AllianceBernstein

EXECUTIVE SUMMARY

The Dawn of Molecular Medicine

The Transformation of Medicine and Its Consequences for Investors

- Rapid scientific and technological advances are ushering in a new age of molecular medicine
- A future of revolutionary testing, diagnostics and targeted medicine beckons
- The implications for healthcare are profound—creating compelling, but complex, investment opportunities

April 2011

About the Authors

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Amy Raskin is Director of Research of US and Global Growth Equities and is responsible for managing the firm's US and Global Growth Equities analyst teams. She is also the Director of Thematic Research, and has overseen the firm's Research on Strategic Change effort since 2003. Raskin has been CIO of AllianceBernstein Venture Capital Funds since 2008. She joined the firm in 2000 as a US growth equity analyst covering networking and telecom equipment. She previously worked as a telecom equipment analyst for Donaldson, Lufkin & Jenrette, as an investment-banking associate for Lehman Brothers and as a telecommunications products manager for J.P. Morgan. Raskin graduated from the University of Pennsylvania with a BSE in engineering.

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Eli Casdin is a Vice President and an Analyst for Research on Strategic Change. He has spent the last seven years researching the investment implications of new technologies for the life science and healthcare sectors. Casdin joined the firm in 2007 and since 2008 his research has focused on molecular medicine. He was previously at Bear Stearns and, before that, Cooper Hill Partners, a healthcare-focused hedge fund. Casdin holds a BS from Columbia University and an MBA from Columbia Business School.

About Research on Strategic Change

Most fundamental research analysts cover an industry and the companies within it. AllianceBernstein's Research on Strategic Change team seeks to find investable ideas stemming from economic or technological changes that are powerful enough to profoundly influence corporate performance across multiple industries. **The Dawn of Molecular Medicine: The Transformation of Medicine and Its Consequences for Investors** is the group's sixth report. Prior publications include **Broadband: The Revolution Underway** (2004); **China: Is the World Really Prepared?** (2005); **The New Industrial Revolution: De-verticalization on a Global Scale** (2005); **The Emergence of Hybrid Vehicles: Ending Oil's Stranglehold on Transportation and the Economy** (2006); **Abating Climate Change: What Will Be Done and the Consequences for Investors** (2008).

Introduction

How We Expect Scientific and Technological Breakthroughs To Transform Healthcare and Society

The year is 2050. The location is a general hospital somewhere in the US. A baby is born, and a sample of her blood is taken for analysis, as is the norm for all newborns. The sample is sent to a molecular testing facility specializing in the analysis of genomes—the entirety of the hereditary information within us all. The complete genomic code of the baby is read, recorded and stored, and a computer program combs the billions of characters in the record of the baby's genomic code, seeking any one of thousands of particular sequences. The matching sequences found reveal profound molecular information about the baby. In a matter of hours, a comprehensive molecular medical record is generated that indicates everything from her body's likely response to particular drugs to her chances of developing various life-threatening diseases.

Meanwhile, in another wing of the hospital, a doctor is performing a procedure to cure a patient's diabetes. In the next room, another physician is discussing with a patient how he might be able to grow a new eardrum to restore hearing that was lost in an industrial accident.

Sound far-fetched? In our view, the scientific and technological advances detailed in this report make such a future likely. Advances in recent years have already transformed the field of molecular biology from an academic discipline into an engine of innovation and a source of revenue growth for the biotechnology, diagnostic, life sciences and pharmaceutical industries.

Mainstream media coverage of genomics over the last two decades has tended to focus on its more extreme aspects. Fears of genetically engineered foods and the discriminatory use of genetic information have dominated headlines. But scientists' increased understanding of this field is beginning to have a hugely beneficial, and less well-appreciated, impact on medicine.

The important ethical debates about genomics are beyond the scope of this report, as are detailed analyses of the implications of advances in molecular medicine for society and for sectors other than healthcare. Our research focuses on how recent developments in the study of the human genome and, more broadly, molecular and cellular biology are revolutionizing medicine; and on the profound investment consequences of this transformation for the healthcare sector.

