

Maintaining Attractive Biopharma Returns in the Face of Healthcare Reform

Perspectives from Health Advances and Cowen Healthcare Royalty Partners

Healthcare reform is the Obama Administration's top domestic priority. The rigorous debates have focused on three key components: access to care, cost of care, and value of care in the U.S. healthcare system.

Investors are grappling with how these three components of reform will affect the favorable returns traditionally captured in the biopharma sector – a sector that is already feeling pressure from patent expirations, fewer drug approvals, and growing development costs. Biopharma executives are working hard to influence the path that the government takes and are seeking solutions that will offset both top-line and bottom-line pressure created by cost containment measures.

While the Administration has succeeded in creating a sense of urgency around the need for some level of reform, it is important to remember that altering almost 20% of the nation's GDP is bound to be incremental and evolutionary, no matter how bold and revolutionary the legislative impetus. As a political process, the complexion of reform is likely to change frequently, both before and after enactment.

Expanding healthcare coverage to some percentage of the uninsured will grow drug unit volume, but per unit price cuts and more restrictive drug coverage will have a negative impact on revenues and profit. R&D expenditures could increase as evidence-based or value-based medicine emerges in the biopharma industry similar to what is occurring within the medical device sector.

So what can be done by biopharma companies? In addition to reducing costs through traditional means, biopharma will need to change fundamental elements of its business model and adopt new solutions. Examples of new solutions to be discussed in this article include:

- ▲ Creating subsidiaries and partnerships to increase participation in the follow-on biologics and/or generics markets, and implementing new lifecycle strategies.
- ▲ Exploring partnerships with healthcare providers to create cost-effective care solutions under capitation systems.
- ▲ Contracting with health insurance providers and pharmacy benefit managers to offer discounts based on patient outcomes and compliance.
- ▲ Exploring integration with device and service companies to reduce costs in the overall healthcare system while capturing more value.
- ▲ Investing in personalized medicine by pursuing research of biomarkers that link treatments to responsive patient segments.
- ▲ Continuing to invest in R&D of high impact therapeutics and novel clinical trial designs that clearly demonstrate strong health economic benefit to both patients and the healthcare system.

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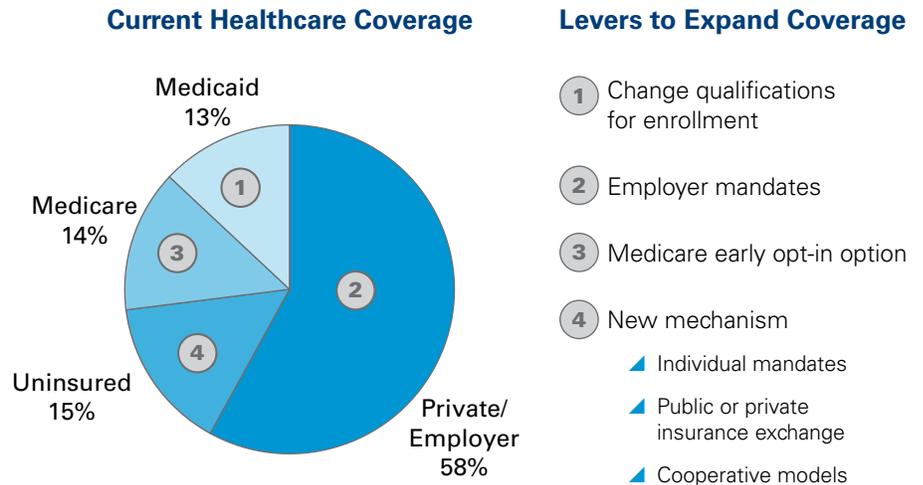
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Access to Care: Expanding the Market for the Biopharma Industry

Access to healthcare in the United States is far from universal; about 46 million Americans (roughly 15% of the population) are currently without healthcare insurance.¹ The need to expand healthcare coverage is thus a driving force in the movement to reform the healthcare system. The debate over this issue centers on the question of what is the most efficient way to provide the uninsured with access to healthcare.

Healthcare coverage could be expanded in a number of ways (see Figure 1). For example, coverage for low-income Americans could be increased by redefining the qualifications for enrollment in the Medicaid program. Allowing a Medicare buy-in for people between the ages of 60 and 64 would also reduce the number of uninsured, and the private insurance market could be expanded by imposing harsh financial penalties on employers who do not provide healthcare insurance for their employees. Other mechanisms for expanding coverage include a mandate that would require all individuals to have healthcare coverage or be subject to a fine, public or private insurance

Figure 1: Healthcare Coverage in the U.S.



Source: Kaiser Family Foundation.

exchanges that would provide more affordable buy-in coverage for people not covered by other programs, and non-profit healthcare cooperatives. Non-profit healthcare cooperatives have received considerable attention recently as Democrats in Congress have begun backing down from a public model. These cooperatives could take many different forms, including patient-owned integrated health systems and purchasing cooperatives. Examples of existing co-ops are HealthPartners, based in Minnesota, and Group Health

Cooperative, headquartered in Seattle.

