Healthcare & Life Sciences

Opportunity & Highlights

Dear Colleague:

Welcome.

As individuals and as groups, we continually seek to improve, mend and alter the overall nature and quality of our lives. Regardless of age, industry, occupation, or affiliation, there is no single imperative more essential than health. As such, the subject of healthcare draws universal appeal whether you are a physician or patient.

As providers, administrators and investors, we strive to improve the institution of American healthcare and navigate its complexity through sensible business development, astute investment and the calculated management of risk.

This industry comprises a variety of markets, each with their own dominant business models, assorted regulatory considerations and disparate commercial dynamics.


Thomas Bird

The healthcare industry has entered a period of expansive and prolonged transformation. This dynamic shift will impact participants in contrasting ways.

Businesses that are reluctant or possess limited ability to adapt will be severely challenged.

However, businesses that can efficiently innovate possess the opportunity to build both market share and favorable returns. These opportunities remain unbounded. Through the adoption of new models and technology, the face of healthcare continues to evolve. While campaigns for compelling innovation are being driven by well financed leaders in health technology, provider care, Big Pharma and Big Biotech – innovative disruption is also being rendered by “two guys in a garage.”

In this healthcare & life sciences report, we highlight today’s growth areas and opportunities, with an aim to provide insight into current trends and business drivers. This report explores the shifts taking place within the US healthcare industry to enable stakeholders to formulate better decisions and strategies. Our overarching goal is to ensure that providers, investors and corporate development professionals remain well-placed to realize healthy returns.

As always, we look forward to continuing our dialog and our work with healthcare and life sciences stakeholders.

Thomas Bird

Thomas Bird
Vice President

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Healthcare Outlook

Highlights

In corporate development there are few investable and actionable certainties. Here today, in 2014, we face one of the most significant certainties that operators and investors will encounter for decades to come – the comprehensive redesign of the health services and life sciences industries.

While discontinued insurance policies, technical failures and anemic enrollment numbers have dominated the headlines, transformative changes are being compelled by more complex and long-term drivers.

Aging demographics, the unrelenting pressures of chronic disease and the addition of 30 million new consumers from the Patient Protection and Affordable Care Act (ACA) are all leading to a critical tipping point and the beginning of sweeping healthcare reform. A new wave of collective change is aimed to provide an enduring solution to these challenges while balancing patient access, physician incentives and the fiscal stability of the US healthcare system.

Healthcare providers and investors will navigate disruption as the industry transitions from legacy businesses to new and lesser understood models. Scientific discoveries and medical advances, next-generation technology solutions, payment reform, changing societal expectations and new models of care are dramatically transforming health care delivery. While there are many issues and unknowns – providers and life science operators with real solutions to these problems possess unprecedented potential to grow.

For the last two years the prevailing strategy amongst most investors and corporate development officers has been the adoption of a wait-and-see attitude. This year is marked as a decidedly different as increased regulatory clarity promotes confidence in future development. Now, we as investors, operators and a nation of consumers, are amidst the most significant wave of long-term change in the history of modern healthcare.

The next decade will be one of the most revolutionary periods the health sector has ever faced as it manages uncertainty in an environment of constrained resources. Substantive structural change is now unfolding in a market where stakeholders have historically been reluctant to embrace reform. These collective changes will influence the success and outcome of every healthcare investment and enterprise for years to come.

Investment Themes

Recognizing long-term reimbursement pressures, regulatory changes and the re-alignment of health services incentives, we believe four dominant investment themes will drive the US health market. Fundamentally, healthcare and life science companies that can demonstrate improved patient outcomes while effectively managing costs, have an unprecedented opportunity to grow and realize outsized success.

Theme 1: Government's expanded role in healthcare

Leaders in all areas of the healthcare industry, including payers and providers, should seek to take advantage of the Affordable Care Act's expanded access. With 30 million new patients entering the system, in addition to growing federal subsidies – returns will go to the most efficient health leaders and systems that can increase market share from a larger pie.

Most likely to come from:

- Managed Care & Primary Care
- Health Services & Distribution
- Generic Pharma

Theme 2: Bending the cost curve

The US healthcare system's rapid growth rate is a counter intuitive risk factor. Federal and state governments simply cannot continue to fund rising healthcare costs. Payers seek sustained savings; providers seek to offset real reimbursement cuts. Hospitals, insurers and healthcare products and services companies are aggressively searching for new cost-saving measures and more efficient business models.

Most likely to come from:

- Health services shifting to lower cost settings
- Healthcare IT, Big Data and Predictive Analytics

Theme 3: Novel science & improved clinical outcomes

Pioneering solutions that fill unmet need through: i) improved patient outcomes or ii) new therapies that provide meaningful disease impact.

Most likely to come from:

- Biotechnology & Life Sciences
- Tools / Diagnostics
- Genomics & Precision Healthcare
- Oncology Therapies, Rare Diseases & Orphan Drug Therapies

Theme 4: Integrated Care

The active management of patient care populations through increased health services coordination will play a pivotal role in near-term healthcare evolution. Fee-for-service treatment models will evolve to value-based systems that incentivize improved patient outcomes and aggregate cost savings. Providers and systems that adopt new models and strategies to reduce costs through holistic care will be financially rewarded as insurers shift the US patient population to integrated care programs.

Most likely to come from:

- Leading Primary & Specialty Care Groups
- HIT & Predictive Analytics
- Personal Health, Preventative Care Tools & Applications
- Remote Health

New medical models and solutions that improve healthcare efficiency or health outcomes, will dominate, especially if they lead to lower healthcare costs.

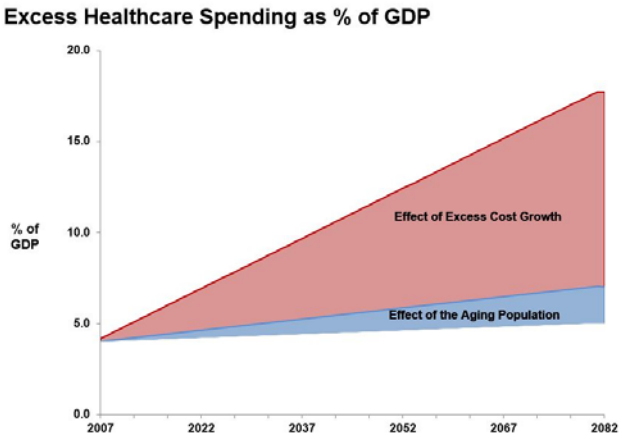
Key Insights by Segment

	Segment Drivers	Actionable Strategies
Healthcare Services 	• Change is accelerating • Reimbursement pressures will continue to drive consolidation, including physician practice acquisition by hospital systems • Administrators will focus on cost containment • Providers actively competing in the market place • Transition from volume to value based care • Increase in patient universe due to the ACA	• Increase focus on primary care and urgent care centers • Contemplate participation in ACOs • Lever HIT for improved CRM and extension of labor force • Realize ACA incentives before they migrate to penalties • Focus on direct consumer demand for more healthcare services
Health Information Technology 	• Systems will require interoperability • Operators & insurers seeking to lever HIT to manage costs • ACA incentives for EHR adoption will turn to penalties • Patients adopt HIT as financial risk shifts • Pharma & Biotech seek HIT to fail faster • Providers seek to use HIT for CRM and operational management	• Focus on predictive analytics and population management • Lever big data and improved research • Integrate between plans, hospitals and physicians • Develop solutions that improve clinical outcomes • Find a way to operate in a value based care market • Mobile health and consumer facing social health applications
Medical Devices, Tools & Diagnostics 	• Ongoing price pressure • Increasing healthcare awareness • Continued reimbursement pressure on labs • Regulatory ambiguity • Decline in genomic mapping costs • Increased testing and diagnostics resulting from population expansion	• Greater emphasis on products that generate cost savings • Increased focus on self-care medical devices • Focus on building scale thru acquisitions • Big device companies partner with early stage • US device companies to go global to lever low cost manufacturing and access growing markets • Lever molecular diagnostics opportunities
Pharma 	• The patent cliff isn't over • Need improved and more efficient drug development • Pharma consolidation continues • Expansion of emerging markets, including China • Research efforts migrating externally • Big pharma demanding product for their pipelines • High cost of development and onerous FDA approval process	• Focus on novel science and improved outcomes • Invest in sound R&D programs • Use collaboration and risk sharing models • Transition from vertical integration to virtual integration • Lever big data and new models to reduce development timelines • Promote "failing faster"
Biotechnology 	• Opaque FDA guidance • Development of precision medicine • Active and competitive M&A market • Cancer immunotherapies dominate spotlight • Advances and cost reduction in whole genome sequencing • Public market scrutiny of relatively early-stage companies	• Biomarkers and companion diagnostics • Emphasis on orphan drugs • Intensify collaboration with academic departments • Focus on working models for predictive and personalized medicine

Healthcare Fiscal Outlook

The US healthcare system continues to struggle with rising costs, uneven quality and differential patient access. Physicians face increasing workloads and/or lower incomes. Patients are paying higher costs while services are being restricted.