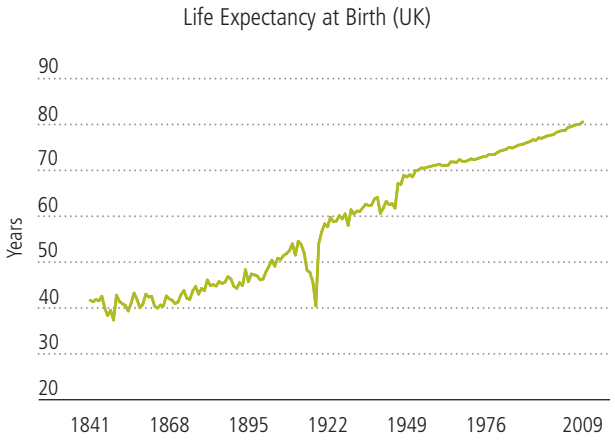
Scientific understanding of molecular biology and its role in human disease is growing quickly. Put simply, in molecular medicine, illness is regarded as a dysfunction in the interactions of biological molecules, rather than simply a collection of symptoms or a breakdown in the function of a particular organ. We would not be surprised if breakthroughs in molecular medicine overturn long-held scientific beliefs. While we do not yet know how scientific understanding will unfold, we are confident that much of what we discuss here will remain pertinent for decades to come.

Germ Theory: A Case History of Medical Revolution

The medical revolution that followed in the wake of the germ theory of disease demonstrates how a major shift in scientific understanding can transform healthcare and extend life expectancy. First proposed in the 19th century, the germ theory held that microbes cause many diseases. This insight led to new standards of hygiene, the introduction and adoption of vaccines, and the discovery of antibiotics.

Display 1

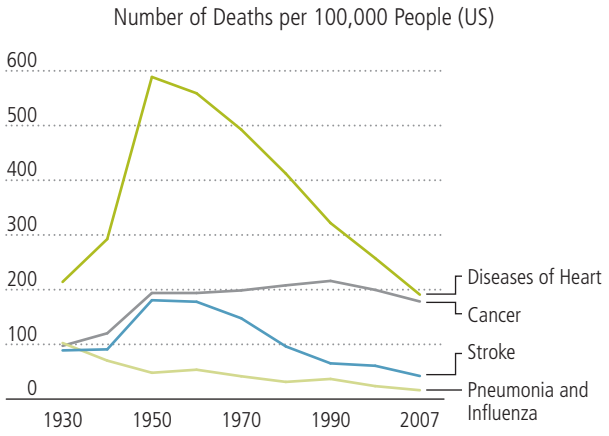
Life Expectancy Has Almost Doubled over the Past 150 Years



Through December 31, 2009
Source: Human Mortality Database

Display 2

Now Versus 1930: Limited Improvements in Survival Rates



Through December 31, 2007
Because of an upward revision of data on diseases of the heart since 1950, the magnitude of increase between 1940 and 1950 may appear more pronounced than it actually was.
Source: US Centers for Disease Control and Prevention

The combination of improved hygiene, vaccination and antibiotics had a dramatic impact. In the UK, which improved hygiene standards early, life expectancy at birth rose from about 42 in 1845 to about 61 in 1930—to 80 today (*Display 1*). Most of the increase in life expectancy through 1940 was attributable to the fact that more children lived past age 10 because they no longer succumbed to infectious disease. From 1940 to 1960, infectious disease declined from the second biggest killer to the sixth. The demographic changes have been spectacular. Prior to 1900, people in their 80s were rare, but they now represent more than 3% of the European population.