Figure 2 shows three pieces of reform legislation that were originally being discussed in Congress. More recently, the Baucus bill came out with more details on its proposal. It is unlikely that any of these bills will be passed in their present state. Although one of their primary goals is to increase access to healthcare, none of these bills would guarantee coverage for all of the 46 million people who are currently uninsured. In their analysis of the proposed legislation, the Congressional Budget Office and the Joint Committee on Taxation estimate that these bills would result in a net increase in the insured population of between 16 million and 37 million, so at best, 9 million people would presumably still be uninsured.²

There are lessons to be learned by looking at the experiences states have had in expanding healthcare coverage. Reform legislation enacted in Hawaii and Massachusetts has taken dramatically different routes. Each approach has succeeded in reducing the number of uninsured in those states, but each has not been without some negative outcomes (see sidebar).

Congress will continue to debate access plans over the next few months. However, the arguments are focused not on whether to provide coverage for the uninsured but on which vehicle offers the best care at the lowest cost

Figure 2: Proposed Legislation

	Senate Health Committee	Senate Finance Committee (Baucus)	House Tri-Committee
Plan Design	<ul style="list-style-type: none"> Expansion of Medicaid eligibility Non-profit Health Benefit Gateways possibly run by the government 	<ul style="list-style-type: none"> Expansion of Medicaid eligibility Network of non-profit health insurance cooperatives in each state with varying plans 	<ul style="list-style-type: none"> Expansion of Medicaid eligibility National Health Insurance Exchange which would offer plans at basic, enhanced, and premium levels
Mandates	<ul style="list-style-type: none"> Individual Employer mandate requires 60% contribution and coverage for all companies > 25 people 	<ul style="list-style-type: none"> Individual Employer mandate requires coverage for all companies > 50 people 	<ul style="list-style-type: none"> Individual Employer mandate with most extensive coverage (65% for single plan) with a penalty of 8% paid into a trust fund
Additional Taxes	<ul style="list-style-type: none"> None outlined 	<ul style="list-style-type: none"> Insurance companies Biopharma Employers 	<ul style="list-style-type: none"> Progressive income taxes on those earning \$350K and higher
Estimated Cost (over 10 years)	\$615 billion	\$829 billion	\$1 trillion

Source: Kaiser Family Foundation, Senate and House reform bills, CBO.

In 1974, Hawaii passed a law requiring employers to provide health insurance coverage for all employees who work more than 20 hours per week. The law set a minimum standard for benefits provided by employer-paid insurance and a maximum for employee contributions to insurance premiums based on income. Today, the Hawaiian health insurance system operates solely through private insurers—no public management or financing is involved—and critics argue that it has created a monopoly of insurance providers. They claim that large insurers use their power in the market to offer low-cost plans to large, low-risk businesses while charging higher prices to small businesses. In addition, although the number of Hawaiians without health insurance has decreased significantly since 1974, 8.3% of the population remains uninsured.³ One reason that the uninsured rate is this high is that the law does not cover dependents of employees, nor does it cover the self-employed and unemployed. Another reason is that many employers avoid the law simply by hiring employees to work less than 20 hours a week. According to a University of Hawaii study, the state's percentage of private-sector, part-time employees without employer-paid health insurance is the highest in the nation.

In 2007, Massachusetts passed legislation that mandated health insurance for all individuals. At that time, the percentage of Massachusetts residents without health insurance was far less than the national average, and employers in Massachusetts were more likely to provide employees with health insurance than were those in other states (70%, as compared with 60% nationally).⁴ The law couples an individual mandate with employer mandates. The results of this legislation have been mixed. On the one hand, the number of people in Massachusetts without health coverage decreased from 6% of the population in 2007 (compared with a national average of 15%) to 2.6% currently.⁵ On the other hand, the state is having a difficult time financing the new system.⁶ Because the fines imposed by the employer mandates were not large enough to motivate all employers to provide coverage, the uninsured population has been larger than the legislators estimated. That, together with a growing unemployment rate, has caused an increase in enrollment in the state's subsidized health care plan (which is currently at about 181,000).⁷ Coupled with decreasing tax revenues, these factors have created what seems to be an unsustainable system.

without restricting individual preferences. While it is hard today to know which plan will move forward, expanded healthcare coverage will increase drug unit volume.

Controlling Costs: Drug Pricing

Regardless of the way in which it is done, expanding access to healthcare will be expensive. The Obama Administration's goal is to keep the increases in healthcare costs to expand access below \$1 trillion over the next 10 years. However, given the growing cost of healthcare, the ultimate price tag could exceed that figure. Over the past 20 years, the cost of healthcare has increased at a rate nearly double that of the overall consumer price index (4.7% vs. 2.5%).⁸ The Centers for Medicaid and Medicare Services (CMS) estimate that the United States spent 16.2% of gross domestic product (GDP) on healthcare in 2007, and they project that healthcare spending will increase to 20.3% of GDP by 2018.⁹ These rates are twice as high as those in Canada and most European countries.¹⁰

Thus, cost reduction is an integral component of the legislation to make health reform in the United States a reality. In 2007, prescription drug spending accounted for 12% of U.S. healthcare expenditures, compared to 31% of expenditures spent on hospital care and 21% spent on physician and clinical services.¹¹ Despite its relatively low share of overall healthcare costs, prescription drug spending receives strong public attention. All three segments will be targets for cost savings.

