.

In 2010, sales of biologics amounted to \$67 billion, approximately 22 percent of total pharmaceutical sales in the United States (IMS Institute for Healthcare Informatics, 2011). Sales of cancer drugs, dominated by targeted treatments, overtook sales of lipid regulators in 2008, and the gap continues to widen: In 2010, total spending on cancer drugs stood at \$22.3 billion, compared with \$18.7 billion for lipid regulators, while, in 2006, the same numbers stood at \$15.8 billion and \$22.4 billion, respectively (IMS Institute for Healthcare Informatics, 2011).

However, it is unlikely that targeted treatments can constitute the sole foundation of a new business model for large pharmaceutical companies for three reasons. First, large pharmaceutical companies are too dependent on innovations by smaller competitors to maintain this pipeline. Second, it is not clear that payers will continue to accept the very high prices for

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<sup>1</sup> As noted by Ling et al. (2007), this is also due in part to the fact that there are a lot more biotech companies than large pharmaceutical firms.

those drugs. Third and most importantly, these drugs are not an ideal fit for the core capabilities of large pharmaceutical companies.

### The Limits of “In-Licensing”

At the moment, pharmaceutical companies can leverage strong cash flow from existing products to close the innovation gap by buying small and innovative competitors or by licensing their products in late-stage development. Seven out of the ten leading biotech firms in 2005 have since been bought up by pharmaceutical firms (Malik, 2009; Whalen and Spencer, 2011). Of the four current top-selling biologics that are being marketed by traditional pharmaceutical companies, three have originally been developed by biotech firms (IMS Institute for Healthcare Informatics, 2011). Tight conditions in capital markets help large companies because smaller competitors face difficulties raising capital to grow independently.

However, using cash flow from products with little remaining life expectancy to purchase innovation is, in essence, a pyramid scheme. As the innovation gap persists, prices for drugs and companies will continuously go up. Growth in U.S. biotech revenue is already twice that of U.S. pharmaceutical companies, according to Goldman Sachs estimates, which expect biotechs to grow, on average, between 14 and 18 percent but pharma by only 6 to 9 percent (Ling et al., 2007). Pharmaceutical companies have also had to pay a large premium when acquiring biotech firms. For example, most recently, Sanofi-Aventis purchased Genzyme for \$74 per share, a price that represented a 48-percent premium. According to Bloomberg, the purchase valued “Genzyme at 4.7 times sales, compared with a median multiple of 4.3 for U.S. drug and biotechnology companies in the past five years” (Torsoli and Tirrell, 2011). It will therefore be increasingly difficult for large pharmaceutical companies to continue to rely on outside innovation, especially once capital markets thaw.

### The Challenge to the Targeted-Treatment Model

There is also a more fundamental challenge to the business model of personalized medicine that affects large pharmaceutical and biotech companies alike. By their very nature, these drugs will work only in the subset of patients who indeed have the targeted dependency. The costs therefore have to be spread over a small denominator, leading to high per-patient prices. For example, the annual cost of targeted cancer therapies can be between \$50,000 and \$100,000 per patient (Aggarwal, 2010). So far, payers have rewarded innovation by accepting these high per-

patient costs. The fact that only few patients benefited from the drugs certainly made paying for them easier. But, as such expensive treatments become more widely available, it is not clear that payers will continue to provide coverage in light of the global purse-tightening. There is also the reputational risk to companies if they are seen exploiting the desperation of cancer patients. As a pharmaceutical executive told us about cancer drug development, “the pricing assumptions behind some of our latest product developments outright scare me.” Lastly, the emergence of biosimilars can erode the profitability of biologics as an important subgroup of targeted treatments.

### The Mismatch Between Big Pharma and Small Volumes

If we expect greater pressure on prices for targeted treatment in the future, their higher development cost puts the large pharmaceutical companies again at a disadvantage against small biotechs. Fewer projects will be commercially viable, and big pharma may even be forced to license out drugs to nimble competitors that can develop them at lower cost. At the same time, it is becoming easier for small companies in niche markets to bring drugs to market and to sell them. Contract research organizations handle clinical development; manufacturing can be outsourced, as can be sales and distribution. So there is no obvious competitive advantage in being a large, integrated company in niche markets. For example, Optimer Pharmaceuticals recently obtained U.S. Food and Drug Administration (FDA) approval for fidaxomicin, a novel antibiotic for hospital-acquired intestinal infections. The company chose to market the drug itself in the United States and only licensed further development in most other countries to Astellas Pharma.

The Optimer/Astellas deal also shows the limits of small biotechs and the area of competitive advantage for big pharma: Large-scale global development, marketing, and distribution require familiarity with regulatory processes in numerous countries, access to national key opinion leaders, and a robust global supply chain, all of which are impossible to maintain and difficult to source for small firms.