Unfortunately, fewer deaths from infectious disease mean that many people now live long enough to get the diseases that tend to occur in older age, such as heart disease and cancer. Survival rates for heart disease and *certain* cancers have shown encouraging improvements over the last few decades amid medical advances, more stringent testing and increased knowledge about the benefits of healthier lifestyles (*Display 2*). But a more refined and complete understanding of the molecular processes involved in particular diseases may improve survival rates much further as new diagnostics and treatments are developed.

Disruption in Healthcare and Beyond

Since its inception in 2003, the Research on Strategic Change team at AllianceBernstein has had the mandate of identifying secular changes in the drivers of economic or industry growth and the companies that are poised to exploit them. Our experience searching for "the next big thing" that may have implications across sectors and industries has taught us that the hallmark of this kind of secular change is a multibillion-dollar shift in value from established companies to emerging ones, usually triggered by a product or business model innovation.

In our view, this kind of disruption is beginning to occur in the healthcare industry. We believe that a sea change is under way in drug research and development and in patient diagnosis and treatment, with major implications for every corner of healthcare, as well as for the technology sector. What's more, this transformation is beginning to accelerate.

The investment implications of these changes will be complex and dramatic. Tremendous opportunities exist for those companies that are helping to make molecular medicine possible and for those that can adapt as old business models are challenged.

For example, we expect that molecular information and technology will create significant revaluation and disruption in the diagnostic industry. We project that molecular diagnostics will generate $21 billion in revenue by 2020—31% of the global diagnostic industry.

We also expect the rise of molecular medicine to transform some devastating acute diseases into chronic, livable conditions. Eventually, some may even become curable. Like germ theory, molecular medicine will likely lead to longer life expectancy in developed countries, which will have vast implications for the provision and use of healthcare and the consumption of goods and services more broadly.

Given the current debate about how to contain rising healthcare costs, it's natural to ask whether molecular medicine will add to the cost of healthcare and if this will be an impediment to its adoption. Clearly, the treatments we envision will be expensive on an absolute basis, but we believe that in many instances, they will prove more efficacious and therefore reduce the need for costly late-stage care. Molecular diagnosis will, we believe, also limit costs because it would determine which patients are unlikely to benefit from potentially expensive treatments because of their molecular makeup. In other words, there is an economic as well as a medical argument in favor of molecular medicine.

In the long term, the longer and healthier lives that could result from widespread adoption of molecular medicine may increase the total lifetime consumption of healthcare. In our view, societies will increasingly need to examine the clinical and economic benefits of treatments. From this perspective, we believe that targeted and precise molecular medical solutions such as drugs and diagnostics will be looked upon more favorably than current treatments that are broad and often ineffective.

When presented with a complex secular investment opportunity such as molecular medicine, investors may be tempted to wait until technologies and markets mature. We believe that would be a mistake. Investors who take a wait-and-see approach risk missing out on opportunities to profit from the companies likely to benefit from the developments we foresee—and instead may invest in companies that could suffer from the disruptive impact of molecular medicine. ■

Key Research Conclusions

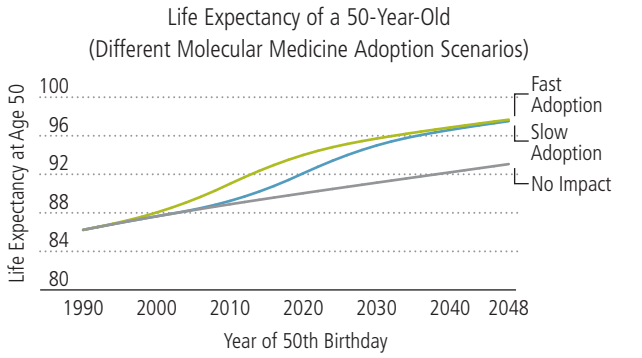
A new era of medicine has begun—the era of molecular medicine. In molecular medicine, illness is regarded as a dysfunction in the interactions of biological molecules, not just as a collection of symptoms or a breakdown in the function of a particular organ. We expect molecular medicine to revolutionize the practice of medicine, transform the global healthcare industry and, ultimately, lead to longer and healthier lives.

