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Healthcare "Moonshot"

Seven Trends Likely to Persist Beyond ObamaCare

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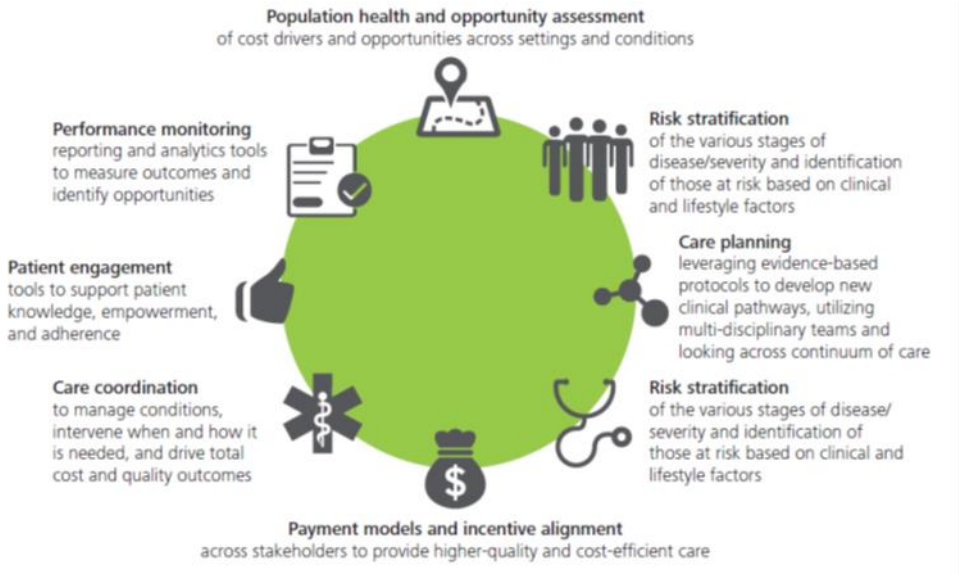
JPM "week" in San Francisco in early January historically has been a sounding ground for issues and trends of major importance to the life sciences. Last year's focus, in simplest terms, centered on evolving alternative payment systems that, by mandate, were to be underpinned by measures of "performance": evidence-based clinical utility, patient satisfaction and cost efficiency as mandated by the Medicare Access and CHIP Reauthorization Act (MACRA) in 2015. Controlling cost represented the lion share of discussion last year, but defining and measuring "value-based care" has turned out to be a far greater challenge, especially within a system rooted in care fragmentation and lack of coordination among sets of providers that CMS believes contributes 20-40% to Medicare costs, a figure supported by a Health Policy Brief published by the Robert Wood Johnson Foundation in November 2015.

Figure 1. Changing Landscape of Healthcare



Source: Deloitte 2016 Healthcare Outlook: Battling Costs While Improving Care

Now that the Trump Administration is officially "off and running", investors have been trying to sort out what will stay and what will go as Trump works to keep his campaign promise of repealing the Affordable Care Act (ACA). Based upon recent speeches and panel discussions held during JPM week this year, as well as discussions sponsored by major consulting firms in which we participated, at a high level, most agree the concept of value-based care is here to stay and with it, most of the value-based MACRA provisions.

"Unpacking" may become a term du jour to describe the process by which various elements of value-based care and its delivery under ACA are eliminated or revised as "unpacking" may end up being the only practical way by which to deal with ACA. Under the assumption that value-based care remains the lynchpin of healthcare delivery going forward, we see certain of the enabling entities such as the Center for Medicare & Medicaid Innovation (CMMI) and the recently formed FDA Center for Innovation continuing to be funded and leading the effort to defragment and better unify the healthcare system. Regardless of how the plethora of issues around this subject play out among the Trump Administration, Republicans, Democrats and other constituents, we believe some of the ACA, MACRA and other value-based care changes already afoot in the pharma/life sciences/healthcare sector may transcend administration changes and political fray in Washington. We highlight a few which, in our opinion, may be particularly significant to early stage life science companies.