To exploit this competitive advantage, it would seem logical for large pharmaceutical companies to focus on developing widely applicable medicines for conditions with high prevalence globally—in particular, the most common: cardiovascular disease, chronic pulmonary conditions (such as asthma and emphysema), diabetes, and mental health. Cancer, on which most companies actually focus today, is much less attractive from a market perspective. Although it

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represents the second-most common cause of death overall, it is not a single disease but a wide variety of malignancies that all require tailored approaches. In 2009, 26.8 million U.S. adults lived with heart disease, dwarfing the number of those living with the two most common cancers, 2.65 million adults with breast and 2.35 million with prostate cancer (American Cancer Society, 2011; Pleis, Ward, and Lucas, 2010). In addition, cancer treatment in early stages relies mostly on surgery and radiation rather than drugs. And finally, chemotherapy is administered for a finite number of cycles, whereas other chronic diseases typically require lifelong treatment.

### **Treatment Gaps in Chronic-Disease Care: The Untapped Growth Opportunity**

“Wait,” the casual observer would say. “Don’t companies focus on cancer because drugs for most of those other conditions are widely available as generics? How can one recoup the investment into yet another antihypertensive, if it competes against drugs that cost pennies?” The answer is that there are still substantial unmet treatment needs for chronic diseases, but the nature of those gaps has evolved. For decades, the ability to control chronic disease was hampered by lack of effective medicines, but today the leading obstacle is the fact that health care systems are ill-prepared to deliver efficient and effective chronic care. There is substantial evidence that patients with chronic conditions are undertreated in emerging economies because they lack access to medicines (World Health Organization, 2003) and in the developed world because they do not adhere to prescribed treatment regimens (Wagner et al., 2011; Miranda et al., 2008; Mendis et al., 2005). This means that the biggest opportunity to close the gap in care does not lie in the development of new molecules but in the development of smarter treatment solutions.

So the shift toward chronic disease has led to a mismatch between what companies offer and what their customers need. Pharmaceutical companies have historically seen their role as developers of new compounds and marketers of pills. Their key customers and decisionmakers used to be clinicians and scientists, with whom they identified and addressed treatment gaps, and regulators, with whom they worked to ensure that drugs were safe and effective. Their new key customers and decisionmakers are payers and governments that are concerned about undertreatment because proper treatment improves prognosis and reduces cost of care.

These new customers (and the patients whom they represent) are looking for providers of therapeutic

solutions, i.e., partners in the care process that can ensure that patients have affordable access to safe and effective medicines and control their diseases reliably in order to avoid disease progression and costly exacerbations. The value of innovation will thus be measured by cost per relevant outcome under real-world conditions rather than differential performance in a clinical trial.

There is substantial evidence that such value can be created because studies of patients with common chronic conditions, such as diabetes, heart failure, and hypertension, show consistently that adherent patients have fewer hospital admissions, lower costs, and better clinical outcomes (Sokol et al., 2005; Ho et al., 2006). If companies can engage their new customers and define new pricing paradigms for drug treatment that are reflective of the created value, it should be possible to secure appropriate financial returns, as we outline later.

To summarize, big pharma needs to rethink its role and broaden its conception of innovation to products beyond the chemical compound to adapt to the changing needs of their customers. In other words, companies should move from maximizing the pill to maximizing total benefit, in which the chemical compound is one contributor. Those innovations, which we call medicines as a service, should address the true needs of patients and payers as the customers and support sustainable commercial models. It should be kept in mind, however, that the attractiveness of such models will differ across companies because of differences in product line-up, geographic reach, internal capabilities, and cost structure. Importantly, companies will have to have the trust of stakeholders in a given market and the ability to engage them effectively in order to deploy service-based models successfully.

### **Medicines as a Service: Innovation Beyond the Pill**

#### **Improving Access to Medicines: An Opportunity in Developing Markets**

In the developing world, patients face fundamental obstacles to access to drugs for chronic diseases, as we have pointed out in a recent report (Mattke et al., 2011). Burdensome administrative and regulatory processes prevent companies from marketing their medicines; poor planning leads to mismatches between demand and supply; weak supply chains raise cost, reduce availability, and allow entry of counterfeit product. Most importantly, the absence of robust primary-care systems means that chronically ill patients are underdiagnosed, undertreated,

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**The shift toward chronic disease has led to a mismatch between what companies offer and what their customers need.**

and undermanaged. For example, the World Health Organization studied treatment of coronary artery disease in ten low- and middle-income countries and found that nearly 20 percent of patient did not receive aspirin, 52 percent did not receive a beta-blocker, 60 percent did not receive an angiotensin-converting-enzyme (ACE) inhibitor, and 79 percent did not receive a statin (Mendis et al., 2005). Clearly, it would be hard for pharmaceutical companies to remove those obstacles, but, given the magnitude of the opportunity, there may be a case for trying.

### Beyond Branded Generics

The clearest near-term opportunity is to implement a safe, reliable, and efficient supply of medicines, and companies have already built significant capabilities in this area. Companies have developed technologies to prevent counterfeiting, manage stocks, and ensure safety of their products. For example, in 2005, Pfizer started tagging all its Viagra® bottles marketed in the United States to counter reimportation and counterfeiting (Barlas, 2005), and AstraZeneca's radio-frequency identification (RFID) tagging of Diprovan® syringes has prevented dosage errors in Japan and Europe (Mintz, undated; Harrop, undated). There are cost-effective technologies to ensure quality of medicines. For example, Merck funded the development of GPHF-Minilab®, a mobile minilaboratory for drug quality verification and detection of counterfeit drugs that allows for the testing of 25 standard drugs and has thus far been distributed to health facilities in 70 developing countries (International Federation of Pharmaceutical Manufacturers and Associations [IFPMA], 2011). AstraZeneca currently supplies about 22,000 pharmacies in the Philippines directly to avoid entry of counterfeit products.

