



## Health Care Innovation: Disrupting the Paradigm

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### Summary

- Over the past ten years, there has been a significant rise in US health care spending, reaching \$2.9 trillion in 2013.
- The health care sector is undergoing a seismic change. Innovation in areas such as genome biology and immunotherapy are drastically improving patients' outcomes against multiple diseases. Novel approaches to address medication compliance and using technology for patient-doctor interactions have the potential to significantly drive down health care costs.
- Scientific advances could produce big winners, as well as many losers, and we continue to evaluate the full range of opportunities focusing on future returns, valuation, and scenario analysis.

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The complexities of the health care environment, in terms of outcomes, cost, and access, are well known by investors. In 2013, the aggregate spend in the US health care industry reached \$2.9 trillion (Exhibit 1). In this paper, we will focus on the 9% of spending attributable to prescription pharmaceuticals, as well as a portion of the 20% spending attributable to physicians and clinics. We will also discuss the improving environment for biopharmaceutical innovation, breakthroughs in genome biology, immunotherapy, gene therapy, and novel approaches to health care delivery.

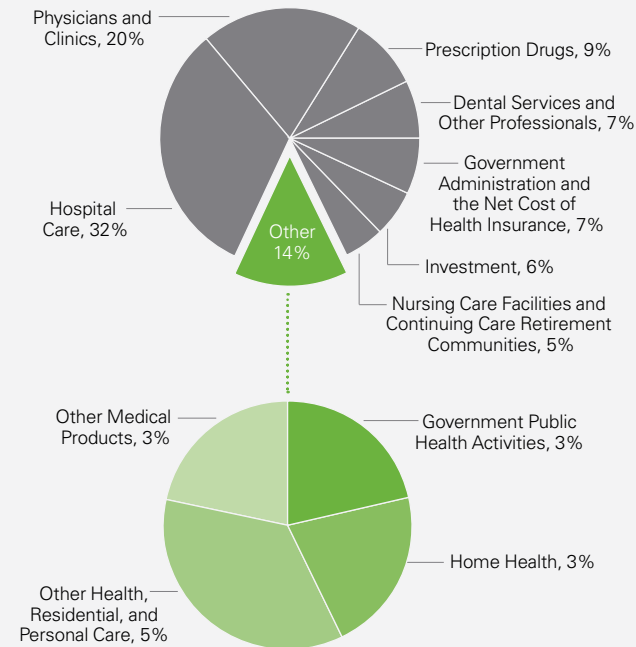
### The Current State of the Health Care Environment

Over the past ten years, there has been an inexorable rise in health care spending in the United States (Exhibit 2). In 2014, health care spending reached 17.5% of GDP, a level that is approximately double that of the rest of the developed world. Currently, health care spending in the United States is on pace to reach nearly 20% of GDP by 2023. The growing magnitude of this spend is one of the strongest arguments for the private sector to invest in potentially disruptive products and technologies that can reallocate the way dollars are currently spent and potentially even bend the cost curve.

Exhibit 3 shows the number of new drug approvals by the Food and Drug Administration (FDA) since 1992 and the average amount of biopharmaceutical industry research and development spend per FDA approval. The growth in the number of FDA approvals over the past decade is an encouraging sign. We believe it reflects both the improved quality of the applications submitted for FDA approval, as well as the FDA's implementation of some creative pathways to