The practice of healthcare should change dramatically. New therapies and approaches will redefine the roles of hospitals and physicians. In time and with proper oversight, payers and providers will likely rely on molecular information to manage scarce healthcare resources. Eventually, diseases that are lethal or debilitating today should become chronic and livable. We expect individual life expectancy as a whole to increase. The unfortunate result of living longer, however, is that illnesses such as Alzheimer's disease that affect people later in life will become more prevalent. In both our fast-adoption and slow-adoption scenarios for molecular medicine, in most developed countries life expectancy at age 50 will reach 97, but in the fast-adoption scenario, it will near that point much sooner (*Display 3*). Demand for goods and services—particularly healthcare, financial and discretionary consumer services—will likely change as a result of new consumption patterns.

The drug and diagnostic industries should be affected most by the adoption of molecular medicine. The economics of individual drug markets should change in the medium term as drugs increasingly address smaller subsegments of disease and, in some cases, are used for greater lengths of time. In the longer term, regenerative medicine that restores faulty biological mechanisms will likely disrupt currently large drug markets, but should create new business opportunities. Molecular diagnostics will be highly disruptive, potentially improving profitability and returns among those diagnostic firms that adapt their business models. Eventually, large new user markets and test categories should emerge.

Display 3

Different Paths to a Longer Life



Historical analysis and projections are not a guarantee of future results.
As of December 31, 2010; assumptions are subject to change.
Fast Adoption: Benefit from molecular medicine begins in 2020. Full benefit occurs by 2040, after which improvement in life expectancy tapers off over a 20-year period due to the impact of diseases of older age; no improvement after age 80.
Slow Adoption: Benefit from molecular medicine begins in 2030. Full benefit occurs by 2050, after which improvement in life expectancy tapers off over a 20-year period due to the impact of diseases of older age; no improvement after age 80.
No Impact: no improvement in life expectancy from molecular medicine.
Source: AllianceBernstein

Our conclusions about molecular medicine's likely impact on six subsectors of the *healthcare* industry over various time frames are summarized in *Display 4.* Overall investment implications for each subsector are rated from +++ (highly positive) to – – – (highly negative). A split rating for a given time period (such as +++/– – –) means that the trend will be positive for some industry players and negative for others. We believe that in the medium to long term, the adoption of molecular medicine will facilitate significant healthcare cost savings.

Display 4

Industry Winners and Losers

	Time Frame*		
Sector	**Short**	**Medium**	**Long**
Drug Industry	++/−−	+++	+++/−
Diagnostic Industry	++/−	+++/−	+++
Healthcare Facilities and Services	+/−	+/−−	+/−−
Medical Supplies and Devices	−	+/−−	++/−−
Payers and Providers	N/A	+	+++
Life Science Industry	++	++	+++
Consumption of Goods and Services	N/A	N/A	++
Financial Services	N/A	N/A	++/−−

+++	Highly Positive	−	Negative
++	Very Positive	−−	Very Negative
+	Positive	−−−	Highly Negative

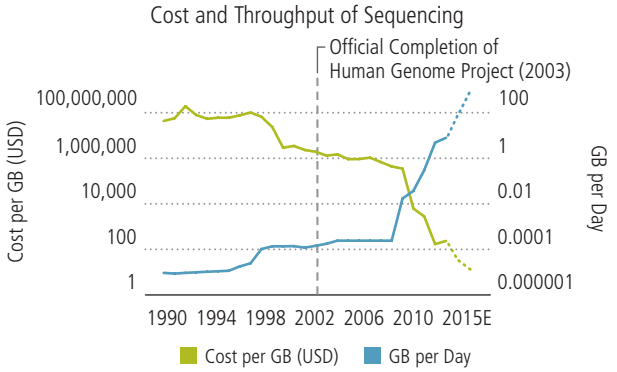
As of March 31, 2011; estimates are subject to change.
**Short is from one to five years; medium, from five to 10 years; and long, beyond 10 years.*
Source: AllianceBernstein