Figure 3 shows the three main segments of the prescription drug market in terms of sales dollars. The largest segment is referred to as branded drugs; these are typically oral agents that are protected from generic substitution. The second largest segment is biologics; these are typically injected and have no direct generic substitutes (there is currently no process in place for FDA approval of follow-on biologics; developing one is part of the Obama Administration's plan). The smallest segment in terms of sales dollars is generics, but these drugs account for

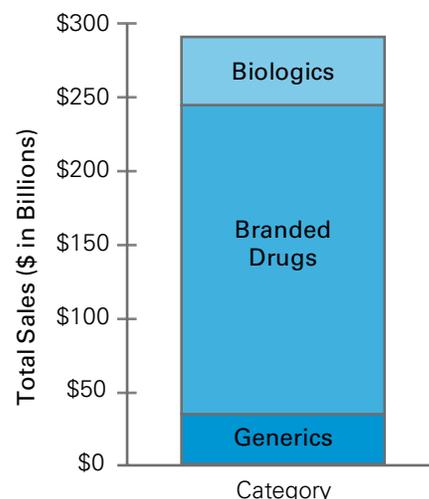
more than 60% of U.S. unit volume.¹² Over the next five years, as patents on major branded drugs expire, branded drugs will continue to lose market share to generics, but are still projected to account for the majority of drug costs. In the short-term, branded drugs will be the segment most affected by cost reductions.

The pharmaceutical industry and its investors are concerned about the reductions that might be forthcoming. Key questions include the following:

- ▲ How will publicized industry commitments to lower drug costs affect revenues?
- ▲ Which segments of the prescription drug market are at greatest risk of cost reduction? Will individual drug classes be targeted?
- ▲ Will formularies become more restricted?
- ▲ How will drug pricing be negotiated?
- ▲ Which changes will be driven by private insurers, and which will be driven by government mandates?

In its plan to provide universal health coverage, the Obama Administration has asked for cuts in the costs of drugs for Medicaid and Medicare enrollees. In June 2009, the pharmaceutical

Figure 3:
2008 U.S. Prescription Sales



Source: IMS Health.

industry agreed to lower drug costs by \$80 billion over the next 10 years; \$30 billion of the proposed reduction is to come through a 50% discount on prescription drugs for select participants in Medicare Part D during the “donut hole” period (i.e., the period in which senior citizens are required to cover their own drug costs).¹³ While the proposal would reduce out-of-pocket expenses for individuals, it would not reduce government spending and because of current bad debt owing to late payments and missed co-payments, it would also not have much of an impact on pharmaceutical revenues.

Details on how the remaining \$50 billion would be applied are still vague, and Congress has not yet approved the industry’s offer. Direct taxes on the industry have also been considered. One of the provisions in the health-care reform legislation announced by the chairman of the Senate Finance Committee for financing the reform included \$3.2 billion in annual “fees” on drug makers, to be assessed on each company based upon market share.

Beyond taxes, many ideas for cost reduction are currently on the table. These programs are structured to curb drug costs through increased rebates or pricing controls, stronger support for lower cost drugs, in particular generics and follow-on biologics, and caps on the overall cost of care. Each can be evaluated for its potential impact on the pharmaceutical industry.

Increased Rebates/Pricing Controls

The prices of many branded drugs—especially those for which no therapeutic equivalents are available have increased significantly over recent years. The government could employ various tactics to counter price increases, as described below.

Public Program Rebates

The Tri-Committee Bill presently before Congress proposes to increase Medicaid rebates from 15% to 22.1% of average manufacturer price (AMP) and to extend Medicaid rebates to dual eligibles (people enrolled in both Medicare and Medicaid) covered by Medicare Part D. Dual eligibles account

for about 25% of Part D enrollees.¹⁴

Anti-psychotic, anti-depressant, cardiovascular, diabetes, anti-epileptic, and ulcer drugs would be the drug classes most affected by the proposed legislation as these drugs are the largest classes prescribed by Medicaid and Medicare programs today. Current projections estimate a 3.2-5.7% sales decline if these rebate changes occur.¹⁵

Direct Government Negotiation

Medicare Part D has a non-interference clause that prohibits the government from negotiating directly with manufacturers on drug prices. In the European Union, national authorities can contract directly with drug manufacturers, which enables them to achieve significant volume discounts and concessions. Given the non-interference clause in Medicare Part D and the impact that a single government purchaser would have on market competition, it is unlikely that direct government negotiation will play a role in the reform of the U.S. health-care system. None of the frontrunners in reform legislation propose removing the interference clause.

Parallel Drug Reimportation

Parallel drug reimportation is the practice of purchasing drugs that have been manufactured abroad at lower prices. Concerns about quality control of imported drugs and the impact of imported drugs on global pricing structures and market entry make it unlikely that parallel drug reimportation will be a part of U.S. healthcare reform. It is even possible to imagine a scenario in which the U.S. pharmaceutical industry stops selling drugs to key international markets that tolerate reimportation. In the EU, where parallel trade is accepted among member countries, manufacturers have protected market-based prices by instituting supply quotas on a regional and/or national basis.

Stronger Support of Lower Cost Drugs

Managed care’s introduction of tiered formularies to manage drug utilization made a significant impact on overall drug spending. Moving forward, both the government and private payers will employ stronger tools to encourage

the use of low-cost drugs over more expensive options.