The current model to monetize the value of these innovations is branded generics that are marketed by, for example, Sanofi and GlaxoSmithKline (GSK) in emerging economies (Singer, 2010). Patients are willing to pay a premium price for those products because of concerns about counterfeiting and quality issues: As much as 20 percent of drugs sold in Brazil are counterfeit ("Medicamentos falsos são consumidos em grande quantidade no Brasil," 2010), and estimates for other developing countries range from 10 percent to 30 percent (World Health Organization, 2006). Manufacturers of branded generics ensure the integrity of their supply chain and provide features for consumers to verify product authenticity, such as packaging and serialization.

This consumer-facing model could be extended to payers. Governments in emerging economies are very interested in ensuring the safe and efficient sup-

ply of medicines, but they commonly lack required resources and capabilities. They would be interested in a partner that can offer a full range of essential medicines and ensure reliable and secure management of the entire supply chain up to the dispensing point. Such an arrangement would be attractive to companies with a robust generics business, such as Sanofi and Sandoz, a subsidiary of Novartis, which operates Arogya Parivar, a sustainable business unit in India that sells both Novartis and sourced generic drugs (Novartis, undated).<sup>2</sup>

### Direct Care Delivery

As we described recently (Mattke et al., 2011), limited access to primary care remains a key obstacle to medication treatment in developing countries. Clearly, pharmaceutical companies are not in an ideal position to take on the complex task of care delivery, but they will need to support the development of a robust infrastructure for care delivery in emerging markets because such an infrastructure is the precondition for accessing patients and meeting their needs and, thus, for establishing a pathway toward future drug sales. Many companies are already supporting pilot projects in partnership with other stakeholders to improve care delivery for patients with chronic conditions. Eli Lilly recently announced a \$30 million investment in pilot projects on diabetes care in Brazil, India, Mexico, and South Africa (Eli Lilly and Company, 2011). Several other companies are entering into partnerships with local governments or non-governmental organizations to improve access to care. Pfizer is undertaking a pilot disease-management program along with the Shanghai Center for Disease Control and Prevention to manage and reverse hypertension and related risk factors. Sanofi, in conjunction with national health ministries and universities, is conducting pilot programs in Mauritania and Morocco to improve care for schizophrenia patients (IFPMA, 2011). These initiatives aim at creating locally sustainable institutions; however, laudable (and image-enhancing) as they may be, they are unlikely to create a scalable care infrastructure that matches the rapidly growing needs in those countries.

An alternative could be development of direct care-delivery models by pharmaceutical companies, centered on key product lines. It may seem like a far-fetched idea, but there are successful precedents. Fresenius Medical Care, for example, started out as a pharmaceutical company, branched out into dialysis products, and then began running dialysis centers.

<sup>2</sup> A sourced drug is one that the company buys from other manufacturers and sells under its own name.

Today, it is the world's largest manufacturer of dialysis products and the world's largest operator of dialysis centers. Other companies have started from care delivery and branched out into products: The Aravind Eye Care System made cataract surgery accessible and affordable in India by developing a highly efficient delivery system. Part of its success in keeping cost down is a decision to manufacture its own supplies, such as intraocular lenses (Miller, 2006). Companies with a comprehensive product line that is focused on distinct conditions, such as Novo Nordisk and other large insulin manufacturers, would be in a good position to introduce such models for diabetes care.

### **Creating Value by Improving Adherence: The Opportunity in the Developed World**

Even in developed countries, where patients generally have access to medicines, treatment gaps persist. In particular, low adherence to long-term treatment regimens remains a big problem: Data continue to show that, on average, approximately half of the patients take chronic drugs as prescribed. It is not surprising that it is hard to convince patients to stay on those drugs (World Health Organization, 2003; Burke, Schlenk, and Rand, 2001; Sokol et al., 2005). Most drugs are used for prognostic indications; they lower a patient's blood pressure or cholesterol to prevent future heart attacks. They do not make you feel better; in fact, many make you feel worse because of side effects. They cost money and require visits to the doctor and trips to the pharmacy. But what is surprising is that the industry has not yet come up with better ways to promote adherence.

The problem has long been known; in the 1990s, the Boston Consulting Group recommended that pharmaceutical companies offer disease-management services to improve medication adherence. But pharmaceutical companies were caught between Scylla and Charybdis. Out of concern about being portrayed as driven by narrow self-interest, companies were hesitant to introduce product-specific interventions. Product-neutral interventions, on the other hand, create a free-rider problem: Although one company bears the cost, the intervention would also increase sales of competing branded or generic products. In the absence of a convincing commercial rationale, pharmaceuticals largely opted to yield this area to players with product-neutral business models. Disease management was spun out into companies that marketed their services to payers, which would ultimately stand to gain from reduced medical cost because of better adherence. Distribu-

tors and pharmacy benefit managers (PBMs), which benefit from an increase in sales volumes irrespective of a particular product, started developing adherence solutions. McKesson Patient Relationship Solutions, for example, offers education and incentive programs to promote patient adherence. Medco's online health resource centers for various chronic diseases provide access to information and consultations with specialty pharmacists.