Healthcare costs are driven by three fundamental inputs, i) cost of units of care, ii) units per patient, and iii) number of patients. Following ACA implementation, efforts to reduce aggregate spend through either unit cost or per patient volume are likely to be offset by the increased number of people being added to the system and the comprehensive benefits required by the ACA.



Source: CBO, Salem Partners

Key drivers impacting unit prices and higher utilization include advances in medical technology, increasing chronic disease prevalence and increased provider consolidation and market power.[1]

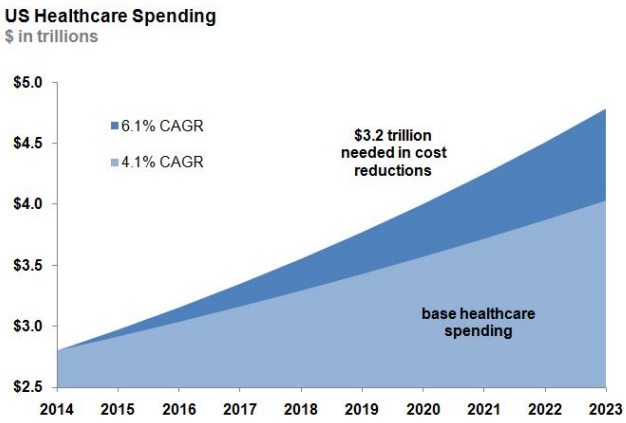
Contrary to perception, analyses by both the National Health Expenditure Accounts (NHEA) and the Centers for Medicare and Medicaid Services (CMS) confirm the ACA does not actually lower health spending trends. Forecasts actually call for an acceleration in spending growth – a 6.1% CAGR for the ten-year period from 2014 to 2023.[2]

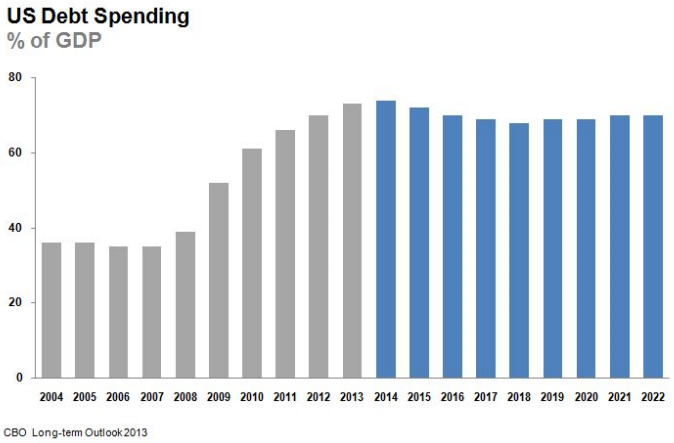
A Burning Platform

The overextension of US healthcare spending is dissimilar from other historical budget challenges – the x-factor being the absolute magnitude and momentum of this spending. The funding obligations and outlook for the federal and state systems are not positive and provide meaningful risk to proper and guided fiscal management.

> **Unabated healthcare spending will grow at a CAGR of 6.1% for the next 10 years,** rising from $2.8 trillion in total spending to $4.8 trillion by 2023. This growth rate and the overall economic burden will be unmanageable for the federal government, state/local governments and private market consumers.[3]

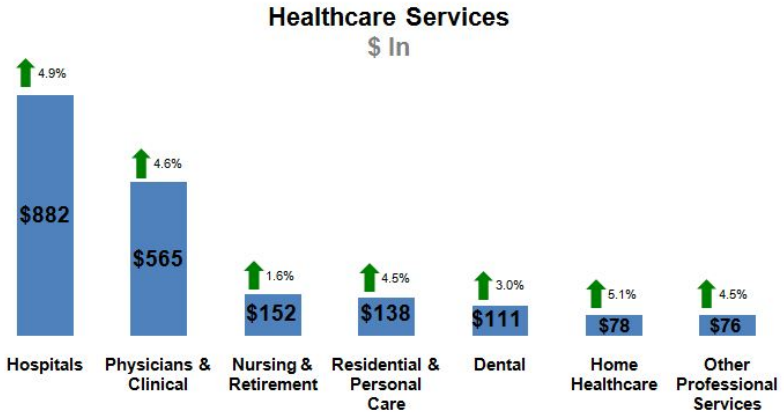
A reduction to a more sustainable 4.1% CAGR equates to taking out $3.2 trillion in aggregate spend by 2018.





Health Service Spending

Health Services spending comprises the single largest subcategory of the US budget at $2.0 trillion annually, $882 billion of which is spent within the hospital system.

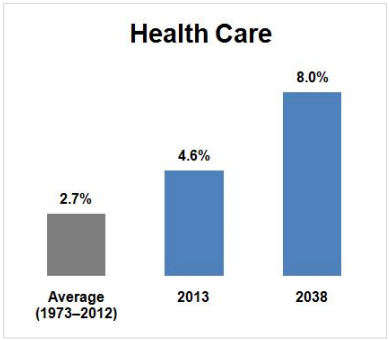


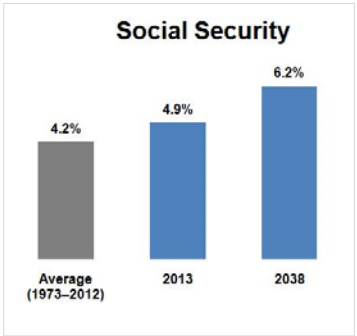
Source: CBO

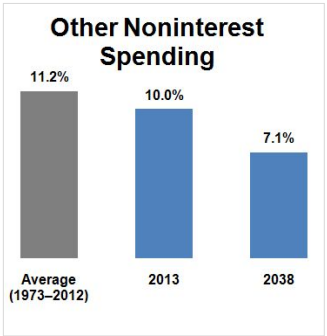
Despite easy calls for reductions in discretionary spending, there are only three categories of federal expenditure significant enough to provide real impact to the deficit: i) healthcare ii) social security and 3) national defense.

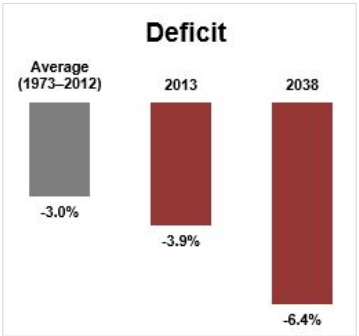
CBO Spending Projections

% of GDP









Source: CBO

U.S. spending for healthcare has been on a relentless upward path – reaching $2.8 trillion in the aggregate, $8,508 per person and 17% of GDP.

The US Healthcare Market

A Heterogeneous Market

The US healthcare market is not a monolith, rather it's an amalgam. The healthy and homogenous bottom 50% of US healthcare consumers only account for 3% of total healthcare costs. While the top 5% of consumers, are incredibly heterogeneous, with varied health issues, chronic diseases and complex treatment and therapies. This top 5% of the population accounts for 50% of all US healthcare expenditures.[4]

As such, the business of managed care and cost control is about large populations – even groups of 5,000 or 20,000 patients may not be enough. Any real savings will be anchored in effectively controlling costs and bending the curve through intense focus on this small minority of patients.

Trends

Millions of Americans are expected to gain health coverage through Medicaid or via new online exchanges. Early estimates projected as many as 30 million people would gain new insurance through the ACA and online exchanges.[5] Whether because of technological hurdles or an overestimation of demand from young healthy consumers, early enrollment numbers remain dramatically below initial projections and the impact to ACA implementation remains unknown. Ultimately, many variables will define the success of the ACA, including who will continue to enroll, the medical requirements of participants, and how effectively the industry will be able to manage these members. Unfortunately none of these variables are likely to change the broader medical cost trend – total healthcare spending will continue to rise with the addition of the newly insured.

The individual market will continue to be marked by turmoil as consumers reconcile discontinued insurance programs along with premium increases. In some cases the dramatic increase in premium rates is the unintended effect of health systems seeking to insulate themselves from uncertainty. Insurers have opted to price policies aggressively to offset the financial risks of providing care to an unknown patient population.

Hospitals, insurers and health services providers are searching for cost-saving measures, focusing on better outcomes and responding to incentives to become more tightly aligned.

Despite uncertainty, healthcare stakeholders should strategize based on a post-ACA landscape, accounting for broader adoption and a migration to longitudinal integrated care.