Therapeutic Substitution

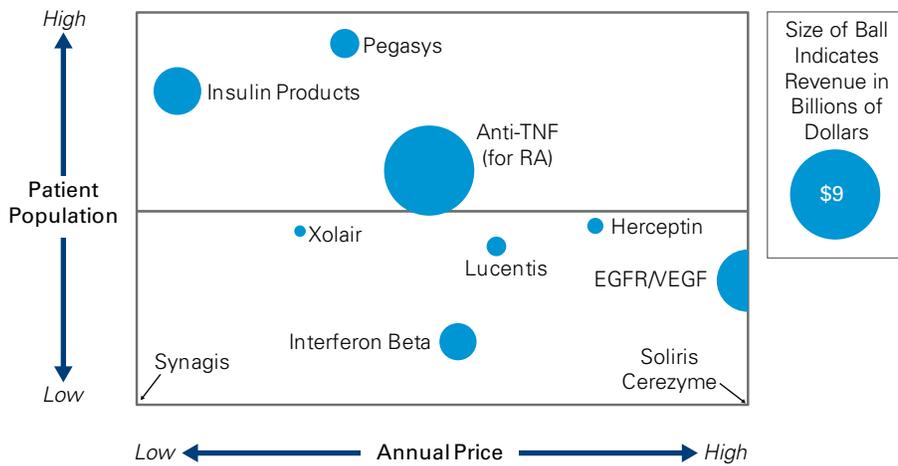
Today, roughly 60% of Medicaid prescriptions are generic. When a branded drug loses patent protection and exclusivity, a generic equivalent can enter the market, and within six to eight months of entry, typically erodes 90% of the branded drug’s sales because of its much lower entry price. This is also because insurance providers often mandate that pharmacists dispense generics even when doctors prescribe branded drugs. However, many patients continue to take branded drugs even though a generic within the same class could provide the same therapeutic benefit (e.g. generic Zocor vs. branded Lipitor within the statin class). Such substitution is called therapeutic substitution, because it is not substitution for the identical molecule. Some states have already mandated therapeutic substitution. The federal government could also mandate therapeutic substitution and thus cause a reduction in the usage of a branded drug class. This could cause a significant decline in several branded drug classes. The drug classes most vulnerable to substitution are statins and anti-depressants, because of their high utilization and the availability of generics; several products within these drug classes could be converted to generics.

Restricted Formularies

Private insurers and large companies that provide health insurance for their employees can control drug costs by excluding expensive drugs from their formularies. For example, Wal-Mart, which is pushing the use of generics and restricting access to branded therapeutic equivalents, has reduced the number of branded drugs in its formulary from 260 to 128.¹⁶ Pharmaceutical companies have responded to restricted formularies by instituting patient assistance programs that minimize the impact of increased co-payments on individuals; however, if payers completely close their formularies, this tactic is less viable.

To date, most strategies like the one used by Wal-Mart have focused on

Figure 4: Example of Current Biologics



Source: Health Advances analysis, NIH, annual reports.

branded drugs, but biologics are also at risk of being excluded in insurance formularies. Typically, insurance providers look at total exposure—not just at the price of therapy—to determine the overall benefit of a drug. Total exposure factors in the price of therapy and the size of the potential patient population. Figure 4 shows that while many biologic therapies are expensive, patient populations tend to be small. A reduction in the price or restricted access to any of these drugs or classes has a lower impact than targeting classes of branded drugs. Only a few classes of biologics have a high risk of being excluded from formularies or being subject to other restrictions. Anti-TNFs, which are biologics primarily used to treat rheumatoid arthritis, constitute one of those classes, given their high pricing and total exposure.

Follow-On Biologics

Creation of a regulatory pathway for follow-on biologics will reduce the costs of certain biologics over the long term. It is estimated that follow-on biologics could undercut the price of some high-priced biologics by 30 to 50%.¹⁷ The determination of a period for data exclusivity must reward innovative products while fostering greater competition (see sidebar for details).

Caps on the Overall Cost of Care

Payers can indirectly manage the costs of drugs by setting limits on what they

will pay for services that include drug administration. Drugs administered at hospitals and clinics are most vulnerable to these tactics.

Capitated Payment Systems

The government can indirectly control increases in drug prices by imposing a cap on payment for episodes of care. One capitated system already in use is the diagnosis-related group (DRG) reimbursement system for hospitals. When payment for repeated episodes of inpatient care has a cap, hospital administrators are more apt to employ cost-effective pharmacy practices and to maintain strict inpatient drug formularies.

An area that is moving to a capitated system is dialysis for end-stage renal disease. In 2008, Congress passed the Medicare Improvements for Patients and Providers Act (MIPPA), which introduced a bundled payment for drugs and services administered at dialysis centers. Before MIPPA was enacted, drugs and services administered at dialysis centers had been reimbursed separately at a rate of average sales price (ASP) plus 6%. Under that system, centers were profiting by using expensive drugs like Epogen. To control drug use and costs, CMS developed the bundled rate, which will be implemented in 2011. Analysts predict that by 2012, the “bundle” will lower sales of Epogen, which currently amount to \$2.5 billion of U.S. dialysis

Focus on Follow-On Biologics

The patents on more than 20 biologics will expire before 2020. Included in this group are several major brands, such as Epogen, Neupogen, Remicade, and Enbrel, whose annual sales by 2020 will have reached nearly \$70 billion in the United States and Europe alone. At present, no pathway exists in the United States for government approval of follow-on biologics. For companies to enter the market with a follow-on biologic once the patent on its biologic counterpart has expired, a full drug approval by the FDA is required, which could cost over \$100 million to complete. The economics currently do not justify entry.