The "Cancer Moonshot" Basic Tenet will Remain in Force

The official mandate for the *Cancer Moonshot* program ended on January 20th, and its specific funding future is uncertain at this writing. But the disparate organizations who participated to date will continue to work towards its goal: compress the legacy 10-year research and investigative timeline to deliver clinical solutions in half the time (5 years) to eliminate/cure cancer at (hopefully) lower cost than historical precedents. Vice President Biden, in both a speech at JPM and again at Davos two weeks ago, reiterated key underpinnings of the initiative that center around the culture of cancer (academic) research and the lack of patient-centricity in cancer treatment. The Vice President's comments were expanded upon in a discussion with Greg Simon, the Executive Director of the *Moonshot* program, during a JPM Panel discussion. Key take-aways we believe are likely to survive with or without the Moonshot program:

1. Cancer Is A World Issue With Enormous Financial Consequences.

The impact of cancer and its cost to individuals and society is felt by all nations. The World Health Organization has estimated that by 2020, 50% of the world's healthcare expenditure, or about $4 trillion, will be spent on three causes of death, cardiovascular disease, cancer and respiratory disease. According to the Vice President, numerous governments joined *Moonshot* discussions over the past year and gave support for unifying approaches to clinical trials, creating standard protocols for clinical trials and harmonizing regulatory pathways to facilitate a more rapid development cycle for effective cancer treatments. Among other things, this commonality of cause may likely accelerate harmonization of EU and US regulatory pathways and may accelerate the speed at which a level of harmonization takes place with other regulatory bodies such as the Chinese FDA. A more rapid EMA and FDA harmonization potentially could diminish the commercial appeal of a regulatory path based upon the CE Mark as the EMA moves to a stance that is based upon clinical validity rather than primarily manufacturing quality.

2. Changing the Basic Research Culture and System, Breaking Down the "Silo" Approach of Basic Academic and Government-sponsored Research. Vice-President Biden specifically targeted the need to move from the Post WWII antiquated "individual achievement" research model (his terminology) for government-backed grant funding and publication to one of "sharing data and collaboration" across various research organizations, stakeholders and collateral areas of experience in order to more widely validate the integrity of basic research and to cut the timeline to commercialization. As an example, he cited bringing in knowledge and research conducted by NASA to inform radiotherapy-based cancer clinical trials and treatments. He went further in proposing penalizing government-funded researchers who are unwilling to "share" their science and data. With numerous examples of unsubstantiated, discredited or incomplete data from sole-source labs and researchers now a matter of public record, we believe investors are becoming much more sensitized to the subject and will more strongly favor companies whose data and clinical results can be or have been vetted/validated by outsiders. This trend could lead to the single inventor/owner/entrepreneur company becoming much harder to fund by traditional means.

The 21st Century Cures Act further supports this notion and has specifically begun to address collaboration in combination product clinical trials. An example of these efforts, the NIH through the NIH Formulary, is now charged with integrating and coordinating many of the corporate interactions required for eventual commercial combination therapies. More specifically, the NIH is building pre-set *standardized* license agreements whereby the intellectual property rights, data ownership and other multi-entity considerations necessary for combination therapies are set out in advance. The concept builds on similar "pre-set" collaboration terms and document sets pioneered by the Harvard Medical System, MIT, and other Massachusetts academic research institutions. It was suggested by speakers on a related JPM panel discussion that the NIH leadership role in standardizing such agreements could cut as much as a year out of the "development/commercialization" timeline for combination product therapies.