### Exhibit 1 US Health Care Spending Was \$2.9 Trillion in 2013

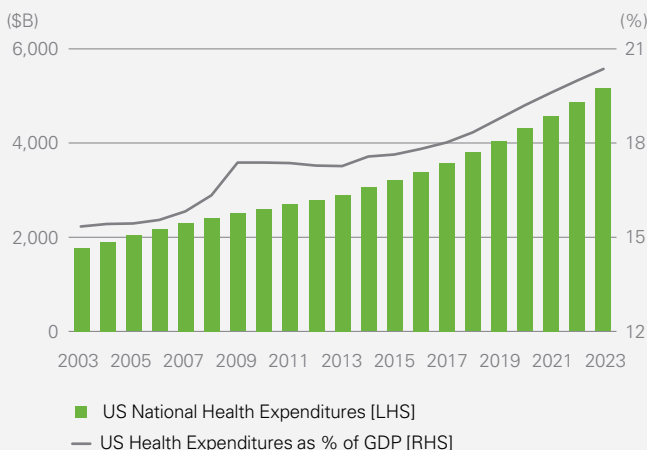
Breakdown of US Health Care Spending



As of April 2015

Source: healthcare-economist.com

### Exhibit 2 US Health Care Costs Continue to Increase



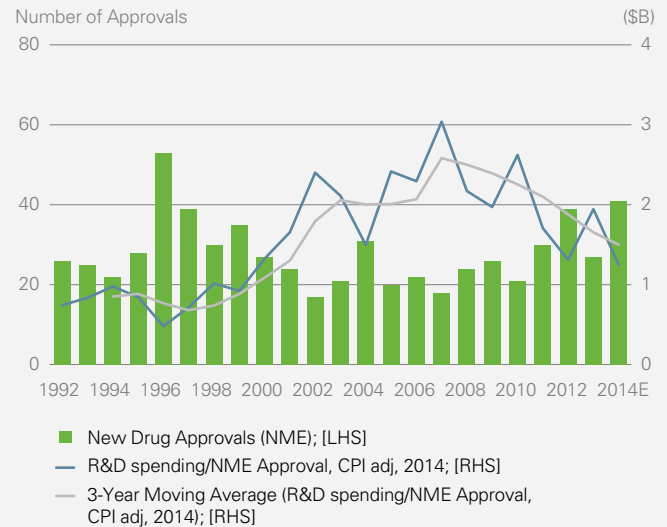
As of June 2015

Health care spending projections are based on the 2013 version of the NHE released in January 2014. Estimated or forecasted data are not a promise or guarantee of future results and are subject to change.

Source: Centers for Medicare & Medicaid Services, Haver Analytics, Lazard

### Exhibit 3 Biopharma Research and Development Spend Is Becoming More Efficient

Drug Approvals and R&D Spending



As of January 2015 (drug approvals); and April 2015 (R&D spending)

NME = New molecular entity. Estimated or forecasted data are not a promise or guarantee of future results and are subject to change.

Sources: FDA, PhRMA, Bureau of Labor Statistics

significantly accelerate the time to market for highly innovative drugs. Following an extended period of time where the average amount spent by the biopharmaceutical industry per approved drug more than tripled, reaching a peak of about \$3.0 billion in 2007, which closely coincides with a perceived innovative trough for the industry, we have seen a steady reversal of this trend over the past seven years. This reflects the combination of more measured research and development spending by the health care industry and the recent increase in the number of FDA approvals.

## The Acceleration of Health Care Innovation

### Genome Biology

One of the greatest life science innovations of the past thirty years has been the advent of DNA sequencing, which led to the sequencing of the first human genome at the start of the last decade. This sequencing effort cost approximately \$2.7 billion, consuming thirteen years of work and millions of labor hours. Since then, the advent of much lower-cost DNA sequencing, spurred on by technological innovations by sequencer manufacturer Illumina (among others), has led to a thriving new field known as genome biology.

In fact, today a human genome can be sequenced in approximately one week at a cost of approximately \$1,000 when done at scale (Exhibit 4). This is important because many diseases, like cancer, are a function of mutation in our DNA. The advent of low-cost DNA sequencing has transformed our understanding of disease biology, as hundreds of thousands of genomes have now been sequenced. Many heritable diseases are being identified, along with a growing number of novel therapeutics to treat them.