Because follow-on biologics—or biosimilars, as they are also called—have considerable potential for cost savings, legislation concerning them has received a good deal of attention in recent months. The key issues being tackled by the legislation include the time period for data exclusivity once a follow-on biologic pathway is available and the allowance of biologic interchangeability.

Efforts to create a biosimilar market have long been discussed and challenged. The salient issues include:

- ▲ Questions about the feasibility of an actual replication of the biologic produced through complex cell expression systems
- ▲ Lack of regulatory guidelines and of experience among the regulatory agencies in designing a fair and reliable approval process
- ▲ Several layers of intellectual property (IP) protection surrounding biological treatments

Most discussions have revolved around data exclusivity. A biologic would be protected from follow-on biologics for the longer of (1) the time that the brand's patent is valid and enforceable or (2) the exclusivity period as determined by law. New small-molecule drugs typically have five years of data exclusivity. Recently, Congress agreed to a 12-year exclusivity for follow-on biologics.¹⁸ This is considered a huge win for manufacturers of branded drugs.

Once there is a pathway for approval of follow-on biologics, biologic interchangeability becomes the critical issue because it can allow for automatic substitution of prescriptions. This factor is the reason that generics rapidly erode the market share of branded small-molecule drugs. Within six to eight months of the time a generic enters the market, it can erode a brand's market share to less than 10% of its original share. However, the complexity of producing protein-based drugs makes it difficult to produce biologics that function in exactly the same way as the original protein-based drugs. In addition, the reform bills now under consideration have rigorous data requirements for follow-on biologics, including data on immunogenicity that can be obtained only in large clinical trials. Thus, it is unlikely that follow-on biologics will be freely substituted for original biologics in the way generics are substituted for branded drugs. Follow-on biologics will not be adopted as quickly as small-molecule generics. The prices will also not be as low as the prices of generics. Most experts believe the prices of follow-on biologics will be 25 to 50% lower than the prices of branded drugs, as compared with the 80 to 95% discounts given on small-molecule generics.¹⁹

sales, by about 30%.²⁰ The Obama Administration will likely look for other areas in which to employ capitated payment systems.

Reduction in Reimbursement for Provider-Administered Drugs

Experts are predicting a reduction in reimbursement for drugs and infusion services administered in physicians' offices. In 2005, when Medicare shifted from reimbursing at average wholesale price (AWP) less 20% to ASP plus 6%, some physicians, particularly oncologists and urologists, stopped administering intravenous drugs in their offices. Instead, they began prescribing subcutaneous drugs that can be administered at home or sending patients to hospital infusion centers. Private insurers have been slow to shift to reimbursement based on the 2005 Medicare guidelines, but in the opinion of most experts, they will gradually shift to a Medicare-like reimbursement. The profit for physicians is significantly less than it was before the reimbursement system was revised. Companies that offer subcutaneous or oral alternatives to their intravenous products have profited from the revision, but the impact on other pharmaceutical companies has been minimal.

Two more changes in Medicare payments could be on the horizon: CMS may shift reimbursement for office-administered drugs to ASP plus 4% and decrease reimbursement for office-administered infusions by as much as 17%. If the reimbursement rate for infusion services is reduced, the use of intravenous drugs, which are usually expensive, would decline further. It should be noted that shifting patients to home-based subcutaneous injections is not always a less expensive option, given the high pricing of some medications.

Value-Based Healthcare

Although trimming costs has become increasingly critical to the success of any healthcare reform package, the Obama Administration has demonstrated its commitment to maintaining a high quality of healthcare and getting more for the healthcare dollar by

looking closely at the value captured through therapeutic interventions. For example, the American Recovery and Reinvestment Act (ARRA), which President Obama signed into law in February 2009, created the Center for Comparative Effectiveness Research (CER). The CER's mandate is to conduct studies comparing alternative therapeutic methods in terms of their outcomes, as well their impact on healthcare costs. In a report to Congress, a committee of the Institute of Medicine (IOM) recommended that the CER conduct studies of treatment strategies for (in order of priority) cardiovascular disease, the elderly population, gastrointestinal disease, inflammatory diseases, and infection acquired in healthcare settings. The committee also recommended that the CER conduct comparative studies of care models and diagnostics. This is an important distinction because across a list of the top 100 recommendations, very few focused directly on comparison of pharmaceuticals or biologics.²¹

In the same report, the IOM committee defined the CER's purpose as "assisting consumers, clinicians, purchasers and policy makers to make informed decisions that will improve healthcare at both the individual and population levels." The pharmaceutical industry has been actively lobbying to obtain a better definition of how the CER's purpose will translate into physicians' treatment decisions, insurers' coverage, and regulatory approvals (at present, the CER is not linked to the FDA process).