Consumer Engagement

As price increasingly flows downstream, money will move differently as consumers exercise greater control over spending. Individual consumers, bearing more financial responsibility for their medical bills, are questioning and sometimes delaying procedures, imaging and elective services. Early data indicates that changes in how the industry operates and how average consumers choose healthcare appear to be having a real effect, primarily a consequence of a behavioral shift in purchasing. Price-sensitive consumers are increasingly distinguishing high-cost care from high-quality care. Two-thirds of polled healthcare services consumers indicated that they do not believe that expensive medical treatment means better quality.[6]

Shifting the Location of Care

With increasing pressure to keep costs down, providers are pushing to deliver health services away from traditional hospital settings. Care is moving outside costly settings to more affordable retail clinics and even to remote and telemedicine health solutions. In addition to costs savings, consumers value the convenience.[7]

Utilization of outpatient care and retail clinics has tripled over the last five years. Differential pricing amongst care settings varies wildly. Emergency room treatment costs for low-risk, low complexity conditions, such as colds or sinusitis, are 7x more expensive than treatment provided through retail clinics and almost 13x more than e-visits.[8]

Pharmacies and retailers are aggressively asserting their place in the market. These retailers are expanding their product and service offerings while making significant capital investments in store networks. Walgreens has initiated an ambitious agenda in rebranding and repositioning itself as a diversified healthcare provider.[9] Pharmacies recurrent touch points in supplying patients products provides a unique opportunity to extend their value proposition to patients.

Top Operators of Retail Clinics

Operator	Number of Clinics
MinuteClinic (CVS)	683
Healthcare Clinic (Walgreens)	384
The Little Clinic	101
Target Clinic	57
RediClinic	30
All Others	220
Total	1,475

Source: Salem Partners

Price Transparency

In 2013, CMS disclosed, for the fist-time ever, Medicare Provider Utilization and Payment Data summarizing inpatient hospital services and the correlated payments. The results: i) pricing variation is massive and ii) there is not rationale for why.[10]

Consumers have long demanded the ability to comparison shop for medical care based on price and quality. New models are bringing increased transparency into the medical services market. Employer led efforts to empower workers to make better informed choices will create a cascading effect throughout the US health system.

Initiatives to provide pricing clarity has historically been a disjointed effort. As corporate employers and employee consumers increasingly value the ability assess and compare health services, a number of ventures have emerged. These new players specialize in converting incomprehensible data into something more user-friendly. Since 2010, more than $400 million in venture capital has been invested in companies attempting to solve for medical cost transparency. [11]

Healthcare Information Technology

Health service providers face a myriad of information technology challenges, including: core mainframe maintenance, the burden of legacy systems, meaningful attestation, EDI integration, patient records management, adoption of ICD-10, as well as the complexities of semantic interoperability between numerous systems.

In addition to managing these core functions, providers will require innovative health technology solutions to extend provider capacity, enable integrated care collaboration and support new value-based compensation models that require complex data analyses. Exceptionally strong opportunities and growth will be centered on big data solutions, predictive analytics, personal HIT, telemedicine programs, as well as the expanding mobile and self-care application markets.

Patient CRM & #Social Media

More progressive consumer facing industries, such as retail, financial services and media, have long ago invested in and deployed successful CRM programs. As health service providers seek to engage a new generation of empowered consumers, the health industry will require advanced technology solutions combined with new cohesive strategies. Providers and networks are now rethinking strategies as a means to increase physician productivity, increase patient engagement and strengthen the provider-patient relationship.

Technology will be used to extend communication reach. Consumers want to connect with their health providers. A survey conducted by PwC's Health Research Institute found that 69% of consumers are willing to communicate with doctors and nurses using email, 49% via online web chat or portal, and 45% using text messages. Healthcare organizations should use technology to extend care and build a workforce that is skilled at engaging digitally with patients.[12]

Workforce Management

The addition of 30 million new customers into the healthcare system, aging demographics and the existing physician shortage will strain hospitals and networks. Facing the challenges, and the already increasingly complexity of operations management, provider systems are deploying health information technology to manage volume and maximize efficiency.

Incentives Shift to Penalties

CMS grants incentive payments to eligible professionals and eligible hospitals, who demonstrate they have engaged in efforts to adopt, implement or upgrade certified EHR technology. To encourage widespread EHR adoption, promote innovation and to avoid excessive burden on healthcare providers, “meaningful use” was deployed as a phased approach, which is divided into three stages which span 2011 (data capture and sharing), 2013 (advanced clinical processes) and 2015 (improved outcomes). The incentive payments range from $44,000 over 5 years for the Medicare providers and $63,750 over 6 years for Medicaid providers. Participation in the meaningful use program is voluntary, however if providers fail to join in by 2015, financial incentives to providers will flip to negative adjustments in their Medicare/Medicaid fees, starting at 1% and escalating to 3% by 2017.[13]

2014 will serve as the performance year for other federal quality reporting program penalties scheduled to take effect in 2016. These programs (Physician Quality Reporting System and VBPM) continue to grow in complexity, while penalties continue to increase each year. Physician group practices will need to report quality measures for each of these programs in 2014 to avoid 2016 penalties that, in total, can amount to up to -6.0% of Part B covered professional services under the Medicare physician fee schedule.[14]

Hospital readmissions remain a considerable cost burden within the healthcare system. The incidence of readmission are estimated to be as high as 30%; while readmission cost for Medicare patients alone is $26 billion annually.[15] The ACA’s new readmission penalties take direct aim at this expense and encourages hospitals to get treatment right the first time. The estimated savings from improved hospital care is $630 million in 2014, increasing to more than $1 billion in 2015.[16]

According to a CMS study, 2012 hospital readmissions dipped to 18.4%, a drop of nearly 70,000, and this trend is expected to accelerate through 2014 as hospitals focus on discharge planning, compliance and the continuum of care.[17]

Market Summary

The transformation of the US healthcare market is driven by legislation and secular change. As a part of this evolution, compelling investment themes will be provided, regardless of pace or path.

Participants that demonstrate improved patient care while effectively managing costs will be well positioned in the industry. Advances in health system management and clinical innovation will accelerate as health information technology proliferates. Leading organizations that balance their core business while aggressively identifying new growth opportunities will lead the new healthcare market. Teams that can maximize efficiency and reduce expense by designing processes to fail faster will create a competitive advantage. Additionally, managers that nourish product pipelines and seek collaboration amongst corporate development arms and venture firms will succeed.

Regulatory Reform

Over the past three years, an opaque regulatory landscape has driven most service providers to the sidelines to adopt a wait and see strategy. The unknown impact of regulatory reform and the adoption of the ACA had generally dampened investment, internal development and mergers and acquisitions.

Legislative & Judicial Recap

In March 2010, President Obama signed the Patient Protection and Affordable Care Act into law. Included in this notable legislation are provisions guiding comprehensive reform through expansion of access, increased insurance coverage requirements and penalties related to hospital readmissions.

In June 2012, the Supreme Court resolved the constitutionality of the ACA with a landmark decision to largely uphold the healthcare reform law, including the individual mandate requirement and the expansion of the Medicaid program.

The court's decision eliminated most of the uncertainty that has constrained healthcare sector performance and investment over the past few years. Following the court's ruling, the healthcare industry has acknowledged the certainty of full implementation and now moves forward with investment, implementation plans and strategies.

Affordable Care Act in Action

Provisions of the ACA include the expansion of Medicare, creation of healthcare insurance exchanges, setting minimum coverage, and establishing employer requirements. In promoting implementation the ACA utilizes a mix of financial incentives and penalties.

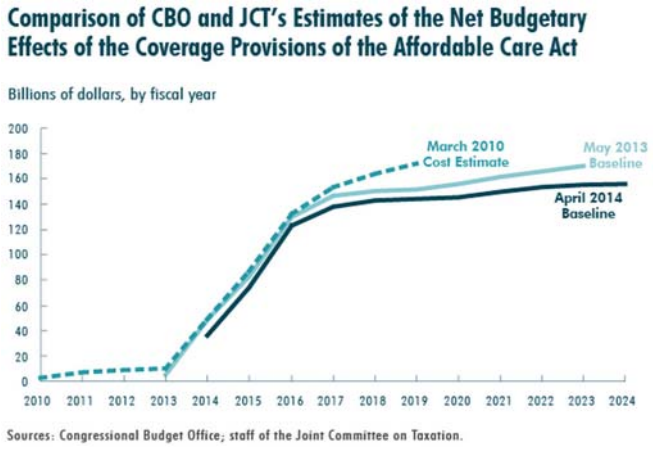
Expenditures allocated to the government

As healthcare spending increases continue to exceed forecasted GDP growth rates, the federal government becomes obligated to larger liabilities.

Increasing government cost pressure will be from ACA Medicaid expansion, the costs of an aging population, as well as higher continued subsidies to a larger private insurance pie (growing from the expansion of private coverage through mandate).