The treatments we envision will likely be expensive on an absolute basis, but we believe that, in many instances, their effectiveness will lessen the need for expensive late-stage care. Molecular diagnosis should facilitate significant cost savings by reducing the use of expensive current treatments in patients who are unlikely to experience any medical benefit. In other words, we see an economic as well as a medical argument in favor of molecular medicine. In our view, societies will increasingly examine the clinical and economic benefits of treatments. Therefore, targeted and precise molecular medical solutions such as drugs and diagnostics should be looked upon more favorably than current treatments that are broad and often ineffective.

Molecular data and research insights have accumulated rapidly in recent years, providing a strong foundation upon which greater knowledge about the molecular biology of disease will be built. Researchers now know the basic composition of the human genome—the entirety of the hereditary information within us all. Complex instruments

Display 5

Sequencing Costs Have Plunged, and Throughput Has Climbed



Historical analysis and projections are not a guarantee of future results.
As of December 31, 2010; estimates are subject to change.
One gigabase (GB) equals 1 billion bases.
Source: Washington University and AllianceBernstein

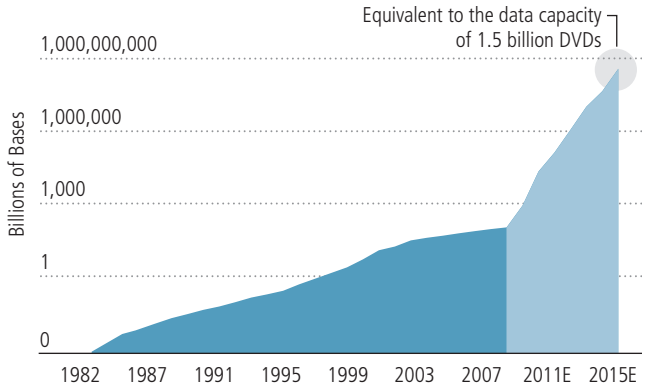
called DNA sequencers read the genomic "code" stored in the biological molecule deoxyribonucleic acid (DNA), which contains instructions regarding biological structure and processes. DNA is the blueprint and production line for human life and disease. Researchers can now probe deeper and ask specific questions about the role of molecular processes in disease.

The rise of molecular medicine is a classic technology-based transformation similar to the advent of the digital information era. In that instance, advances in semiconductor technology drove down the cost of computing, which allowed a growing number of users to apply powerful computing technology to routine activities. Processing speeds doubled every two years and applications for computing exploded, which attracted even more users. The growing user base attracted more innovators to create even more applications and uses for information technology, which then expanded the applicable user population yet again, and the virtuous cycle took off. In the case of DNA sequencing, technology improvements are occurring at an even faster rate, doubling every six months (*Display 5*).

Decreasing costs and increasing speeds have made experiments to uncover links between variations in DNA and human disease much more accessible. Scores of research institutions (and, increasingly, commercial entities) are using sequencers and the molecular data that they generate to

Display 6

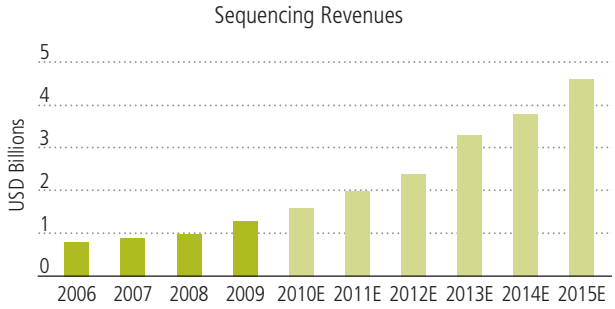
Sequencing Data Generation Should Rise Rapidly, in Our View