While insurers may look to studies that the CER publishes to inform their reimbursement decisions, in the near term, the CER is likely to take on secondary and observational studies rather than head-to-head trials between branded products. One reason for this is cost. Head-to-head trials, which often require large numbers of patients to show statistically significant differences, can cost \$35 million per trial.²² It does not appear that during the next five years, the CER will function like the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom (which makes recommendations to the National Health Service

whether or not to reimburse specific drugs).

Some pharmaceutical companies are anticipating increased scrutiny of the quality of their products by incorporating the concept of quality, from both a patient and system perspective, into their long-term planning. This may include integrating comparative effectiveness into the drug development process. Developing "me-too" drugs and charging a significant premium for more convenient dosages and routes of administration may not be sustainable strategies in the future.

Although it may be too early for pharmaceutical companies to invest in pure comparative research, over the next few years, they will need to continue building internal capabilities in pharmacoeconomics. Longer-term, direct comparison of new agents with existing standards of care could be likely.

Industry Solutions

In addition to investing in pharmacoeconomic capabilities, key strategies pharmaceutical companies should pursue over the next few years to position themselves successfully under reform include:

- ▲ Participating in generics/follow-on biologics markets
- ▲ Forming partnerships with providers of quality healthcare
- ▲ Integrating products into broader solutions to capture additional value while lowering overall costs
- ▲ Contracting with healthcare insurers on a pay-for-performance basis
- ▲ Investing in personalized medicine

Participation in Generics/ Follow-On Biologics Markets

The pharmaceutical industry has already recognized the growing importance of both standard generics and follow-on biologics. Many manufacturers of branded drugs have begun participating in the small-molecule generics market by selling authorized generics (generics that are exclusively licensed

from a brand company in exchange for a royalty or profit share) or by creating a generics subsidiary. Examples of generics subsidiaries include Novartis' Sandoz and Pfizer's Greenstone LLC. Several companies, including Merck, Wyeth, and Boehringer Ingelheim, have announced launches of businesses dedicated to follow-on biologics. The potential to retain more market share and higher price levels than is possible in the small-molecule market makes the follow-on biologics business attractive to brand manufacturers.

The branded drug and follow-on biologics/generics markets could converge over the next 10 years, with more integration and partnerships between companies and new models for managing the lifecycles of products. The evolution of the traditional pharmaceutical model into a hybrid pharmaceutical/generic or biotechnological/follow-on biologics model could change the dynamics of competition.

Provider Partnerships

When drug therapy is a single component of a comprehensive healthcare plan—which is very often the case—therapeutic decisions about other components of the plan greatly influence how effective any drug is in producing a positive outcome. Over the past few years, an increasing amount of data has shown that outcomes vary by healthcare provider and healthcare model. By partnering with providers of high-quality healthcare, drug manufacturers have a better chance of demonstrating the value of their products. Such partnerships can also reduce the financial risk that capitated and pay-for-performance programs pose for both pharmaceutical companies and healthcare providers.

Michael Porter and Elizabeth Olmsted Teisberg argue that to improve outcomes for patients and at the same time reduce the cost of healthcare, reform should focus on creating value-based competition among healthcare providers. In their opinion, “a move by providers to measure results, make results transparent, and use results information to improve value would be the single most important step in transforming the healthcare system.”²³

Cleveland Clinic is a healthcare provider

renowned for delivering high-quality service. It has been publishing outcome reports on thoracic and cardiovascular surgery, heart disease, digestive diseases, nephrology, and other medical specialties since 1999. These reports compare the clinic's outcome data with national benchmarks even though the clinic is known to take on more difficult cases than most hospitals across the country. It is currently planning to implement a policy that requires each of its clinical departments to develop and publish outcome measures and results. The Cleveland Clinic's model has encouraged the University of Pennsylvania Hospital and Dartmouth-Hitchcock Medical Center to generate similar reports. Porter and Teisberg note that the outcome reporting by Dartmouth-Hitchcock is particularly interesting because the center does not rank at the top on all the outcomes reported.²⁴

The dialysis provider industry is one that has been particularly scrutinized on treatment costs and outcomes in the U.S., given it is largely funded by CMS. Recent legislation, under MIPPA, established quality standards that will take effect in 2012. Dialysis facilities that fail to achieve the established quality standards will have payments reduced by 2%. Furthermore, facility performance scores will be made available to the public. Manufacturers of leading drugs used by dialysis centers, such as erythropoietin-stimulating agents,