GAO Analysis

According to a comprehensive investigation conducted by the US Government Accountability Office (GAO), federal healthcare spending is expected to continue growing faster than the economy. In the near term, this is driven by increasing enrollment in federal healthcare programs due to expanded eligibility, easier access and legislated mandate. Over the long-term, the ACA projects a decline in healthcare spending and the rate of total cost growth. Slowing the rate of healthcare cost growth is critical in ensuring the US budget is on a viable path. There is general agreement that advances in technology will be a key factor in creating efficiencies and removing costs from the system, but considerable uncertainty remains as real cost savings will be difficult to realize.



The effect of the ACA on the long-term fiscal outlook depends largely on whether elements in the ACA designed to control costs are effective and can be sustained.
The GAO has projected an improvement in the long-term outlook; however it should be noted the GAO models utilize the ACA's own assumptions regarding broad expansion of coverage (including younger healthier participants) and the implementation and effectiveness of the proposed cost-containment provisions over the entire 75-year simulation period.[18]

The feasibility of forecasted ACA cost-savings, based on perpetual increases in healthcare productivity, remains unknown – however the unsustainable path of the federal budget is a certainty.

Organizational Strategy & Change: ACOs

The development of accountable care organizations (ACOs) is one of the most notable changes currently taking place in the healthcare industry. As a cost saving strategy, ACOs have been proposed as a new model to proactively manage patient care and expenses.

ACOs have big ambitions – to increase quality, reduce costs and to create healthier patients through a model of coordinated treatment. Under the ACO delivery model, service providers such as hospitals and physicians organize as a group to contract with payer organizations and to assume responsibility for the care of a defined patient population. If this group meets quality goals, projected outcomes, and manage to reduce costs, the resulting savings are shared between the providers and the payer.

In addition to cost containment, ACOs illustrate the movement towards new integrated care models. As ACOs form, providers are subtly positioning for the shift away from episodic care to longitudinal value-based care.

Hundreds of hospitals, physician groups and insurers are assembling into ACOs. CMS has approved more that 250 Medicare ACOs, including naming 123 organizations to the 2014 Medicare Shared Savings Program – increasing the total number of beneficiaries to 4 million.[19]

Early data from a federal pilot program of Medicare patients point to modest savings – virtually all ACOs achieved slower cost growth compared to non-ACO peers, however a minority generated significant enough savings to benefit from the shared savings program. The Physician Group Practice pilot program, saved $137 million over 5 years across 10 participating physician groups, an average of $114 per year per beneficiary.[20] Similarly, in 2009, spending grew about 2% less per quarter for enrollees in Blue Cross Blue Shield of Massachusetts' ACO-like program compared to its traditional programs. Blue Cross Blue Shield reported that 2010 savings were even higher.[21]

Cigna believes its ACOs can bring costs down and is aiming for 1 million members by forming 100 ACOs by the end of 2014. Cigna estimates per patient annual cost growth is 50% lower for members in ACOs compared to members covered by the traditional fee-for-service models. Cigna estimates emergency room visits fell 7% across the system, while quality indicators for procedures such as mammograms and cervical cancer screenings are up about 5%.[22]

It should be noted that the concept of an ACO is not a new idea. Critics contend that this strategy is reminiscent of the failed managed care experiments of the 1990s. Proponents counter that this new model is different by being provider led. While the idea is promising, many healthcare executives remain skeptical as the model remains largely unproven and preliminary savings have only been modest. Additionally, participation and reporting ACO operations require investment in new technology systems and infrastructure, thus potentially pushing costs higher.
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The Physician

Primary and specialty care physicians find themselves in an especially challenging market crowded with frenetic change. As government reimbursement pressure continues, the impact is widely felt amongst hospital systems and the physicians that serve them.

Bad Medicine of the SGR

The Sustainable Growth Rate (SGR), a policy signed into law in 1997 by President Clinton, ensures that if Medicare begins to grow at an unsustainable rate, payments to physicians will be cut to offset the growth in Medicare spending.

For each year since 2002, the SGR formula has called for substantial reduction in Medicare physician reimbursement rates. For 2002, payment rates were reduced 5.4%. In each subsequent year, congress has overridden the formula, specifying small reimbursement rate increases or payment freezes instead of large cuts. This intervention has only deferred rather than cancelled the reductions in payment rates. At this point, a pending cumulative payment rate reduction of 26% has been accrued.[23]

On Dec. 26, 2013, President Obama signed into law the Pathway for SGR Reform Act of 2013 as part of the December budget agreement. This law included a three month reprieve as a legislative window to consider actual repeal of the SGR. Then in April 2014, President Obama signed the Protecting Access to Medicare Act of 2014, creating another one-year SGR patch and successfully kicking the $180B cut down the road to April 2015.

With extensive cuts looming and the distraction of a yearly “doc fix,” physician groups continue to face the threat of a disastrous fee reduction. The end of SGR may be the catalyst for a broad shift away from historical fee-for-service models.

Countdown to ICD-10 transition

ICD-10 is the international medical code system that describes roughly 70,000 diseases, symptoms, abnormal findings and external causes of injury. ICD-10 is 4x larger than ICD-9 and presents a monumental challenge for health service providers. This year, practice professionals face the challenging task of preparing their organizational infrastructure and staff for the ICD-10 compliance deadline.

Critical issues that will need to be addressed include upgrading practice software, ensuring that patient encounters are appropriately documented, adequately training clinical and administrative staff, testing internally and with external trading partners, and establishing contingency plans for the likely disruption of cash flow.

While the comprehensive nature of ICD has provided some humor, the training, costs and technological challenges of adoption are less funny.

Physician Practice Acquisitions

Hospitals have aggressively ramped up their physician practice acquisition and employment activity. In 2014, we expect higher M&A volume for both the primary and specialty care segments. In a recent poll, nearly 50% of surveyed hospitals indicated they were actively involved in practice acquisitions – with family practice and internal medicine as leading targets.[24]

Physician and practice managers will need to remain proactive and agile in 2014. While the influx of new ACA patients may provide positive volume, it should be noted that the payment capabilities and reimbursement rates may not be ideal. Physicians should expect increased competition from retail clinics.

Pharma & Biotech

The outlook for pharma and biotechnology in 2014 remains positive as companies benefit from the addition of 30 million consumers into the US market, reduced FDA review timelines, emerging market growth, technological advances supporting drug development, and the emergence of precision medicine.

Despite strong tailwinds, the industry continues to face pressure to backfill therapeutic pipelines. Drug companies with deep pockets and shallow pipelines are aggressively seeking acquisitions and have shifted to consider earlier stage products, even with prominent targets trading at record highs.

Pipeline Fatigue Isn't Over

Big pharma has been facing significant aggregate patent losses for years – a challenge that continues today. Between 2009 and 2014, the industry lost 18% of total sales to generic competition.[25] In 2013, products generating roughly $28 billion in sales lost patent protection. In 2014, estimated sales exposure approaches $34 billion; popular block buster drug loss will include Nexium ($4B), Cymbalta ($5B), Celebrex ($1.8B), Evista Sandostatin, and Exforge.[26] While 2014 expirations are a bitter pill, a bigger challenge will be next year, in which $55 billion in sales will be in jeopardy.

In response, companies have cut jobs, reorganized units and sold off non-core assets. That has boosted cash in hand for many, opening the way for acquisitions.

Despite strategic initiatives, the pharmaceutical industry continues to face exposure to large market share losses from generic competition. Many of the industry's largest firms have focused on mergers and acquisitions as a strategy to accelerate growth and provide product diversification. Other firms have pursued plans to diversify into biologics, which have little generic competition in the U.S. market.

Transaction Trends

M&A activity in 2013 was strong; prices remained high and a number of deals saw hefty premiums. Specialty pharmaceutical and biotech unseated Big Pharma as the year's most aggressive buyers. Amgen's $10.4 billion purchase of Onyx Pharmaceuticals was the industry's largest. In Perrigo's acquisition of Elan for $8.6B, Perrigo picked up a promising pipeline along with a new Dublin domicile. Allergan sought to solve its headache with the acquisition of MAP Pharmaceuticals. Later end of year deals included gastroenterology-focused Salix Pharmaceuticals' acquisition of Santarus for $2.1B and Akron's acquisition of drug maker Hi-Tech Pharmacols for $640 million.

M&A in the healthcare sector will be up materially in 2014 at all size levels and across all subsectors

Following last year, deal activity has already taken off in 2014. Immediately entering the New Year, Forest Laboratories bought the pre-IPO Aptalis Pharma for $2.9 billion to add treatments for gastrointestinal ailments and cystic fibrosis. Subsequently, Actavis acquired Forest Laboratories for $25 billion. Also, in February Mallinckrodt accelerated its push into specialty pharma with the acquisition of Cadence Pharmaceuticals for $1.4 billion, and then followed it up with the purchase of Questcor for $5.6 billion.