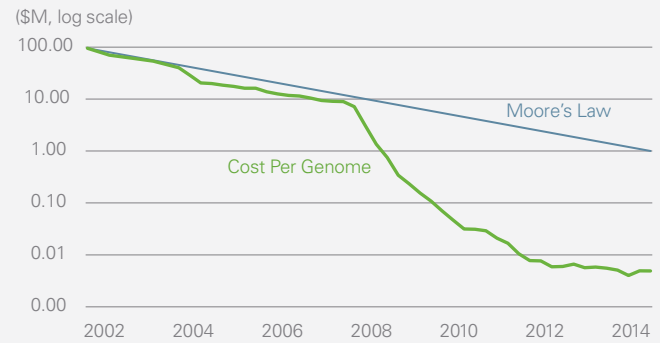
At the same time, advances in genome biology are transforming the drug development process. Exhibit 5 shows drug development timelines for a number of breakthrough cancer medications that have been commercialized over the past fifteen years. Novel insights from genome biology are one factor shortening these timelines. One of the best examples is Pfizer's Xalkori, which treats a subset of lung cancer. This drug went from discovery to FDA approval in just four years. Contrast this with the time it took to commercialize Novartis's Gleevec,<sup>1</sup> one of the most successful cancer drugs of all time, which went from discovery to approval in 41 years.

## Immunotherapy and Gene Therapy

Advances in genome biology are also unlocking some of the most complex systems of human biology, leading to the identification of novel "druggable" targets. The scientific community's enhanced understanding of the workings of the immune system, particularly in the context of fighting cancer, provides an illustrative example through the advent of immunotherapy, which represents one of the biggest paradigm shifts in the treatment of cancer in several decades. While cancer is very clever at evading the immune system, when one intervenes with a PD-1 antibody it essentially removes the brake on the immune system that otherwise would be active. The identification of a

**Exhibit 4  
Costs Are Decreasing in Genome Sequencing**

Cost per genome



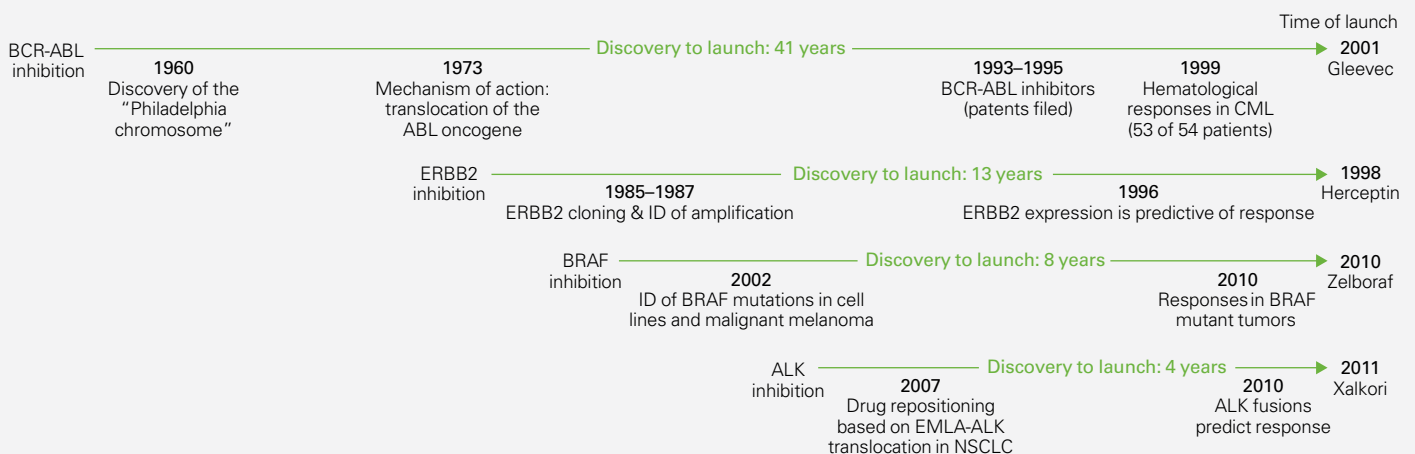
As of June 2015

Source: National Human Genome Research Institute (<http://www.genome.gov/sequencingcosts/>)

critical checkpoint in the functioning of the immune system, or PD-1 receptor, which normally serves to suppress the immune system when it interacts with a tumor cell, has led to the emergence of a highly promising class of therapeutic monoclonal antibodies.