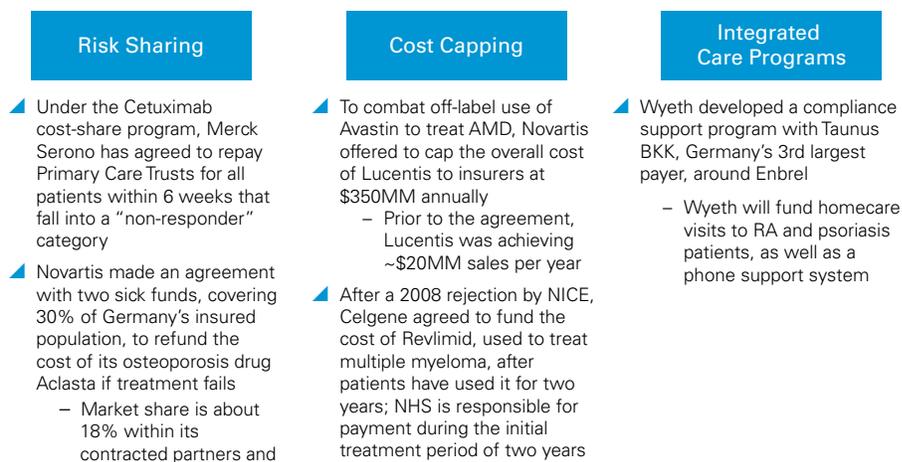
vitamin D analogs, and IV iron, are marketing their products to key dialysis companies by demonstrating how they may achieve strong outcomes in a cost-effective manner. Furthermore, drug companies are exploring partnerships with key dialysis chains to track quality measures associated with their products and to co-administer programs to increase patient adherence.

Given the concern today about the quality of care in a reformed healthcare system, the trend toward outcome reporting will no doubt continue to grow. Although outcome measurement as a means of managing the total cost of care will likely remain provider-driven, increasingly biopharma companies will look to partner with providers in this area.

Pay-for-Performance

Pay-for-performance refers to an increase or decrease in payment that is based on patient outcomes. Although healthcare providers have been the usual participants in pay-for-performance programs, drug manufacturers have recently entered this arena. Outside the United States, pharmaceutical companies have been signing risk-sharing contracts with insurance providers based on the outcomes that their drugs produce. A landmark example is the contract between Janssen-Cilag (a division of Johnson & Johnson) and NICE regarding reimbursement for the multiple myeloma drug Velcade. In exchange for NICE's approval of Velcade

Figure 5: Innovative EU Manufacturer-Payer Programs to Control Drug Costs



Source: Health Advances interviews, ISPOR, Datamonitor 2008, In Vivo 2009, Europharmatoday.com.

for use in patients in their first relapse, Janssen-Cilag agreed to charge for the drug only if patients responded to it and to reimburse the price of the drug when patients did not respond, which the company estimated would be 15% of patients. The Velcade Response Scheme (VRS) set a precedent for risk-contracting with NICE, which was later pursued by companies like Merck, Celgene, and Roche.²⁵ Figure 5 details other innovative cost control partnerships between biopharma companies and payers in the EU.

In the United States, CIGNA and other large health insurance companies have also begun exploring pay-for-performance contracts. For example, CIGNA and Merck signed a contract in which Merck agreed to increase rebates on the diabetes drug Januvia/Janumet if patients comply with treatment and achieve improved HbA1C levels.²⁶

To remain competitive as the focus on pay-for-performance increases, pharmaceutical companies will have to continue to adopt creative contracting strategies. These strategies could entail reimbursing or reducing prices based on patient outcomes or compliance, or sharing costs with insurers based on duration of therapy or competing alternatives.

Device or Service Integration

As reimbursement for certain prescription drugs is decreased, biopharma companies are looking at other ways to capture value. Some companies are looking at selling “total solutions” versus just the product. A simple example is with insulin delivery systems. Currently, medical device companies are being reimbursed for insulin pumps separately from insulin. Insulin companies could consider expanding into insulin delivery devices to help gain market share and potentially increase the sales per patient, while driving overall costs to payers down.

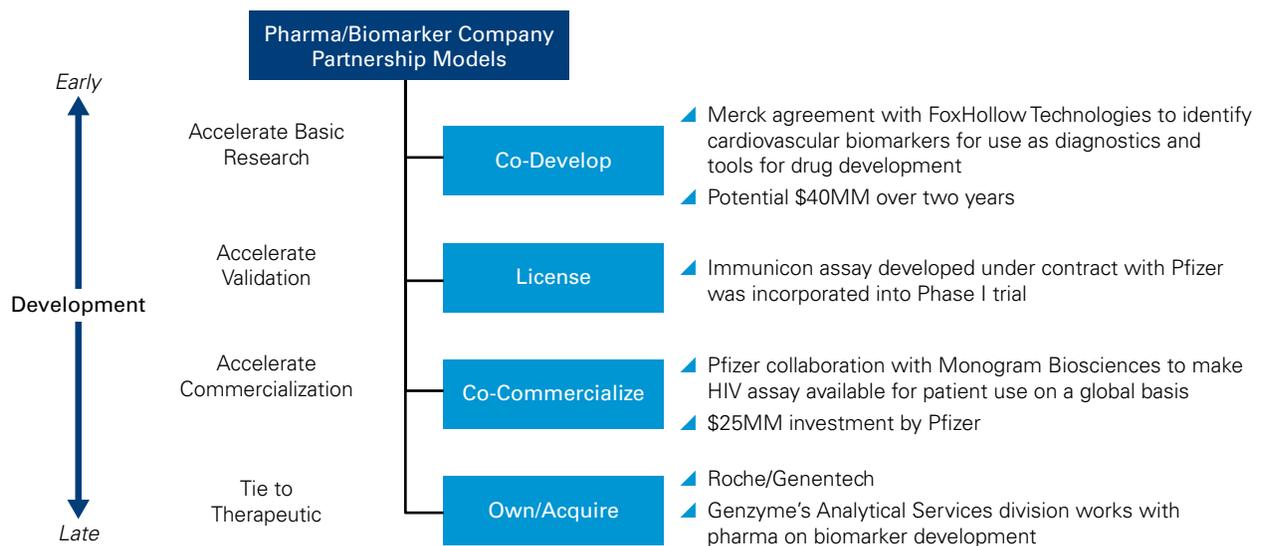
Integration has also been seen between service providers and drugs in the dialysis industry. Fresenius, the leading dialysis chain in the United States, acquired PhosLo, a generic calcium-based phosphate binder. PhosLo is significantly cheaper than branded non-calcium alternatives, such as Renagel, but has side effects associated with higher calcium intake. However, by instructing the technicians in its dialysis centers to adjust a patient’s calcium levels during a dialysis session, Fresenius can manage these side effects while keeping overall costs down. Creating such cost-effective integrated care solutions will receive increased attention in the coming years.