Even more recently there has been a wave of mega deals, including Valeant Pharmaceuticals $53 billion hostile offer to buyout Botox maker Allergan, GlaxoSmithKline's $20 billion acquisition of Novartis' oncology drug business and Pfizer's $118 billion dollar hostile bid for AstraZeneca. Notably, the to-be-determined AstraZeneca deal would represent the biggest deal for the healthcare sector since Pfizer's purchase of Warner-Lambert for $112 billion in 2000.

Healthcare companies with deep pockets and shallow product pipelines are poised for a busy year of acquisitions, with biotechnology firms likely to be among the most prominent targets even as they trade at record highs.

A strategic success has been Gilead Sciences 2011 acquisition of hepatitis C drug maker Pharmasset for $11 billion – since the deal was announced; Gilead's stock has almost tripled, adding almost $85 billion in market value and making Gilead the biggest biotechnology company in the world. The drug Gilead gained in the deal, Sovaldi, was approved by the FDA in December 2013 and is projected to generate $2.5 billion in revenue this year.

Evergreen R&D Restructuring

The restructuring trend continues to endure as a recurring theme. Blockbuster patent protection and increasing generic competition, along with weak R&D productivity, paint the backdrop for the industry's conventional strategic solution to Eroom's Law – R&D restructuring.

Big Pharma continues to advertise robust R&D divisions and a commitment to the internal development of innovative new drugs, but R&D setbacks exact a financial toll that is commonly followed by heavy cuts and broad restructuring. Notwithstanding, firms continue to project the delivery of multiple products each year for the next few years even as they prep reductions to R&D budgets.

Most recently, a series of pipeline setbacks and a plunge in profits forced Merck into announcing its intent to cut $2.5 billion in annual expenses. Executives outlined plans to sell off products, including some R&D projects, as they push for a major top-to-bottom R&D reorganization.

Pipeline fatigue has pushed for sober assessments of output; and many firms have responded with varied degrees of R&D reform. Both GlaxoSmithKline and AstraZeneca embraced change, so much so that AstraZeneca restructured twice.

A notable move was Pfizer's shock and awe approach to global R&D operations, which included realigning therapeutic priorities, discontinuing programs, shutting down facilities and broad reassessment of pipeline strategy. Other reformers include Novartis, Shire, and Sanofi, and most recently, struggling pharma giants Eli Lilly and Bristol-Myers Squibb.

Destination Dublin

International strategic consolidation is driven by a host of motivations, including, pipeline prospects, research and development assets, commercialization opportunities, and increasingly, geography. Currently, the international destination of choice is Ireland; the most dynamic M&A market for life sciences. Virtually every pharmaceutical and biotech concern domiciled in Ireland has made its way onto an M&A target list somewhere.

The latest company to enter Ireland is Horizon Pharma via its acquisition of Vidara. The attraction towards Ireland is straight-forward – tax efficiency; and the model has been well proven. Following Michigan-based Perrigo's purchase of Elan, the new Irish domicile saves the company an estimated $150 million in reduced taxes. Other such precedents include Warner Chilcott by Actavis, Alkermes' purchase of Elan's drug technology business, and Jazz Pharmaceuticals acquisition of Azur Pharma. US painkiller manufacturer, Endo Health Solutions, announced it was acquiring Canadian drug maker Paladin, which possessed substantial operations in Ireland, enabling it to reincorporate in Ireland and cut its tax to 20% – compared with the US rate of 35%.

Biobuck Earnouts

Earnouts defer a portion of a purchase price and are dependent on the occurrence of certain future events. The most common earnout milestones are coupled to clinical advancements, such as, IND filings, the initiation of a specified Phase, success in a designated Phase II or III study, achieving endpoints, NDA submissions / approvals and even progression in international approvals.

Buyers continue the use of these structured payments in life sciences transactions. While specific terms generally remain confidential, there is little doubt that optics of M&A pricing and deal announcements exceed the ultimate total of actual consideration paid. Some recent acquisitions have had 90%, or higher, of the buyout tied to either regulatory or commercial sales hurdles. As an example, Dianippon Sumitomo's acquisition of Boston Biomedical for $2.6 billion, paid out only $200 million upfront with the remaining 92% dependent on development and sales targets.

Trials

Close cooperation amongst a diverse group of stakeholders, including research sponsors, clinical investigators, patients and regulators, is a requirement in conducting a clinical trial today. Medical product discovery, development, manufacturing and consumer use, in geographic isolation no longer exists.

The increasing trend toward conducting clinical trials outside the United States is an important consideration in improving the efficiency of drug development. The percentage of patients enrolled in clinical trials is decreasing in the US and increasing abroad. This year, more than 50% of all trials will be conducted outside the US, requiring sponsors to better understand different cultures, foreign infrastructures and evolving regulatory requirements. [27]

Clinical trials in many countries cost less than they currently do in the United States. If a large outcome trial requires enrolling tens of thousands of patients, selecting trial sites in Russia or India instead of the United States can result in hundreds of millions of dollars in savings. Some also argue that clinical trials conducted outside of the United States are of higher quality because of better adherence to trial protocols and better patient follow-up. [28]

Specialty Pharma Offset

Although generic drug use will remain high, there will be a major counterweight to aggregate cost savings – an increase in the use of complex, expensive specialty drugs.

Less than 1% of prescriptions filled in 2012 were for specialty medications, yet they accounted for 25% of total prescription drug expenditures. By 2019 or 2020, specialty drugs are expected to represent 50% of plan sponsors' overall drug spend. The top three therapy classes – inflammatory conditions, multiple sclerosis and cancer – are expected to account for more than 50% of that overall spend.[29]

The primary driver of specialty drug spend will be a continuing increase in drug costs – more-sophisticated therapies with price tags worth tens and hundreds of thousands of dollars are now being brought to market.

Prescription drug spending on 8 of the top 10 specialty therapy classes will continue to increase over the next 3 years. This is due to both the robust pipeline of new biologics and physicians delaying treatment of patients until the new drugs are available. By the end of 2015, we expect that cancer, multiple sclerosis and inflammatory conditions such as rheumatoid arthritis (all specialty conditions) will each command higher drug spending than any other therapy class except diabetes.[30]

U.S. spending on specialty prescription drugs — those used to treat chronic, complex diseases such as cancer, multiple sclerosis and rheumatoid arthritis — is projected to increase 67% by the end of 2015.

Change in US Specialty Drug Spending

Therapy Class	2013	2014	2015	3-Year Compound Total
Inflammatory Conditions	25.1%	17.2%	17.4%	72.2%
Multiple Sclerosis	19.8%	18.5%	16.8%	65.6%
Cancer	21.3%	20.9%	21.0%	77.4%
HIV	9.2%	9.6%	9.4%	30.9%
Hepatitis C	33.0%	58.5%	168.4%	465.8%
Growth Deficiency	6.2%	5.9%	6.5%	19.9%
Anticoagulant	-0.3%	-0.2%	0.0%	-0.6%
Pulmonary Hypertension	11.0%	11.1%	10.5%	-14.2%
Respiratory Conditions	24.8%	29.5%	27.9%	36.6%
Transplant	-2.2%	1.0%	-1.2%	-2.4%
Total Specialty	17.8%	19.6%	18.4%	66.8%

Source: Express Scripts, Salem Partners

FDA & Regulatory

The regulatory environment has shifted to become somewhat more accommodating than prior years. There is the notion the FDA is not being as much of a drag to progress and in some cases may actually be encouraging bringing innovation to market.

An example of this new willingness would be the FDAs breakthrough therapy track to speed important drugs through the approval process – part of a movement on the agency's part to give patients and their physicians more of a say in weighing medicines' risks and benefits.

In addition to developing new programs to adapt to the changing scientific landscape and ensure the safety, efficacy and timely approval of new treatments and therapies for patients, the FDA is also taking steps to reform its existing regulations. Executive Order (EO) 13563 outlines ongoing plans to create a simpler and smarter regulatory system while improving health and safety. One specific ambition of EO 13563 is to increase flexibility by purging burdensome regulations that are outdated, inefficient or excessive.

Approvals

The new drug approval rate has waned. In 2013, the FDA approved 27 novel new molecular entities, including biologics – a considerable decline from prior highs (39 approvals in 2012). The FDA has attributed the decline to a total drop in the number of new drug applications – even after starting the year with the new Breakthrough Therapy Designation program (BTD). Ultimately, the regression has raised extensive questions about the productivity and sustainability of the world's multibillion-dollar R&D business.

The FDA's BTD program has been designed to shuttle major therapeutic advances through an expedited approval process. While a pioneering step for the administration, the program contributed marginally in new drug approvals in 2014. However, as a promising indicator, the BTD program did successfully cut several months off the regulatory pathway for lymphoma therapy Imbruvica (ibrutinib).

Despite the new designation, the slide in approvals to a three-year low has inspired a complete rethinking in the way most Big Pharmas develop new products. Interestingly, as some of the biggest pharma companies, like Eli Lilly, continue their long losing streaks in the clinic, innovative biotechs, like Biogen Idec and Gilead, are driving through new franchise therapies with enormous potential.