Conversely, manufacturers seem to have all but given up: We searched the websites of the five top-selling branded drugs for content related to adherence. Only the Lipitor and Advair® websites provide specific recommendations on increasing adherence; the websites of Nexium®, Plavix, and Abilify® state that drugs should be taken as prescribed but do not provide adherence strategies. Television commercials encouraging consumers to "ask your doctor whether X is right for you" are ubiquitous, but they do not mention the importance of actually taking the drug.

Yet the untapped opportunity in improving adherence is substantial. Estimates for the medical cost that could be avoided with better adherence range from \$80 billion to \$290 billion per year in the United States (New England Healthcare Institute, 2009; Hicks et al., 2011; Osterberg and Blaschke, 2005; Berg et al., 1993), compared with an estimated size of the overall prescription-drug market of about \$307 billion in 2010 (IMS Institute for Healthcare Informatics, 2011). A recent study estimated that better adherence could save \$7,823 annually for patients with congestive heart failure (CHF) and \$3,756 in diabetics.<sup>3</sup> If we extrapolate to the national level, we find that the size of the adherence market would be \$46 billion for heart failure and \$71 billion for diabetes.<sup>4</sup> For comparison, 2010 sales of Crestor®, the

<sup>3</sup> Roebuck et al. (2011) estimate the changes in medical use and pharmacy and medical costs resulting from improved medication adherence for a large sample of patients with four targeted conditions, including CHF and diabetes (16,353 patients with CHF and 42,080 patients with diabetes), using a three-year panel data set and econometric model specifications accounting for the endogeneity in the relationship between adherence and health service use and cost. For their adherence measure, the authors created a binary adherence variable on the basis of the medical adherence ratio for each patient-year, in which a Medication Possession Ratio (MPR) less than 0.8 was considered nonadherent and MPR greater than or equal to 0.8 was considered adherent. Measures of health service use and cost included annual numbers of inpatient hospital days, emergency department visits, outpatient physician visits, and annual pharmacy (ambulatory, community based, or mail service), medical (from medical claim data), and total health care costs (sum of pharmacy and medical costs).

<sup>4</sup> We estimated the size of the national adherence market for heart failure and diabetes using the results from Roebuck et al. (2011) and the most-recent estimates for patients with heart failure from the American Heart Association (AHA) and for patients diagnosed with diabetes from the Centers for Disease Control and Prevention (CDC). In effect, in 2012, the estimated number of American adults with heart failure is 5.7 million, and the number of Americans diagnosed with diabetes is 18.8 million, so the potential annual savings in medical spending from improved adherence for Americans with heart disease is \$46 billion (5.7 million × \$7,823) and that

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best-selling lipid drug, were \$3.8 billion; of Actos, the best-selling diabetes drug, \$3.5 billion; and, of Avastin®, the best-selling targeted cancer drug, \$3.1 billion (IMS Institute for Healthcare Informatics, 2011). In other words, just realizing one-tenth of the value left in lack of adherence would trump the revenue of a new blockbuster drug.

Large pharmaceutical companies have the capabilities to capture some of that value that disease-management companies, PBMs, distributors, and providers currently leave on the table. They have deep insights into the biology of diseases and the differential importance that adherence to different drugs plays for different diseases. Increasingly, they are using those insights to develop diagnostic tests to identify patients who will respond to a drug or experience side effects. They have robust health economics and outcomes research capabilities to project the effectiveness and cost-effectiveness of different adherence solutions. And they are versed in interacting with multiple stakeholders to ensure market access for novel products. Thus, they are in an excellent position to develop and commercialize innovative service-based models. In other words, they would shift from selling drugs to selling outcomes.

### Bundling Medicines with Adherence Solutions

As a first step, companies can add patient-engagement solutions to medicines, which would promote adherence but also help with concomitant lifestyle changes that are critical to therapeutic success. This strategy can leverage the increasing knowledge about how to change patient behavior and encompass a variety of tools, such as packaging, educational materials, incentives, social media, and “gamification.” Models do exist in consumer-focused pharmaceutical products. Birth-control pills, whose users admittedly have strong incentives to be adherent, come in monthly blister packs that allow verifying easily which doses were taken. The over-the-counter weight-loss drug Alli® offers an educational and support program, but, interestingly, the prescription version of the same compound (Xenical®) does not even have its own website. Of the five top-selling drugs, only the Lipitor website has a patient-engagement tool (HeartWise) to promote healthy lifestyles and adherence.

For higher-cost products, drugs could be marketed with technologies that promote adherence. The Vitality GlowCap™ technology (Vitality, undated), for example, consists of a cap for standard pharmacy

containers that has an embedded microchip. The program on the chip reminds the patient to take a drug, notify caregivers of adherence, and reorder drugs from the pharmacy. Proteus Biomedical, a Californian start-up, has developed a so-called smart pill (“Pills Get Smart,” 2010). It contains a tiny transmitter that gets activated by gastric acid when the patient has swallowed it. The information gets sent to the patient’s doctor, who can ascertain precisely when drugs were taken. Novartis is testing this technology with immunosuppression drugs in patients after heart transplant, when precise adherence is critical for avoiding a rejection and keeping the patient alive. As the cost of such technologies comes down, their use in mainstream medicines is conceivable.