Personalized Medicine

Personalized medicine refers to the practice of developing drugs for segments of patients whose genetic and disease markers make it likely that they will respond to a specific therapy. With an increased focus on quality of care, drug manufacturers will be under more pressure to demonstrate that their products have positive outcomes. Personalized medicine is therefore of growing interest to manufacturers. Biomarkers have been discussed for the last 10 years, and although some markers have failed, the science is progressing rapidly. In the short term, it is unlikely that each patient will have a personalized healthcare plan. However, more specific segmenting of patient populations will ultimately lead to higher response rates.

Oncology has been at the forefront of personalized medicine, and it has given rise to some successful diagnostic-therapeutic partnerships. Four therapies that require a diagnostic prior to use are currently on the market, and two of them relate to oncology. Most notably, Genentech’s Herceptin is linked to the genetic marker HER2/Neu, which predicts response to the therapy. Another example is the diagnostics company DxS. Since the end of 2008, DxS has entered into four partnerships with

Figure 6: Pharmaceutical-Biomarker Company Partnership Models



Source: Health Advances analysis, Company press releases.

pharmaceutical companies (Roche, Amgen, Boehringer Ingelheim, and Astra Zeneca); the goal of these partnerships is to adapt DxS's Therascreen K-RAS and EGFR mutation kits to predict response to cancer therapies.

Although oncology has dominated the field of personalized medicine, to date there has been an increasing amount of collaboration between diagnostic and pharmaceutical companies in other therapeutic areas. For example, in 2009, Bristol Myers Squibb formed a partnership with XDX for the purpose of identifying biomarkers for lupus, which Bristol Myers Squibb will use in developing a drug to treat the disease.²⁷ While much biomarker research is in its early stages, pharmaceutical companies are already showing a strong commitment to personalized medicine. There are precedents for success in this dynamic field: a ground-breaking example occurred in 2006, when Pfizer and Monogram Biosciences agreed to co-market the Trofile assay, which is required to identify responders to Pfizer's novel HIV drug Maraviroc, a CCR5-inhibitor.²⁸ To stay ahead of the changes that healthcare reform is likely to bring, pharmaceutical companies should keep themselves informed of biomarker discoveries in their markets. Figure 6 describes the spectrum of partnership models biopharma companies can pursue with biomarker companies.

Conclusion

It is impossible to predict at this point exactly what the contents and effects of the final healthcare reform bill will be. Among the pressures that healthcare reform is likely to put on biopharma companies are more aggressive efforts to restrict the use of high-priced branded drugs for large patient populations, more use of capitation systems to manage the costs of care, and closer scrutiny of the value of new treatments.

No doubt, certain drug classes are more at risk of losing value, especially if one of the more aggressive proposed bills passes. To respond to the pressures of reform, drug companies will have to develop novel solutions.

And in the long term, the pharmaceutical industry will have to work harder to achieve the same levels of return for its investments as it has in the past.

Some products and companies will continue to provide attractive returns, but others will struggle. Finding the best investment opportunities will require a new set of diligence questions that focus more on the economics of overall care than on the cost benefit of drugs alone. In selecting the winners, it is important to recognize the need for reform to address those areas which can most readily affect healthcare on a national scope. As such, expensive therapies for widely prevalent disorders are most vulnerable to regulation, especially if effective substitutes exist. On the other hand, highly differentiated products addressing niche markets, especially if the underlying disease is severe or life-threatening, are more likely to escape relatively untouched, as even stringent regulation will do little to impact overall resource utilization.

The debate over healthcare reform

promises to be sustained and vigorous, and the nature of the political process ensures that any successful legislation will be a compromise between conflicting interests. It is not possible to predict which of the above elements and tools will be enacted or which of the reforms passed into law will be able to have a material effect on the system. While therapies are effective at forestalling downstream system costs, their costs are highly visible to consumers to an extent disproportionate to their 10% of healthcare expenditures. As a result, the industry must position itself to succeed in a more cost-constrained, value-sensitive environment.

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Cowen Healthcare Royalty Partners ("Cowen Royalty") is a leading global healthcare private equity firm with over \$800 million in capital under management. The Firm invests principally in commercial stage healthcare companies and products through the purchase of traditional passive royalties, the creation of Synthetic Royalties[®], and structured debt and equity instruments.

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