Historical analysis and projections are not a guarantee of future results.
As of February 8, 2011; estimates are subject to change.
Projections begin on January 1, 2009, and are in terms of bases from finished sequences, rather than the total number of bases generated (which is considerably higher, as multiple runs are needed to arrive at a complete sequence); DVD comparison assumes conversion rate of one base per byte.
Source: Cisco Systems, GenBank and AllianceBernstein

Display 7

We Expect Rapid Growth in Sequencing Revenues



Historical analysis and projections are not a guarantee of future results.
As of February 15, 2011; estimates are subject to change.
Source: Strategic Directions International and AllianceBernstein

understand molecular biology better. Similar to the digital era described above, a virtuous cycle is in effect: more molecular data are generated as sequencing costs fall and speeds rise, so new insights are gained; researchers purchase even more sequencers to investigate these insights; and through these experiments, researchers generate more data and information about disease at the molecular level.

The collection, processing and storing of molecular information will become a new and large driver of demand for information technology. We expect that the exponential increase in research activity will produce tremendous amounts of molecular data (that will need to be converted into digital information), as seen in *Display 6*. This display shows the amount of molecular data generated by DNA sequencers that is (and will likely be, according to our projections) stored on GenBank, an open-access sequence database. Providers of traditional technologies that analyze digital information should increasingly gear their businesses to serve this new type of user.

The earliest investment opportunities in molecular medicine should occur among the leading suppliers of DNA sequencing technology. We estimate that the sequencing market generated $1.6 billion in annual revenue in 2010 and that it will reach $4.6 billion by 2015—far more than most market participants expect (*Display 7*). Companies competing in this market must continue to innovate to keep pace.

We expect the future clinical application of molecular information to be even more financially and socially rewarding. The applications of molecular medicine are likely to occur in three distinct phases, each significantly disrupting segments of the healthcare industry and prompting innovation in business models.

The first impact should occur over the next few years in the nascent field of molecular diagnostics. We expect the growing use of molecular diagnostics to transform the entire diagnostic industry. We estimate that revenues for molecular diagnostics will increase from 11% ($4.4 billion) of the $40 billion in vitro diagnostic (IVD) industry today to $21 billion (or 31% of an estimated $67 billion industry) by 2020 (*Display 8*). For investors, three areas are noteworthy:

- Use of information from a patient's genome will facilitate more precise prediction of the diseases the individual is most at risk of developing (*Display 9*).
- Molecular information will be applied to the diagnosis and prognosis of cancer (*Display 10, page 8*), dramatically improving patient treatments and outcomes.
- Molecular tests known as companion diagnostics, which determine which drugs work for which patients, will become standard.

As a result of these and other applications, the role of diagnostics in the clinical medicine value chain will change. Successful firms with clinically relevant tests will garner higher unit prices and higher gross margins than historically have been observed in the IVD industry.

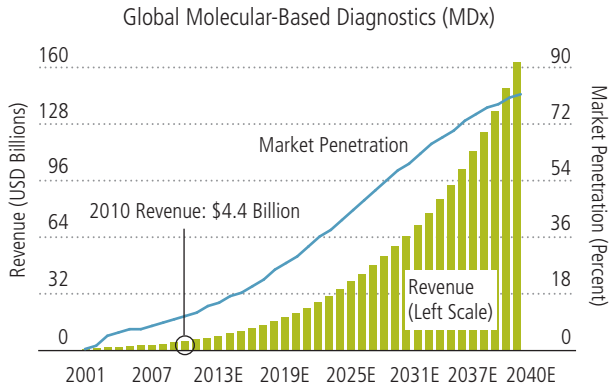
Our research suggests that traditional IVD companies are almost universally unprepared for this transition; many will likely see their businesses disrupted. Success in the field of molecular diagnostics requires expertise in information technology and clinical drug development, as well as diagnostic development and distribution. Today, most companies in the IVD industry lack many of these capabilities. Also, their business models are generally geared to benefit from large economies of scale and distribution rather than research and development of innovative diagnostic tests. To remain competitive, partnerships and the restructuring of business models will occur.