FDA Guidance

The administration has released its 2014 guidance agenda for the Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER), listing dozens of guidance documents it plans to release during the 2014 calendar year.

Based on planned reports, the FDA intends to direct considerable attention to both biotech and bioequivalence. The FDA intends to release two Guidance documents on biopharmaceuticals and five guidance documents on biosimilars – the most ever released in one year.

The FDA can and will make radical change to its position when new data comes to light. As binary events like FDA decisions and clinical trial results remain the riskiest part of investing in the sector, investors should factor into their risk-reward scenarios the possibility for delays in approvals and even the potential for drugs already on the market to be removed.

The regulatory landscape continues to shift and the FDA will continue to amend policy based on a myriad of inputs.

OGD & GDUFA

The Generic Drug User Fee Amendments of 2012 are designed to speed generic drug access to the public and reduce administrative costs of the approval process. The law requires applicants to pay user fees to supplement the costs of inspecting facilities and reviewing generic drug applications.

The Office of Generic Drugs' (OGD) Regulatory Counsel has provided additional guidance related to ANDAs:

- Prioritization of the Manual of Policies and Procedures, which will outline internal procedures, priorities, assignment of managers and general principals of managing inquiries
- Guidance on the Quality of 505(j) Applications - to provide guidance on improving application quality
- ANDA Amendment Tier Guidance to help clarify the statute and GDUFA metrics as they apply to amendments to pending applications
- Supplemental guidance to describe how Prior Approval Supplements will be treated under GDUFA
- Definition and guidance related to Controlled Correspondence

Unfortunately, the FDA has not addressed concerns about outsized GDUFA user fee burdens on small companies.

Biosimilar Pathway

One of the most significant changes in regulatory law was created thru the Affordable Care Act and its provision for the Biologics Price Competition and Innovation Act (BPCIA), creating an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product.

In effect, the most significant hurdle will likely be the technical challenge in assessing whether a biosimilar product is interchangeable with the original reference listed drug. Chemical drugs, can be closely or exactly approximated, and be therapeutically equivalent based on bioequivalence and pharmacokinetic / pharmacodynamics data. Unlike smaller drugs, biologics and biosimilars are radically more complex and commonly possess inherent differences potentially resulting in dissimilar efficacy, safety and immunogenicity.

As a result of this complexity, it has been unclear just how 'abbreviated' an abbreviated approval process for biosimilars could be. Would clinical trials in humans be mandatory? How large would those clinical trials need to be? Companies interested in entering the biosimilars field have been anxiously awaiting guidance from the FDA since the 2010 passage of the ACA.

Following prolonged delays, the FDA released draft guidance for drug makers interested in making generic forms of biological drugs such as enzymes and antibodies. The move could open the door for cheaper versions of some of medicine's most expensive drugs, but it is still unclear how many companies are willing to take on the challenges and uncertainties of producing biosimilars.

Ultimately, the FDA provided few concrete details about what would be required, preferring to review on a case-by-case basis. This policy bandage preserves regulatory flexibility but ultimately deters corporate investment. Ambitious drug makers willing to proceed are assuming substantial risk. Applicants pushing biosimilar development in an ambiguous regulatory complex are potentially subjected to repeated reviews with no assurance of outcome.

Little has been established in the way of guidance and regulatory pathways by which a company could expect to understand how a biosimilar product would best obtain FDA approval, leaving the industry to watch and wait for further instruction.

Biologics Price Competition and Innovation Act of 2009

The BPCIA is somewhat analogous to the Hatch-Waxman Act, which established an abbreviated pathway to bring generic drugs to the market, but there are some key distinctions between the laws and the products, which will impact the ability of generic manufacturers to bring products to the market in a cost-effective manner that saves consumers money through discounted generic products.

Comparison of Generic Drugs and Biosimilars

	Generic Drugs	Biologics
Definition	Bioequivalent to an approved brand drug Bioequivalence defined as the relationship between the brand drug and the generic drug. One way bioequivalence is measured is by evaluating the time it takes the generic drug to reach the bloodstream in 24 to 36 healthy, normal volunteers. This determines the rate and extent of absorption - or bioavailability - if the generic drug, which is then compared to that of the brand (reference product). The generic version must deliver the same amount of active ingredients into a patient's bloodstream in the same amount of time as the brand drug.	Biological products are highly similar to the reference product; no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency; must have the same mechanism of action, condition(s) of use, route of administration, dosage form, and strength.
Regulatory Law	Hatch-Waxman Act of 1984 of the Food Drug, and Cosmetic Act	Biologics Price Competition and Innovation Act of the Public Health Service Act of 2009
Approval Process	Abbreviated New Drug Application (ANDA) - 505 (j) application	351 (k) application

Key Features of Hatch-Waxman Act of 1984 and Biologics Price Competition and Innovation Act of 2009

	Hatch-Waxman Act of 1984	Biologics Price Competition and Innovation Act of 2009
Key Features	• 1 dimension for approval: generic • 5 years of market exclusivity for the reference product	• 2 dimensions of approval: biosimilarity and interchangeability • 12 years of market exclusivity for reference product - FDA cannot approve a biosimilar until 12 years after the reference product is first licensed • 12 to 14 months exclusivity granted for 1st biosimilar product found to be interchangeable • Interchangeable product can be substituted without authorization from the health care provider

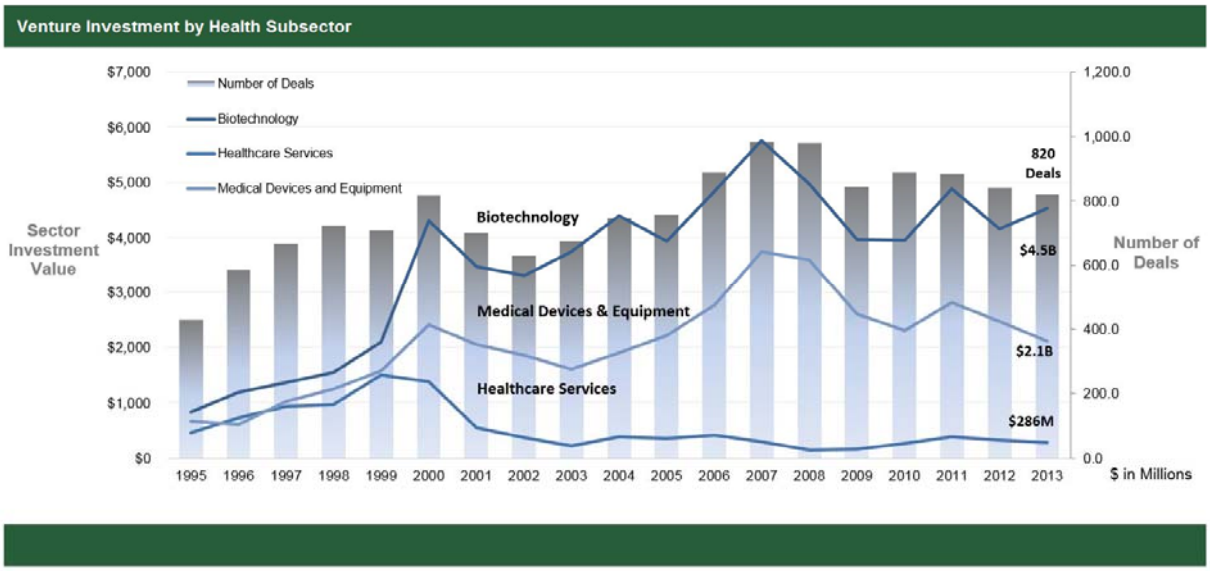
Bonilla J., Beaver N. The new US biosimilar legislation, one year later. BioProcess International. 2011: 22-30.
The National Law Review. New U.S. law establishes long awaited abbreviated approval pathway for biosimilar. March 18, 2013.
National Association of Boards of Pharmacy. Paving approval pathway for biosimilars presents unique challenges for FDA. May 23, 2013.
Bryant K., US Pharm. 2013:38(6)(Generic Drugs suppl):11-17, Biosimilars: The Long and Winding Pathway to Approval.

Industry Transaction Trends

Venture Investment

Traditional venture firms and corporate capital continue to actively fund healthcare and life sciences start-ups. Corporations are launching venture arms and they are involved in a growing share of healthcare deals. In recent years, corporate venture firms invested in almost one in three dollars on life sciences' newcomers, investing more money in biotechnology than any other sector except software.

Aggressive corporate arms seek to differentiate by leveraging other benefits, including regulatory expertise, industry connections, reimbursement know-how, and marketing muscle.