In the long run, deeper insights into users’ minds that are gained by such monitoring technologies can inform patient-centered drug development that takes into account, for example, which side effects drive drug discontinuation and what influences lack of adherence in different populations, and combines an effective compound with a targeted engagement strategy. This approach would go beyond conventional disease management, which takes an existing product and applies a generic educational intervention. In other words, it would represent a form of personalized medicine that does not rely on targeted molecules but on tailored patient-engagement interventions.

### Integrated Medication Management

A paradigm shift in how medical products and services will be paid for in the future opens up new paths for pharmaceuticals to introduce service-based models. Payers are starting to test payment systems under which they reward results instead of purchasing products and services. For example, in the United States, Accountable Care Organizations (ACOs) are emerging that contract for the provision of all required care for a population under explicit quality targets and gain-sharing agreements.<sup>5</sup> In the UK, plans are under discussion to form Clinical Commissioning Groups, large primary-care practices that would receive risk-adjusted budgets to manage care for an assigned population (King’s Fund, 2011).

Such arrangements could transform care delivery because they give providers greater flexibility in how to allocate resources and remove the incentive to orient care decisions according to particularities of the

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**Just realizing one-tenth of the value left in lack of adherence would trump the revenue of a new blockbuster drug.**

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from diabetes is \$71 billion (18.8 million × \$3,756) (CDC, 2011; AHA, 2012).

<sup>5</sup> Under gain-sharing agreements, the cost of care for a patient population is estimated in advance. If a provider can provide care at lower-than-expected cost, it gets to keep part of the savings. Sometimes, if a provider has higher-than-expected costs, it is subject to penalties.

reimbursement system. But they also shift financial risk and additional care-management responsibilities to providers, which will be interested in finding competent partners to help them share risk and master their new tasks.

Pharmaceutical companies have made initial steps with crude, outcome-based payments for targeted cancer treatments, such as the Velcade® Response Scheme in the UK, under which the manufacturer reimburses the National Health Service if a patient does not respond to the drug (National Institute for Health and Clinical Excellence, 2009; Hughes, 2007). Similarly, Italy has introduced outcome-based payments for new oncology drugs.<sup>6</sup> Although those schemes are mostly meant to ensure market access for high-cost drugs, they illustrate that risk-sharing and payment based on outcomes can be mutually beneficial for companies and payers.

An advanced risk-sharing model could offer overall medication management for entire patient populations on a per-patient fee basis. The fee would reflect expected drug treatment cost based on patient characteristics, as well as expected cost of care for defined exacerbations, such as hospital admissions for uncontrolled hypertension. Thus, the pharmaceutical company would assume financial risk and can reap rewards, if it manages drug therapy for a patient well, and lose money otherwise. This entity, which could be called an Accountable Treatment Organization (ATO), could partner directly with an ACO to agree on a formulary and treatment algorithms, and thus cut out intermediaries, such as distributors and PBMs. The attraction of this particular model is that it aligns the commercial interest of manufacturers in increasing sales with the policy goal of optimizing patient care. It also encourages rational use of later-generation originator drugs with improved tolerability and potency for patients with conditions that cannot be controlled with generics or who experience side effects because companies would be able to benefit from sales of generics as well. Part of rational use could be genetic testing to identify patients whose molecular or genetic disease dependencies makes them likely to benefit from a given drug or who cannot tolerate a given drug.

Clearly, designing and implementing such models is challenging; it requires advanced statistical methods to predict future medication cost based

on patient characteristics and research to determine which exacerbations can be deemed to be under the control of the ATO. But large pharmaceutical companies have all the building blocks to develop such models: unrivaled knowledge of disease biology, huge volumes of clinical data from trials and observational studies, and robust health economics capabilities. They also have the means to make the required investments into future business models and the balance sheets to assume financial risk.

Such models would be attractive for companies that have strong portfolios in selected disease areas, such as GSK and AstraZeneca in asthma and chronic obstructive pulmonary disease (COPD) or Sanofi in diabetes. They could also be explored in high-risk populations that are traditionally underserved by the established medical care system and commonly experience high-cost exacerbations, such as complex geriatric care and care for patients with severe mental health conditions. Both patient groups are frequently institutionalized, and stabilizing them and keeping them in a community setting would be rewarding, as well as cost-saving. In particular, the integration of medical and social protection systems, such as is planned in the UK, creates opportunities for such models.

## Conclusions

At the dusk of the blockbuster era, large pharmaceutical companies find themselves in dire need for innovation to sustain their revenues and profits. Our analysis has shown that moving from mass-market drugs to niche products with very high prices cannot be the only solution. As in many mature product markets, companies need to find a way to marry their products to value-added services and define business models to turn the value into revenue, i.e., move from selling pills to selling outcomes. The opportunity is clearly there because prescription drugs are underused, and better adherence to evidence-based treatment regimens could both save lives and reduce cost.