Immunotherapy can transform and extend a cancer patient's survival. Exhibit 6 shows a conceptual survival curve, where the green line represents the expected short survival that cancer patients would experience if given no treatment, while the blue line represents the relatively limited survival benefit that would be conferred by current treatments (mainly chemotherapy), which has been the treatment used over the past forty to fifty years. By comparison, the first generation

**Exhibit 5  
The Cancer Drug Timeline Has Decreased Significantly**



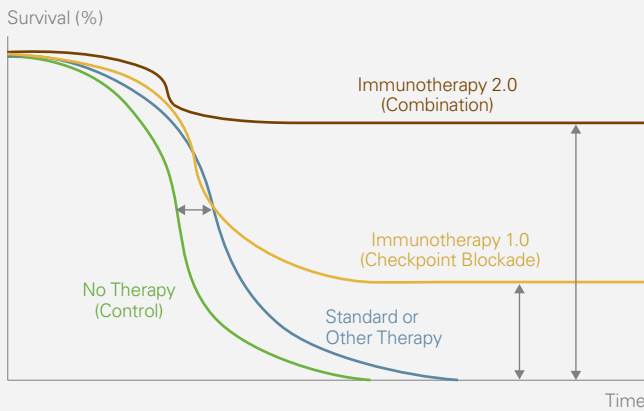
As of December 2014

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Source: Nature Journal, Goldman Sachs Research



### Exhibit 6 Immunotherapy Can Potentially Increase Cancer Survival Rates



As of May 2014

Immunotherapy 1.0 comprises the anti-PDL1 and Anti-PD-1/PD-L1s treatments. This information is for illustrative purposes only.

Source: Merck

of immunotherapies or PD-1 antibodies—as depicted with the yellow line—shows a dramatic longer-term survival improvement, with an estimated 25% to 35% of patients experiencing a long duration of effect, likely lasting years. The brown line shows the promise of future iterations of immunotherapy, whereby a vast majority of patients would experience the long-lasting benefit and multi-year survival that a minority of patients are now receiving with the first-generation agents. Ultimately, the science behind immunotherapy holds out the promise of a functional cure.

For example, historical data suggest that patients with refractory squamous lung cancer have an incredibly poor prognosis and are likely to pass away in nine to twelve months in the absence of immunotherapy. However, when given Bristol-Myers Squibb's Opdivo (an immunotherapy treatment) 41% of patients in this particular trial were alive at the one-year mark, a truly remarkable result.<sup>2</sup> In fact, given the breakthrough nature of this advance, the FDA approved Opdivo for second line squamous lung cancer in early March 2015, a record review time of just over two months, where typical reviews would normally take a year, and priority reviews would take six months. This underscores the significance of this advance for patients and lung cancer treatments in general. Today, there is a significant presence of both major biopharmaceutical players, as well as a number of emerging- and early-stage biotech companies, participating in the exciting immunotherapy area, underscoring the level of investment it is currently receiving.

Another exciting area of medicine that holds great promise is gene therapy, a potentially curative technology. An example of a burdensome disease that could be transformed with gene therapy is hemophilia, where affected patients are deficient in a key blood clotting protein due to a genetic defect. Using gene therapy, a working

copy of the needed gene could be inserted into the liver, enabling patients to produce sufficient levels of the needed clotting protein, thereby potentially freeing them from lifelong clotting factor infusions that currently occur two to three times per week. Other diseases that could benefit from this approach include sickle cell disease, macular degeneration, inherited retinal dystrophies, and perhaps even Parkinson's disease.