PwC MoneyTree, National Venture Capital Association, Salem Partners

Select Recent VC Rounds

($ in millions)

Date	Company	Investors	Sub-Sector	Round Size	Funding to Date
Jan-14	MedHOK, Inc.	Bain Capital Ventures; Spectrum Equity Investors	Healthcare Technology	$78	$78
Jan-14	AqueSys, Inc.	Accuitive Medical Ventures; Longitude Capital; Rho Capital Partners, Inc.	Healthcare Equipment	$44	$100
Jan-14	Complexcare Solutions, Inc.	Warburg Pincus LLC	Healthcare Services	$40	$40
Feb-14	Melinta Therapeutics, Inc.	Grupo Santo Domingo; Vatera Healthcare Partners	Biotechnology	$70	$263
Feb-14	ZS Pharma	Alta Partners LP; RiverVest Venture Partners; Salem Partners	Pharmaceuticals	$55	$110
Feb-14	Voyager Therapeutics, Inc.	Third Rock Ventures	Pharmaceuticals	$45	$45
Mar-14	Invuity, Inc.	HealthCare Royalty Partners; InterWest; Kleiner Perkins Caufield & Byers	Healthcare Equipment	$36	$86
Mar-14	Exosome Diagnostics, Inc.	Arcus Ventures; B-To-V; Forbion Capital; NGN Capital; Tiger Partners	Biotechnology	$40	$69
Mar-14	Lumena Pharmaceuticals, Inc.	Adage Capital Management; Alta Partners; NEA; Pappas Ventures	Biotechnology	$46	$71
Mar-14	Kolltan Pharmaceuticals Inc.	Boston Asset Management; Deerfield Management; Osage Partners	Pharmaceuticals	$60	$135
Mar-14	Alphatec Spine, Inc.	Deerfield Capital, LP	Heathcare Equipment	$50	$134
Apr-14	Otonomy, Inc.	Ally Bridge Group, Aperture Ventures, Avalon Ventures; Clough Capital	Pharmaceuticals	$49	$147
Apr-14	Doximity Inc.	Draper Fisher Jurvetson; Emergence Capital ; InterWest; Morgan Stanley	Healthcare Technology	$54	$81
Apr-14	Avalanche Biotechnologies, Inc.	Adage Capital Management; Cowen Capital; Redmile Group	Biotechnology	$55	$61
Apr-14	ProNAi Therapeutics, Inc.	Adams Street Partners; Amherst ; Apjohn Ventures; Capital Midwest Fund	Biotechnology	$60	$88
Apr-14	Adaptive Biotechnologies Corp.	Viking Global Investors	Tools & Diagnostics	$100	$433
Apr-14	NantHealth LLC	Kuwait Investment Authority	Healthcare Technology	$100	$125
Apr-14	Alignment Healthcare LLC	General Atlantic	Healthcare Services	$125	$125
Apr-14	Intarcia Therapeutics, Inc.	Farallon Capital Management; RA Capital Management	Biotechnology	$200	$630
Apr-14	ABILITY Network Inc.	Summit Partners	Healthcare Technology	$550	$579

Source: CapIQ and Salem Partners Analysis

Mergers & Acquisitions

The year-to-date level of announced M&A activity in the healthcare sector is at its highest level since 1980. Approximately $163 billion worth of healthcare deals have been proposed so far this year -- up almost 50% from last year and 211% above the post-financial crisis low of $53 billion in 2012. Approximately 71% of that volume is in the pharmaceutical sector, followed by healthcare equipment and technology.

Mega Deal-making

Recently there have been a number of high profile deals, including Valeant Pharmaceuticals $53 billion hostile offer to buyout Botox maker Allergan, GlaxoSmithKline's $20 billion acquisition of Novartis' oncology drug business and Pfizer's $118 billion dollar hostile bid for AstraZeneca. Notably, the to-be-determined AstraZeneca deal would represent the biggest deal for the healthcare sector since Pfizer's purchase of Warner-Lambert for $112 billion in 2000.

Select Recent M&A Activity

($ in millions)

Date	Target	Acquirer	EV	Revenue	EBITDA	EV/Rev	EV/EBITDA
Oct-13	Warner Chilcott, plc	Actavis plc	$8,431	$2,480	$1,338	3.4x	6.3x
Dec-13	Elan Corporation, plc	Perrigo Company	$6,484	--	--	--	--
Jan-14	Thermo Fisher Scientific Inc.	GE Healthcare Ltd.	$1,060	$252	--	4.2x	--
Jan-14	Aptalis Holdings Inc.	Forest Laboratories Inc.	$2,900	$707	$276	4.1x	10.5x
Jan-14	Ortho-Clinical Diagnostics, Inc.*	The Carlyle Group	$4,150	$1,886	--	2.2x	--
Feb-14	ArthroCare Corporation	Smith & Nephew , Inc.	$1,515	$379	$85	4.0x	17.8x
Feb-14	Cadence Pharmaceuticals Inc.	Mallinckrodt plc	$1,194	$113	--	10.6x	--
Feb-14	Forest Laboratories Inc.*	Actavis plc	$22,425	$3,347	$418	6.7x	53.6x
Feb-14	Emeritus Corporation*	Brookdale Senior Living Inc.	$5,363	$1,915	$344	2.8x	15.6x
Feb-14	Paladin Labs Inc.	Endo International plc	$1,590	$274	$89	5.8x	17.9x
Mar-14	Revive Pharmaceuticals*	Concordia Healthcare Corporation	$265	$50	--	5.3x	--
Mar-14	Nordion Inc.*	Sterigenics International, Inc.	$477	$250	$60	1.9x	7.9x
Mar-14	CDMI, LLC	Magellan Rx Management, LLC	$370	$43	--	8.6x	--
Mar-14	Vidara Therapeutics*	Horizon Pharma, Inc.	$660	$59	--	11.2x	--
Apr-14	AccessClosure, Inc.*	Cardinal Health, Inc.	$320	$80	--	4.0x	--
Apr-14	Questcor Pharmaceuticals, Inc.*	Mallinckrodt plc	$4,801	$889	$516	5.4x	9.3x
Apr-14	Iquum, Inc.*	Roche Molecular Systems, Inc.	$450	--	--	--	--
Apr-14	INSIGHT Pharmaceuticals, LLC*	Medtech Products, Inc.	$750	$174	--	4.3x	--
Apr-14	LVB Acquisition, Inc.*	Zimmer Holdings, Inc.	$13,926	--	--	--	--
Apr-14	Furiex Pharmaceuticals, Inc.*	Forest Laboratories Inc.	$1,535	--	--	--	--
Apr-14	iPierian, Inc.	Bristol-Myers Squibb Company	$725	--	--	--	--
Apr-14	Allergan Inc.*	Valeant Pharmaceuticals International	$44,216	$6,317	$2,126	7.0x	20.8x

Mean	5.4x	17.7x
Median	4.3x	15.6x

*** Denotes Announced Deals**
Source: CapIQ and Salem Partners Analysis

Initial Public Offerings

The IPO market regained its luster in 2013, ending the year with a total of 178 IPOs – a 75% increase from 2012. In 2014, the appetite for new public companies remains strong. In the first quarter of 2014, 103 IPOs were filed, a 178% increase from a year ago. The first quarter of 2014 saw robust activity in the IPO market with healthcare leading all other sectors. Forty-three healthcare companies went public year-to-date, generating $3.0 billion in proceeds with average first day returns of 14.2%.[31]

IPO Industry Breakdown (Year-to-Date)

Industry	Number of Deals	Total Proceeds	Average First Day Return
Healthcare	43	$3.0 bil	14.2%
Technology	31	$6.1 bil	25.2%
Financial	14	$5.6 bil	0.9%
Energy	9	$4.1 bil	4.5%
Consumer	6	$1.2 bil	15.8%
Business Services	5	$2.5 bil	10.6%
Capital Goods & Services	4	$0.4 bil	12.0%
Transportation	3	$0.6 bil	6.8%

As of May 2014

Source: Renaissance Capital, Salem Partners

Select Recent IPOs

($ in millions)