The second major impact will arise from the incorporation of molecular information into drug discovery and development, which is likely to dramatically improve productivity and profitability over the coming decade. The rise of the biotechnology industry in the 1990s was the first wave of molecular medicine, but, in aggregate, the drug industry remains profoundly unproductive. Less than 30% of drugs in development are ultimately marketed, and development times hover around 10 years.[1,2] Consequently, the capital cost of developing a single drug typically exceeds $1 billion, often more than the future profits of the drug warrant. Innovative drug companies will use molecular information to reduce development costs and expand their drug pipeline. In our view, smaller, more nimble biotechnology companies will lead the adoption of molecular technologies in drug research and development.

Drug markets that are currently large will likely become collections of smaller niche markets, each focused on diseases that are rarer because they are tightly defined in molecular terms. We believe that the future drug market will have more "orphan" drug products than blockbuster drugs. While the size of each orphan market may be smaller than current target markets, drugs that deliver superior efficacy may, in many instances, garner higher pricing and substantial revenue. Further, drugs currently on the market, especially those with observable variability in effect, will be used less frequently as physicians rely on molecular tools to better determine which patients are likely to benefit from these drugs.

Display 8

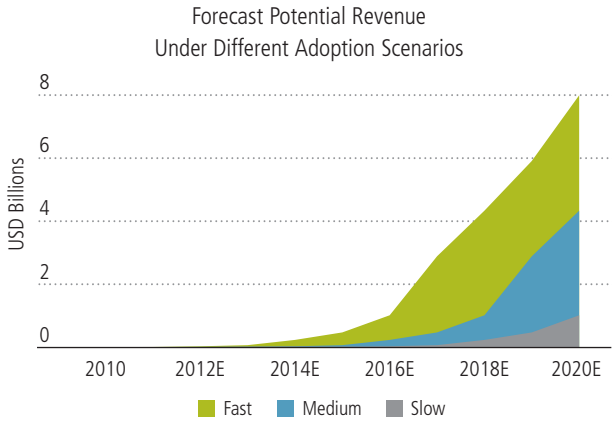
We Expect MDx Revenue and Penetration to Grow Quickly



Historical analysis and projections are not a guarantee of future results.
As of January 5, 2011; estimates are subject to change.
Source: AllianceBernstein