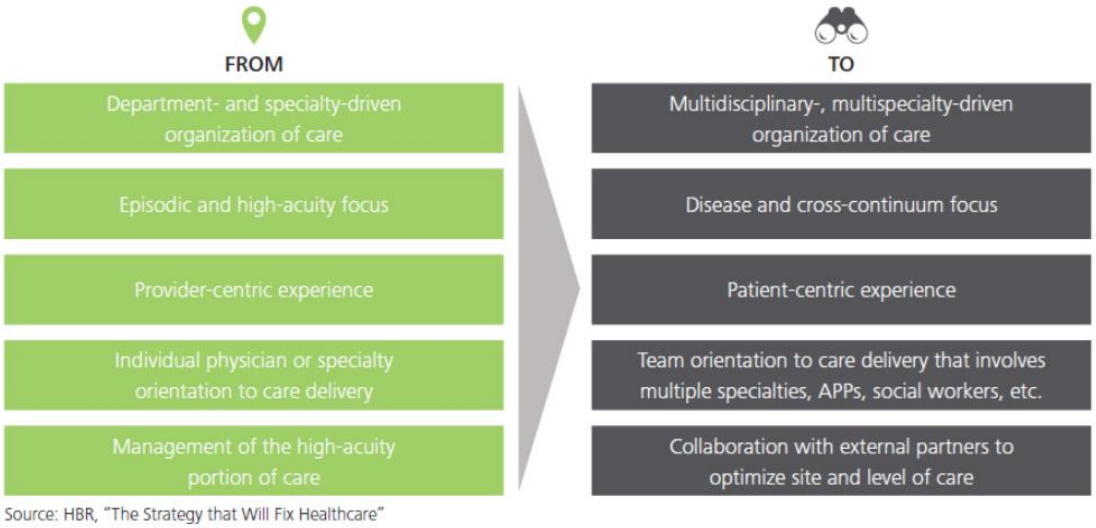
3. Collaborative "Big Data" Needs to be Available to All Stakeholders. The *Moonshot* initiative enabled a new partnership among the NCI, Amazon Web Services and Microsoft whose goal is to build a model for maintaining cancer genome data in the cloud, so that genomic data is accessible by *all* cancer researchers, on a global basis. The need for such collaboration was illustrated by an example cited by Mr. Simon involving a pancreatic cancer patient. The NCI's current cancer genome atlas has data from only about 100 patients, yet a US drug developer has data on over 1000 pancreatic cancer patients. The oncologist in this patient's particular case was unaware of the substantially more robust corporate pancreatic cancer database. The "proprietary" nature of such corporate data may become subject to challenge by a potential greater need to benefit all patients, if that data originated with any government-sponsored funding.

Tumor profiling or "liquid biopsy" are slated to become "obsolete" terms as payers seek to eliminate substantial "data" noise in many liquid biopsies technologies and reduce the burden of false positives in screening diagnostics. "Big Data" is being billed as the solution to cleaning out data noise. Creating personalized treatment value will likely force a consolidation in molecular diagnostics that ends up with value being determining by what are the real clinically relevant and actionable pieces of information based upon a totality of patient outcomes. This trend has already been set in motion by CMS's requirement for clinical utility studies, but we would expect that payers will also drive what kinds of "clinical utility" will be deemed clinically relevant. By necessity, fulfilling this requirement will push towards more sensitive "blood profiling" to gain further insights into (cancer) patient-specific etiology. *Moonshot* has already spurred the integration of this kind of data into shared networks such as CancerLink, Project Genie and the 3D Cancer Atlas. A collaboration among government, academia, pharmaceutical and diagnostic companies called the Blood Profiling Atlas Project is being established as a result of *Moonshot* to accelerate informative blood profiling diagnostic technologies that directly result in patient benefit. We see these trends being highly impactful on the economic viability of many molecular (liquid or not) diagnostic companies and will likely drive further market segmentation in diagnostics.