Date	Company	Ticker	Sub-Sector	Cap Raised	Market Cap	1st Day Return
Jan-14	Ultragenyx Pharmaceutical Inc.	NasdaqGS:RARE	Biotechnology	$121.0	$1,139.8	101%
Jan-14	Dicerna Pharmaceuticals, Inc.	NasdaqGS:DRNA	Biotechnology	$90.0	$294.7	207%
Jan-14	Trevena, Inc.	NasdaqGS:TRVN	Biotechnology	$64.8	$119.4	-7%
Jan-14	GlycoMimetics, Inc.	NasdaqGM:GLYC	Biotechnology	$56.0	$142.8	13%
Jan-14	Cara Therapeutics Inc.	NasdaqGM:CARA	Biotechnology	$55.0	$318.5	17%
Feb-14	Eleven Biotherapeutics, Inc.	NasdaqGM:EBIO	Biotechnology	$50.0	$178.1	9%
Feb-14	Revance Therapeutics, Inc.	NasdaqGM:RVNC	Pharmaceuticals	$96.0	$602.1	68%
Feb-14	Concert Pharmaceuticals, Inc.	NasdaqGM:CNCE	Biotechnology	$84.0	$157.7	1%
Feb-14	Auspex Pharmaceuticals, Inc.	NasdaqGM:ASPX	Biotechnology	$84.0	$506.0	31%
Feb-14	Inogen, Inc.	NasdaqGS:INGN	Healthcare Equipment	$70.6	$309.3	-5%
Feb-14	Genocea Biosciences, Inc.	NasdaqGM:GNCA	Biotechnology	$66.0	$327.8	-8%
Feb-14	Flexion Therapeutics, Inc.	NasdaqGM:FLXN	Biotechnology	$65.0	$195.9	13%
Feb-14	Egalet Ltd.	NasdaqGM:EGLT	Pharmaceuticals	$50.4	$216.9	5%
Feb-14	Eagle Pharmaceuticals, Inc.	NasdaqGM:EGRX	Biotechnology	$50.3	$163.8	-14%
Mar-14	Achaogen, Inc.	NasdaqGM:AKAO	Pharmaceuticals	$72.0	$250.4	19%
Mar-14	Castlight Health, Inc.	NYSE:CSLT	Healthcare Technology	$177.6	$1,456.1	149%
Mar-14	Versartis, Inc.	NasdaqGS:VSAR	Biotechnology	$126.0	$681.8	49%
Mar-14	Akebia Therapeutics, Inc.	NasdaqGM:AKBA	Biotechnology	$100.0	$478.4	57%
Mar-14	Applied Genetic Technologies Corp.	NasdaqGM:AGTC	Biotechnology	$50.0	$190.1	23%
Apr-14	Cerulean Pharma Inc.	NasdaqGM:CERU	Biotechnology	$59.5	$112.7	-2%
Apr-14	TriVascular Technologies, Inc.	NasdaqGS:TRIV	Healthcare Equipment	$78.0	$322.1	15%
Apr-14	Phibro Animal Health Corporation	NasdaqGM:PAHC	Pharmaceuticals	$191.0	$739.4	13%
Apr-14	IMS Health Holdings, Inc.	NYSE:IMS	Healthcare Technology	$1,300.0	$8,135.4	15%
Apr-14	Vital Therapies, Inc.	NasdaqGS:VTL	Biotechnology	$54.0	$262.1	0%
Apr-14	Corium International, Inc.	NasdaqGM:CORI	Pharmaceuticals	$52.0	$121.7	0%
May-14	Agile Therapeutics, Inc.	NasdaqGM:AGRX	Pharmaceuticals	$55.0	$110.4	-8%
May-14	Alder Biopharmaceuticals Inc.	NasdaqGM:ALDR	Biotechnology	$80.0	$312.8	0%
May-14	K2M Group Holdings, Inc.	NasdaqGS:KTWO	NasdaqGS:KTWO	$132.3	$554.1	0%
May-14	SCYNEXIS, Inc.	NasdaqGM:SCYX	NasdaqGM:SCYX	$62.0	$68.0	-10%

Conclusion

While regulatory reform and exchange implementation have driven recent headlines, the broader success over the coming years will be determined by how well the industry addresses a range of foundational business challenges – providing seismic hurdles for some and tremendous market opportunities for others.

Rapid innovation and competition from non-traditional players will provide a disruptive influence in a healthcare landscape historically led by the old guard. Empowered consumers, integrated care and a shift to value-based incentives will provide sweeping change in the delivery of health services.

By the end of this decade, successful health plans will have moved from financing healthcare to coordinating health. As organizations work toward becoming diversified health and wellness solution companies, many will need to grow larger, become leaner, and leverage their brand.

Digital health companies are using their technology to help providers deliver improved patient care. Health information technology faces a particularly exciting future. Healthcare's stubbornly analog disposition will give way to applied CRM, EHRs, outcomes-based care, big data, precision medicine, consumer oriented by health tools, and new clinical solutions.

Despite the healthcare industry's transformation through the Affordable Care Act and digital health, nothing will change the fact that doctors continue to play the leading role in delivering healthcare. As physicians continue to strive for improved patient outcomes; operators, systems and investors which empower lean provider networks will prosper.

We believe the current trends are a prelude to the most significant change in the American healthcare model in 50 years, since President Lyndon B. Johnson signed Medicare and Medicaid into law. While developments will come in spurts, some dramatic and others slight, the collective outcome will be tectonic. This transformation will affect nearly every individual and nearly every enterprise. The near term will be marked by furious innovation yielding both extraordinary successes and disappointing failures. As healthcare professionals, the next five years provide exceptional opportunity for forward thinking innovators and stakeholders as opportunities continue to emerge.

Salem Partners' Healthcare & Life Sciences Practice

Salem Partners was founded in 1997 with the objective of providing sophisticated, independent advisory services to our long-term client partners.

We have pursued our objective by ensuring that regardless of transaction type, size or industry, clients receive the focus of senior bankers and the benefits of our network of contacts. We view each transaction not only as a business opportunity, but also as a chance to build a lasting relationship.

Salem Partners is a leading adviser to early stage and growth stage healthcare and life sciences companies.

- We build relationships where our judgment, objectivity and expertise create significant long-term value for our clients.
- Our investment banking professionals leverage deep domain knowledge and industry relationships to provide insightful strategic advice and successful transaction execution.
- Our wealth management professionals provide customized investment solutions in a multi-family office environment.

Salem Partners consists of a diverse team of seasoned bankers and has completed billions of dollars of transactions for clients in industries ranging from healthcare & life sciences to aerospace & defense.

Healthcare & Life Sciences Areas of Focus:

- Healthcare Services
- Health Information Technology
- Diagnostics & Supplies
- Specialty Pharmaceuticals

Capital Raising

- Salem Partners' clients know that they will have a trusted and experienced advisor protecting their interests in all phases of a transaction.
- Salem Partners acts as the exclusive agent in private placements of equity and debt securities.

M&A Advisory

- We bring a full range of M&A capabilities to every deal, including negotiation, due diligence, valuation and regulation.
- Access to an extensive network of institutional investors, family offices and value-added individuals.

Valuations & Opinions

- Salem Partners provides financial fairness opinions to board of directors, investors, trustees, management and other stakeholders in order to fulfill the fiduciary obligation to verify the financial fairness of a pending transaction.
- The Firm is routinely called upon by some of the world's largest financial institutions to provide validation of asset or company valuations in connection with credit facilities.

Representative Transactions

Salem Partners' clients know that they will have a trusted and experienced advisor protecting their interests in all phases of a transaction. We bring a full range of capital advisory and M&A capabilities to every deal, including negotiation, due diligence, valuation, regulation, tax and accounting.

The firm's deep industry knowledge and access to key executives ensure that clients receive the most advantageous terms available in a transaction.

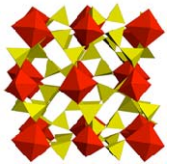
Adams Case Study

- Private, pre-revenue company when Salem met management in 1999.
- Adams had successfully raised a small friends and family round and needed significant institutional capital to fund development of Mucinex™.
- One of the most successful specialty pharmaceutical companies in the U.S. with product sales in excess of $500 million.
- Later acquired by Reckitt Benckiser for $2.3 billion in cash.

Salem Partners

- Salem acted as exclusive placement agent for Adams in three private rounds, raising in excess of $80 million from leading institutions.
- Achieved increasing valuations in each round.
- Engaged by Adams management to advise on the IPO process.
- Hired as wealth manager for several Adams founders and investors.

ZSPharma INC.



ZS Pharma Case Study

- ZS Pharma management team licensed ion-binding crystal technology from a large chemical company and needed significant funding to continue development, test safety and to conduct clinical trials.

Salem Partners

- ZS management engaged Salem Partners in late 2010 and Salem secured a term sheet for an interim financing that would fund proof-of-concept (POC) studies.
- Salem and ZS navigated through regulatory challenges and closed a $5.3 million convertible note financing in late 2011.
- Upon receiving positive POC clinical data, Salem Partners coordinated a competitive process to raise $46 million Series C Preferred Stock from leading venture capital firms.
- Salem participated as a significant principal investor in the transaction.
- Salem actively advised and directed IPO process, registered 2014.

exemplar

Exemplar Case Study

- Private specialty pharma company focused on aerosol drug products delivered to the lung.
- Founded in 2002 by aerosol pioneers Dr. Charles Eck and The Armstrong Family.
- Due to a downturn in its contract services business during 2012, Exemplar's financial performance deteriorated and the Company required an immediate capital infusion.

Salem Partners

- Salem arranged and closed a significant debt & equity investment with a well-known biotech hedge fund investor in less than 30 days.
- Simultaneous with the financing, Exemplar's largest customer, MAP Pharmaceuticals was acquired by Allergan, Inc.

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