## Innovation Focused on Patient Behavior and Interaction

The delivery side of health care continues to be a major challenge, with medication compliance (i.e., patients not properly adhering to their prescribed treatment) being one of the single biggest problems in health care. For instance, many chronic care medications are used just 50% to 60% of the time.<sup>3</sup> Importantly, these poor compliance rates lead to worse disease control and health outcomes, driving up health care costs. Furthermore, today's health care system is optimized towards treating acute conditions, not managing patients with ultimately expensive lifelong diseases. Unfortunately, chronic, often lifestyle-related diseases like diabetes are among the world's biggest health care problems.

In response, Proteus Digital Health, a private company, has developed a digital health feedback system that captures information on medication compliance, patient activity, and rest. This system consists of three components: a tiny ingestible, inert sensor that is activated by stomach fluids; a disposable, wearable patch that captures signals from the sensor, for example, whether a medication was taken, the patient's heart rate, activity, and rest patterns; and a blue-tooth enabled device that records information from the sensor. Recorded information can be remotely shared with physicians, caregivers, and family members. Today, version 1.0 of this product—which is FDA approved—is taken as a tablet together with a patient's regular drug prescription. Version 2.0, likely would formulate the ingestible sensor into a manufactured drug product. Future iterations of this technology potentially may be capable of monitoring other critical health parameters such as blood sugar and cholesterol. This technology represents an innovative way to improve patient compliance and remotely monitor a patient's health status, thereby driving improved health outcomes.

Telehealth, which is a way of facilitating interactions between physicians and patients by leveraging existing telecommunications technologies, is another health care innovation in focus today. Novel ways of providing quality, affordable care are desperately needed. Underscoring this point is that by 2025 there will be a projected shortage of more than 50,000 physicians in the United States.<sup>4</sup> Therefore, improved models of health care access are needed. Telehealth enables real-time interactions between a doctor and patient via video. It also facilitates asynchronous interaction or transmission of data—an example would be a transmission of a health care evaluation based on a patient's records from one health care provider to another. Telehealth also includes remote patient monitoring, such as the Proteus product discussed earlier.

Today, many US health plans are forging telehealth partnerships. United Health already has six telehealth partners, managing roughly 350,000 telehealth consultations daily. Furthermore, privately held Teladoc is the market leader in real-time interactions. Its business model consists of partnering with health plans and employers to provide physician access via PCs and mobile devices. The cost of their service is quite competitive, with an average cost of \$40 per interaction versus \$85 for a typical Minute Clinic/CVS visit or \$170 for a typical physician office visit. Importantly, the results to date from Teladoc appear compelling, with 90% of Teladoc patients reporting resolution of their medical issue. The net result from these innovations is improved patient health and improved outcomes.

## Conclusion

The health care industry remains in the midst of seismic change. Scientific advances, which are occurring at an accelerating rate, could produce big winners, as well as many losers. Investors recognize this potential and hence are increasingly paying for potential long-term optionality that exists with many biopharmaceutical companies. We continue to evaluate the full range of opportunities focusing on future returns, valuation, and scenario analysis. As always, we see attractive risk/reward in attractively valued health care companies that feature sustainable revenue growth, high or increasing levels of profitability, strong balance sheets, as well as improving shareholder-friendly capital allocation.

## Notes

- 1 This drug is used for treating chronic myelogenous leukemia and was approved in 2001—41 years after the discovery of the Philadelphia chromosome mutation.
- 2 Source: Bristol-Myers Squibb's presentation, CMSTO Meeting, October 2014
- 3 Source: CDC (<http://www.cdc.gov/primarycare/materials/medication/docs/medication-adherence-01ccd.pdf>)
- 4 Source: AAMC (<https://www.aamc.org/download/426260/data/physiciansupplyanddemandthrough2025keyfindings.pdf>)

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