We have laid out several business models of increasing complexity that would allow pharmaceutical companies to capture the value of improving adherence. Implementing those models will require a great deal of technical sophistication and political savvy. Any service model marketed by pharmaceutical companies will be scrutinized by multiple stakeholders for potentially being a disguised sales tool. Thus, companies need credible partners in the development phase and must work closely with stakeholders to achieve transparency. They need sound procedures to ensure that medication choices are

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**An advanced risk-sharing model aligns the commercial interest of manufacturers in increasing sales with the policy goal of optimizing patient care.**

<sup>6</sup> Between July 2006 and June 2009, risk-sharing agreements have been adopted with respect to 13 drugs (for 17 treatments), including sorafenib for hepatocarcinoma, dasatinib and nilotinib for acute myeloid leukemia, temsirolimus for renal-cell carcinoma, and pegaptanib and ranibizumab for age-related macular degeneration (see Lucioni, Mazzi, and Polcaro, 2010; Messori, 2010).

driven by clinical evidence and patient needs without bias for own products. And they must subject their models to objective and rigorous evaluation. None of that will be easy, nor will it be possible for every company in every market. Because substantial investments will be required, all stakeholders involved will have to engage in an open dialogue on how to ensure appropriate financial returns for companies.

But the successful implementation of such models would redefine the role of the pharmaceutical industry as part of the solution to ever-increasing health care costs. And it would make its success less dependent on high-risk product development in an uncertain environment.

## References

Aggarwal, Saurabh, "Targeted Cancer Therapies," *Nature Reviews Drug Discovery*, Vol. 9, June 2010, pp. 427–428.

American Cancer Society, "Cancer Prevalence: How Many People Have Cancer?" last revised October 18, 2011. As of May 24, 2012:  
<http://www.cancer.org/Cancer/CancerBasics/cancer-prevalence>

American Heart Association, *Heart and Stroke 2012 Statistical Update*, c. 2012. As of May 24, 2012:  
[http://my.americanheart.org/professional/General/Heart-Stroke-2012-Statistical-Update\\_UCM\\_434526\\_Article.jsp](http://my.americanheart.org/professional/General/Heart-Stroke-2012-Statistical-Update_UCM_434526_Article.jsp)

Bain and Company, "Has the Pharmaceutical Blockbuster Model Gone Bust?" press release, New York, December 8, 2003. As of May 24, 2012:  
<http://www.bain.com/about/press/press-releases/has-the-pharmaceutical-blockbuster-model-gone-bust.aspx>

Barlas, Stephen, "Pfizer RFID Tags Its Lot of Viagra," *Healthcare Packaging*, December 10, 2005. As of May 24, 2012:  
[http://www.healthcarepackaging.com/archives/2005/12/pfizer\\_rfid\\_tags\\_its\\_lots\\_of\\_v.php](http://www.healthcarepackaging.com/archives/2005/12/pfizer_rfid_tags_its_lots_of_v.php)

Berg, J. S., J. Dischler, D. J. Wagner, J. J. Raia, and N. Palmer-Shevlin, "Medication Compliance: A Healthcare Problem," *Annals of Pharmacotherapy*, Vol. 27, No. 9, September 1, 1993, pp. 1–24.

Burke, Lora E., Elizabeth A. Schlenk, and Cynthia Rand, "Behavioral Strategies to Improve Medication-Taking Compliance," in Lora E. Burke and Ira S. Ockene, eds., *Compliance in Healthcare and Research*, Armonk, N.Y.: Futura Publishing Company, 2001, pp. 57–72.

Centers for Disease Control and Prevention, "National Diabetes Fact Sheet," 2011. As of May 24, 2012:  
[http://www.cdc.gov/diabetes/pubs/pdf/ndfs\\_2011.pdf](http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf)

DiMasi, Joseph A., Ronald W. Hansen, and Henry G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics*, Vol. 22, No. 2, March 2003, pp. 151–185.

Eli Lilly and Company, "Lilly Invests \$30 Million in Partnership to Address Non-Communicable Diseases," press release, Indianapolis, Ind., September 13, 2011. As of May 24, 2012:  
<http://newsroom.lilly.com/releasedetail.cfm?ReleaseID=604828>

Garnier, Jean-Pierre, "Rebuilding the R&D Engine in Big Pharma," *Harvard Business Review*, May 2008.

Harrop, Peter, "RFID in Healthcare: An Enabling Technology," *Asian Hospital and Healthcare Management*, undated. As of May 24, 2012:  
[http://www.asianhbm.com/knowledge\\_bank/articles/RFID\\_Healthcare.htm](http://www.asianhbm.com/knowledge_bank/articles/RFID_Healthcare.htm)

Hicks, K. A., S. J. Karve, A. Vlahiotis, S. G. Frazee, Y. Tian, and S. R. Earnshaw, "PHP59 Estimation of Increases in Direct Medical Expenditures Associated with Medication Nonadherence and Potential Savings from Increased Adherence," poster presented at the International Society for Pharmacoeconomics and Outcomes Research 14th Annual European Conference, Madrid, Spain, November 5–8, 2011.