4. Patient Centricity, Putting Decision-Making and Access into Patients' Hands. From full access to their entire medical record, to patient controlled "directed" medical record sharing, determining who contributes to the record (does the pharmacist or patient's spouse know more about the patient's status than the primary physician) and to clinical trial access, the concept of patient centricity is especially important to the cancer patient and rare-disease communities. The FDA, through the 21st Century Cures Act, must now consider quality of life and patient-perceived treatment benefits as part of new drug/treatment approvals. Furthermore, the FDA is pushing trial sponsors to broaden patient access to clinical trials and reduce trial bias by sharing trial protocols outside of cancer centers of excellence or academic settings. We expect to see an increased burden on clinical trial sponsors to fund improved patient access to trials. One example cited was the use of "credits" for patient transportation to and from treatment or requiring institutional treatment access for late stage patients who find it especially difficult to reach a single trial or treatment centers. We believe the concept of patient-

centricity will expand over the upcoming and near future years as treatment innovators and payers wrestle with how to determine the real cost of a disease and the real economic and social benefits to the patient/society of the treatment within a (fair) practical pricing model. We expect to hear more companies address treatment value in terms of the "value of statistical life" (VSL) or Quality-Adjusted Life Year (QALY) both of which attempt to take a holistic view of care that includes not only the immediate patient benefit, but avoided costs such as chronic care, transplants, etc. , augmented by "societal" benefits of a return to productivity (paying taxes). The graphic below, adopted from a 2015 Harvard Business Review publication, is a fair depiction of the primary role of patient-centricity in value-based care.

Figure 2. Towards Value-based Holistic Health care



Source: Deloitte 2016 Healthcare Outlook

Moves by the FDA Likely to Continue Forward

The FDA has already embarked on implementing some innovations derived from its partnership with CMS, such as the still little-used Parallel Review regulatory path. But a number of other changes, some incorporated into the 21st Century Cures Act and others not, are likely to be watched closely by industry and we believe, will continue to move forward under the new administration. We categorize these into two general buckets: "Standardization" and "Real World Evidence". Both of these core tenets will require new thinking on the part of product innovators.

5. Standardization. We expect the FDA will continue to become more proactive in moving towards the standardization in at least two primary ways aimed at achieving heightened clinical validity and transparency. First, there is a huge disparity in how data such immunohistochemistry or pathology and in other types of technician-read data is currently reported. Substantial enough variation among academia, corporate sponsors and others exists that it is now extremely difficult to match results across research organizations and across clinical trials testing drugs of the same class or even drugs for the same indication. The move towards standardization of reporting will also likely encompass the "statistics" and the methodologies used in validating the treatment or test's benefit in a "statistically significant population." With an increasing number of trials being targeted to highly refined genomic sub-populations, we expect companies will have increased dialog and input from the FDA as to which statistics and what populations will be required for approval and label claims.

A second wave of potential standardization lies in actual clinical trial management. The FDA has already given a nod to the concept of standardized placebo arms for specific drug classes or indications in an effort to improve transparency and speed trial review. As more companies seek to take advantage of various designations that

insure heightened interaction or faster review with the FDA, we can envision innovators being asked to or eventually perhaps being mandated to accept standardized placebo arm design and reporting.

6. The New Buzzword: "Real World". Only about 20-30% of molecular diagnostics and liquid biopsy tests are fully reimbursed because of a lack of translation of the statistical power of benefit from a very narrow clinical trial patient base to use in the "real world". The FDA has discussed changing the view of what is statistically significant or changing a definition of "relevant population" and in doing so, is encouraging companies to open trials to "real world" people (those who might otherwise be fall into various protocol exclusion categories or those with co-morbidities) who could be entered into non-data (non-reporting) trial arms. Another FDA "complaint" around this subject comes from "artificial" clinical trial bias that derives from cancer trial patient populations being affiliated primarily with particular cancer academic centers. The FDA is accepting of adaptive trial and Simon 2-stage trial designs that add-on patients or arms under certain circumstances. We see these trial designs becoming more commonplace or perhaps supplanting the traditional serially phased clinical trial program, thus potentially offering companies a method by which to run various protocols or patient populations side by side, thus saving time and money. As we move further into the realm of personalized medicine and further from the historical "blockbuster" (volume of scripts) model, the FDA may be challenged to reconsider the definition of statistical significance in very small or genetically narrowly defined patient bases.