Display 9

The Risk-Prediction Market Has Enormous Revenue Potential

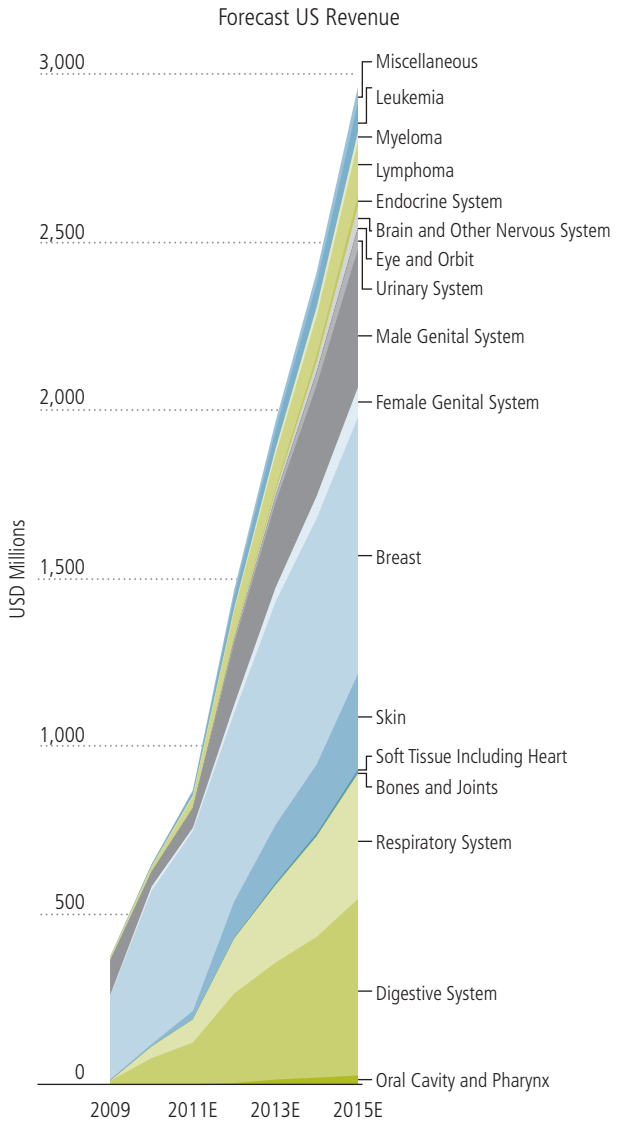


Historical analysis and projections are not a guarantee of future results.
As of December 31, 2010; estimates are subject to change. Forecasts assume each test costs $400, with 20 million tests sold in 2020 under the fast-adoption scenario.
Source: AllianceBernstein

[1]*Joseph A. DiMasi and Cherie Paquette, "The Economics of Follow-on Drug Research and Development,"* PharmacoEconomics *22, no.2 supplement 2 (2004):1–14.*
[2]*Bernard H. Munos (advisor, corporate strategy, Eli Lilly and Company), "The Dynamics of Pharmaceutical Innovation and Their Implications for Investors," (presentation, Sanford Bernstein Long View Conference, May 5, 2010).*

Display 10

Cancer: A Large Diagnostic Opportunity



Historical analysis and projections are not a guarantee of future results.
As of December 31, 2010; estimates are subject to change.
Assumes that molecular tests (costing $3,800 each) will be used on approximately 776,000 new cancer cases (about 50% of the expected number of new cases) by 2015.
Source: National Cancer Institute and AllianceBernstein

Some drugs that are seldom prescribed today because of the adverse response of small sets of patients may see increased use, since it will be possible to identify those patients and avoid prescribing the drugs to them.

The blockbuster drug model is likely to be redefined. Three new types of blockbuster drug markets could emerge. The first will result from the identification of drugs that have specific molecular targets that are common to seemingly disparate diseases. Certain disorders that appear different could be caused by similar molecular dysfunctions, so a single drug could be designed to treat multiple conditions. Another type of blockbuster may emerge when new medications are so efficacious that patients who historically would have had short life spans go on to live much longer and thus consume more drugs over their lifetimes. The third blockbuster route could be through the construction of drug portfolios that treat a variety of subtypes of a given disease and therefore capture large market shares around particular diseases. For example, many companies (including Eli Lilly, Roche and AstraZeneca) are pursuing cancer-focused portfolio strategies.

Companies may be able to repurpose previously failed compounds or drugs pulled early from the market. New insights into molecular biology and its role in disease could breathe life into discarded drug projects.

The third, perhaps most profound, impact will come from the branch of molecular biology known as synthetic biology, which entails directly manipulating, engineering and manufacturing cells. Synthetic biology is only a fledgling scientific endeavor, but in the coming decades it will redefine how researchers study disease and develop drugs and how physicians treat patients. Drug developers can use specific cells to study disease, identify potential drugs and test those drugs more accurately during preclinical development. This will likely lead to a proliferation of new drug candidates and yield many more therapies.

In time, cellular biology should allow physicians to harness the power of regenerative medicine. Researchers will be able to devise cellular therapies to fix broken biological machinery such as hearts, neurons and pancreases. We project that by 2030, regenerative medicine will account for at least 25% of drug industry revenue. Regenerative solutions will, in many cases, cannibalize existing drug revenues and obviate the need for organ transplant surgeries. Clinical research into cellular therapies for eye-related diseases, kidney disease, central nervous system disorders such as Parkinson's disease, skeletal diseases such as osteoporosis, and various blood disorders is at different stages of development. ■

About AllianceBernstein

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