Ho, P. Michael, John S. Rumsfeld, Frederick A. Masoudi, David L. McClure, Mary E. Plomondon, John F. Steiner, and David J. Magid, "Effect of Medication Nonadherence on Hospitalization and Mortality Among Patients with Diabetes Mellitus," *Archives of Internal Medicine*, Vol. 166, No. 17, September 2006, pp. 1836–1841.

Hughes, Bethan, "Novel Risk-Sharing Scheme Puts the Spotlight on Biomarkers," *Nature Reviews Drug Discovery*, Vol. 6, December 2007, p. 945. As of May 24, 2012:  
<http://www.nature.com/nrd/journal/v6/n12/full/nrd2478.html>

Hunt, Vivian, Nigel Manson, and Paul Morgan, "A Wake-Up Call for Big Pharma," *McKinsey Quarterly*, December 2011.

IMS Institute for Healthcare Informatics, *The Use of Medicines in the United States: Review of 2010*, Parsippany, N.J., April 2011. As of May 24, 2012:  
[http://www.imshealth.com/deployedfiles/imshealth/Global/Content/IMS%20Institute/Static%20File/IHII\\_UseOfMed\\_report.pdf](http://www.imshealth.com/deployedfiles/imshealth/Global/Content/IMS%20Institute/Static%20File/IHII_UseOfMed_report.pdf)

International Federation of Pharmaceutical Manufacturers and Associations, *Non-Communicable Disease Health Partnerships and Programs Worldwide*, Geneva, May 2, 2011.

- King's Fund, "Clinical Commissioning: What Can We Learn from Previous Commissioning Models?" updated August 12, 2011. As of May 24, 2012: [http://www.kingsfund.org.uk/current\\_projects/the\\_nhs\\_white\\_paper/gp\\_commissioning.html](http://www.kingsfund.org.uk/current_projects/the_nhs_white_paper/gp_commissioning.html)
- Ling, Anthony, Sarah Forrest, Marc Fox, and Stephan Feilhauer, "Introducing GS SUSTAIN," Goldman Sachs Group, June 22, 2007. As of May 24, 2012: [http://www.unglobalcompact.org/docs/summit2007/g\\_s\\_esg\\_embargoed\\_until030707pdf.pdf](http://www.unglobalcompact.org/docs/summit2007/g_s_esg_embargoed_until030707pdf.pdf)
- Lucioni, C., S. Mazzi, and F. Polcaro, "Il Risk Sharing Come Applicazione del Value Based Pricing," *Pharmacoeconomics*, Vol. 12, No. 2, July 1, 2010, pp. 71–80.
- Malik, Nafees N., "Biotech Acquisitions by Big Pharma: Why and What Is Next," *Drug Discovery Today*, Vol. 14, No. 17–18, September 2009, pp. 818–821.
- Mattke, Soeren, Marla C. Haims, Nono Ayivi-Guedehoussou, Emily M. Gillen, Lauren E. Hunter, Lisa Klautzer, and Tewodaj Mengistu, *Improving Access to Medicines for Non-Communicable Diseases in the Developing World*, Santa Monica, Calif.: RAND Corporation, OP-349-IFPMA, 2011. As of May 24, 2012: [http://www.rand.org/pubs/occasional\\_papers/OP349.html](http://www.rand.org/pubs/occasional_papers/OP349.html)
- "Medicamentos falsos são consumidos em grande quantidade no Brasil," *Portal Educação*, August 2, 2010. As of May 24, 2012, in Portuguese: <http://www.portaleducacao.com.br/farmacia/noticias/41480/medicamentos-falsos-sao-consumidos-em-grande-quantidade-no-brasil>
- Mendis, S., D. Abegunde, S. Yusuf, S. Ebrahim, G. Shaper, H. Ghannem, and B. Shengelia, "WHO Study on Prevention of Recurrences of Myocardial Infarction and Stroke (WHO-PREMISE)," *Bulletin of the World Health Organization*, Vol. 83, No. 11, November 2005, pp. 820–829.
- Messori, Andrea, "Outcome Based Schemes Are More Common Than You Think," *BMJ*, Vol. 341, July 2010, p. c3588.
- Miller, Stephen, "McSurgery: A Man Who Saved 2.4 Million Eyes," *Wall Street Journal*, August 5, 2006, p. A6.
- Mintz, Cliff, "E-Pedigree Track and Trace: What Are the Next Steps?" *Life Science Leader*, undated. As of May 24, 2012: <http://www.lifescienceleader.com/magazine/past-issues3/item/3339-e-pedigree-track-and-trace-what-are-the-next-steps>
- Miranda, J. J., S. Kinra, J. P. Casas, G. Davey Smith, and S. Ebrahim, "Non-Communicable Diseases in Low- and Middle-Income Countries: Context, Determinants and Health Policy," *Tropical Medicine and International Health*, Vol. 13, No. 10, October 2008, pp. 1225–1234.
- National Institute for Health and Clinical Excellence, "NICE Recommends a Scheme to Make Bortezomib (Velcade) for Multiple Myeloma Accessible to NHS Patients," press release, last updated June 18, 2009. As of May 24, 2012: [http://www.nice.org.uk/newsroom/pressreleases/pressreleasearchive/2007\\_018\\_nice\\_recommends\\_a\\_scheme\\_to\\_make\\_bortezomib\\_velcade\\_for\\_multiple\\_myeloma\\_accessible\\_to\\_nhs\\_patients.jsp](http://www.nice.org.uk/newsroom/pressreleases/pressreleasearchive/2007_018_nice_recommends_a_scheme_to_make_bortezomib_velcade_for_multiple_myeloma_accessible_to_nhs_patients.jsp)
- New England Healthcare Institute, *Thinking Outside the Pillbox: A System-Wide Approach to Improving Patient Medication Adherence for Chronic Disease*, research brief, August 2009. As of May 24, 2012: [http://www.nehi.net/publications/44/thinking\\_outside\\_the\\_pillbox\\_a\\_systemwide\\_approach\\_to\\_improving\\_patient\\_medication\\_adherence\\_for\\_chronic\\_disease](http://www.nehi.net/publications/44/thinking_outside_the_pillbox_a_systemwide_approach_to_improving_patient_medication_adherence_for_chronic_disease)
- Novartis, "Social Business Initiative," undated web page. As of May 25, 2012: <http://www.novartis.com/corporate-responsibility/access-to-healthcare/our-key-initiatives/social-business.shtml>
- Osterberg, Lars, and Terrence Blaschke, "Adherence to Medication," *New England Journal of Medicine*, Vol. 2005, No. 353, August 4, 2005, pp. 487–497.
- Paul, Steven M., Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg, and Aaron L. Schacht, "How to Improve R&D Productivity: The Pharmaceutical Industry's Grand Challenge," *Nature*, Vol. 9, March 2010, pp. 203–214.
- "Pills Get Smart: Potential Encapsulated," *Economist*, January 14, 2010. As of May 24, 2012: <http://www.economist.com/node/15276730>
- Pleis, J. R., B. W. Ward, and J. W. Lucas, "Summary Health Statistics for U.S. Adults: National Health Interview Survey, 2009," *Vital Health Statistics*, Vol. 10, No. 249, 2010.
- Rasmussen, Bruce, *Response of Pharmaceutical Companies to Biotechnology: Structure and Business Models*, Victoria University of Technology, Centre for Strategic Economic Studies Working Paper 33, August 2007. As of May 25, 2012: [http://www.cfses.com/documents/pharma/33-Pharmaceutical\\_Business\\_Models\\_Rasmussen.pdf](http://www.cfses.com/documents/pharma/33-Pharmaceutical_Business_Models_Rasmussen.pdf)