7. And Finally, Payment and Pricing: Payment-for-Benefit is Rapidly Approaching

Judging from the continued conversation around payment (reimbursement) and drug (treatment) pricing from various of the JPM panel discussions, to us, the genie is clearly out of the bottle. Steven Ubl, President and CEO of PhRMA, the pharmaceutical industry's major trade association, distilled the pricing issues down to the end-game, which in his view, amounts to how much will a patient be willing to pay as a co-pay and what will the "system" do to impact that eventual co-pay. Since more therapies hold the potential for "cure" in much smaller select populations, the need to define *total* value to the patient will continue to force the move to the payment-for-benefit paradigm and away from discreet (volume) drug pricing. Smaller players may not yet fully grasp the implications of what is being described as an approaching sea-change in reimbursement: from legacy "payment for blockbusters" to annuity or other "payment-for-benefit" schemes, which may result in a "bolus" payment upon treatment initiation and periodic payments upon achieving benefit metrics (i.e., each year of sustained life or reduced chronic drug treatment). Larger drug companies, however, are beginning to act to inform the public about the value of innovation and as one CEO mentioned, transmit transparency as to how pharma arrives at drug pricing. This is a progression in thought on payment-for-benefit that Big Pharma was not having some months ago and, in our view, represents a significant change towards acceptance. In the NY area, PhRMA has already begun running TV ads promoting the 'benefits" of today's innovative drugs.

The following are among notable comments made during a JPM panel discussion entitled, "The Great Debate: Pricing, Innovation & Delivering Value in the New Era of Medicine" (JPM, 1/9/17): "80% of healthcare expenditures are by super-users (multiple chronic diseases), this makes drug prices in isolation, the wrong target, the target should be disease-focused." "There is an under appreciation of the role of private payers in restraining costs- five payers and three PBMs control 80% of (US drug) pricing and have been very effective in restraining cost growth." (Steve Ubl, President & CEO of PhRMA) "We need to identify whose benefit—the hospital, the payer, the patient or the taxpayer?" (Bristol-Myers CEO, Giovanni Caforio) "We need to shift away from drug transactions to outcomes", "How do you bring a holistic view (of treatment) to the payer? We need to articulate a lower total cost of the holistic patient outcome based on medical value (extension of life), patient value (quality of life), healthcare system (lower hospital costs) and societal value (increased patient productivity). We can only do this as an industry by becoming more transparent in how we price." (Novartis CEO, Joseph Jimenez). We believe that Mr. Jimenez's last comment is particularly apropos in that innovators

will increasingly need to substantiate in quantitative terms a rationale for treatment pricing. We believe this will be a challenge for smaller life science companies, but one they will have to meet as investors, over time, are likely to become even more demanding of managements to seek very early interactions with both regulatory and payer bodies in order to have at least a working "thesis" on patient treatment value before funding clinical trials.

Comment

The other side of the payment vs pricing issue is wasted expenditures. As acknowledged by CMS and others, about 1/3 of current healthcare expenditure is non-productive, and therefore, wasted, by virtue of being falsely needed or an overtreatment (i.e., mammograms, PSA tests and falsely needed biopsies), by money wasted treating non-responders (on average, only about 10-20% of patients respond to standard cancer treatments thus the real benefit of blood profiling), by highly fragmented and uncoordinated care (non-patient centric) and of course, fraud. We would also include the cost of failed clinical trials. We believe the trends as described above, in aggregate, represent an opening of the door to significantly reducing the level of wasted healthcare expenditures. If nothing else, this would be a major achievement and is a primary reason why we believe these trends will persist with or without the *Cancer Moonshot* or the ACA. *SG*

Health Affairs article:
http://content.healthaffairs.org/content/34/4/576.abstract?rss=1&utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%253A+yahoo%252FpeRX+%28Healthcare+Industry+News%29

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