Roebuck, M. Christopher, Joshua N. Liberman, Marin Gemmill-Toyama, and Troyen A. Brennan, "Medication Adherence Leads to Lower Health Care Use and Costs Despite Increased Drug Spending," *Health Affairs*, Vol. 30, No. 1, January 2011, pp. 91–99.

Singer, Natasha, "Drug Firms Apply Brand to Generics," *New York Times*, February 15, 2010. As of May 24, 2012:  
[http://www.nytimes.com/2010/02/16/business/16generic.html?\\_r=1](http://www.nytimes.com/2010/02/16/business/16generic.html?_r=1)

Sokol, Michael C., Kimberly A. McGuigan, Robert R. Verbrugge, and Robert S. Epstein, "Impact of Medication Adherence on Hospitalization Risk and Healthcare Cost," *Medical Care*, Vol. 43, No. 6, June 2005, pp. 521–530.

Torsoli, Albertina, and Meg Tirrell, "Sanofi to Buy Genzyme for Sweetened \$20.1 Billion After Nine-Month Pursuit," *Bloomberg*, February 16, 2011. As of May 24, 2012:  
<http://www.bloomberg.com/news/2011-02-16/sanofi-aventis-agrees-to-buy-genzyme-for-74-a-share-in-19-2-billion-deal.html>

Vitality, "Introducing GlowCaps™," undated web page. As of April 11, 2012:  
[http://www.vitality.net/glowcaps\\_howglowcapswork.html](http://www.vitality.net/glowcaps_howglowcapswork.html)

Wagner, A. K., A. J. Graves, S. K. Reiss, R. Lecates, F. Zhang, and D. Ross-Degnan, "Access to Care and Medicines, Burden of Health Care Expenditures, and Risk Protection: Results from the World Health Survey," *Health Policy*, Vol. 100, No. 2–3, May 2011, pp. 151–158.

Whalen, Jeanne, and Mimosa Spencer, "Sanofi Wins Long-Sought Biotech Deal," *Wall Street Journal*, February 17, 2011. As of May 24, 2012:  
<http://online.wsj.com/article/SB10001424052748703373404576147483489656732.html>

World Health Organization, *Adherence to Long-Term Therapies: Evidence for Action*, Geneva, 2003. As of May 24, 2012:  
[http://www.who.int/chp/knowledge/publications/adherence\\_report/en/index.html](http://www.who.int/chp/knowledge/publications/adherence_report/en/index.html)

———, "Counterfeit Medicines: An Update on Estimates," November 15, 2006. As of May 24, 2012:  
<http://www.who.int/medicines/services/counterfeit/impact/TheNewEstimatesCounterfeit.pdf>

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