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Expert Insight

Why PM1.0 Will Not Create Radical Health Care Change Prompting the Need for PM2.0

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Peter Keeling of Diaceutics explores the concept of PM2.0 in this article for the pharmaphorum website.

The six forces behind 2.0 anything…
The nomenclature '2.0' has become synonymous with second generation trajectories. We have all experienced the benefit of the Web2.0 movement, a term coined in 1999 by Darcy DiNucci and subsequently popularized at conferences from 2004 onwards. On the surface Web 2.0 suggested a new version of the internet, however, it was not intended to refer to an update to any single technical specification, but rather to cumulative changes in the way web pages are made and used with particular reference to social media.[1]

A closer analysis of the 2.0 concept suggests that five dynamics align to create the conditions which trigger a step past a '1.0' trajectory, including:

1. A better understanding of the limitations and potential of current technology by those closest to it.
2. An adequate flow of investment towards continuous experimentation.
3. A formal or informal systems integration of previously disparate stakeholders around that new trajectory.
4. Greater transparency of the significant (versus moderate) returns available.
5. Advent of individual or corporate leadership accelerating the change.

Let's consider these five forces at work in a familiar example. On my first birthday in 1961[2] the then US president, John F Kennedy, announced before a special joint session of Congress the dramatic and ambitious goal of sending an American safely to the moon before the end of the decade.

All five 2.0 forces can be seen at work in achieving this clear technological leap. Firstly, President Kennedy did not set this new vision without NASA informing him of the limitations and possibilities of 1950s rocket propulsion systems as witnessed in the Gemini and Mercury programs. Secondly and thirdly, NASA acted as funder and systems integrator for this goal, managing the most complex of supply chains from life support systems to lunar landing modules and, in doing so, triggered one of the most rapid periods of continuous experimentation in history. In terms of incentive, the political returns to winning the cold war against the USSR were deemed enormous, particularly after the shock that it was not an American, was the first man in space in 1957. Lastly, despite the many social and racial problems of the era and potential application of federal dollars, JFK's leadership in setting the new space trajectory set the world alight, resulting in Armstrong and Aldrin landing on the moon on July 20, 1969. By setting the moon landing goal, JFK ensured the world stepped past 'space exploration 1.0'.

Let's face it, the PM 1.0 definition has had an inauspicious start…
How do these concepts help us assess where we are with personalized medicine? First of all we need to contextualize personalized medicine or PM1.0. Let's face it, PM1.0's definition has really had an inauspicious start. Simultaneously slighted by investors and industry leaders as relating to a niche (read minor fringe activity), only for those experimenting in oncology, or confused as an ersatz buzz phrase for everything from sports monitoring devices to regenerative ageing surgery[3], in the first part of the last decade personalized medicine was often overhyped and constantly reshaped in favour of someone else's preferred definition. I have personally witnessed the targeted therapy and companion diagnostic space being subjected to constant (and frankly confusing) renaming, with terms like theranostics, pharmacogenetics, personalized healthcare, precision medicine and stratified medicine. More telling perhaps has been the label (communicated up to the 'C suite' and from there to investors) from many close to the pharmaceutical science that 'the science is not there yet. A phrase used to correctly suggest that we still have a long way to go to understand one (and only one) dimension of personalized medicine, namely the genetic and molecular underpinnings of personalizing treatment.

Our own in-depth analysis of PM1.0 suggests that despite recent industrial thawing towards a personalized medicine-enabled business model, itself triggered by accelerated approvals of biomarker aided therapies[4], personalized medicine is really still a series of disconnected building sites and stakeholders. Moreover, PM1.0 is often too narrowly confined from within the pharmaceutical industry, to investments in responder testing for targeted therapy. Nor have the incentives for PM1.0 been clear. Given the financial uncertainties implied by subsetting small patient cohorts for therapies subject to $1 billion development fees, the response by many in the pharma industry is to default to a personalized medicine approach versus a 'one size fits all' therapy launch only when the regulatory pathway dictates such an approach. Whilst leading companies have supported some degree of central strategic planning and training, our observation is that in the majority of cases where a therapy will be commercialized with a test, it is the FDA or EMEA that are arbitrating the choice of personalized medicine on a particular asset versus a CEO-led strategic missive.

If we look instead at payers, likely the only other major industrial player with the wherewithal to organize an acceleration of personalized medicine, the picture is equally reactive. Yes, there are payer-led initiatives. United Healthcare[5], for example, currently supports up to $.5 billion on genetic testing for their patients [2013]. Aetna has had a central personalized medicine person in place assessing the space for as long as Diaceutics has existed. However, by the nature of their industrial architecture payers are highly data-driven[6] and too often this has been lacking in PM1.0 and has consequently not triggered a payer-led drive towards accelerating personalized medicine.

In my view, whilst pharma and payers will increasingly be willing participants in PM1.0 this incrementalism will not translate into the radical health care change implied (and feasible) by an era of personalized medicine. However, our research also suggests that the forces for PM2.0 and a more radical acceleration of personalized medicine are aligning in anticipation of individual or corporate leadership. We outline in broad terms our case for PM2.0 below.

The case for PM2.0.

To assess the case for PM2.0 with a structured lens we applied the five forces (cited above) aligning for a 2.0 trajectory to personalized medicine and further discuss below.

1. Understanding the limitations and potential of PM1.0 technology
With some 70 targeted therapies and companion diagnostics (biomarkers) on the market[7] and the now almost daily translation of genetic research into bedside intervention, the last ten years have seen a period of rapid learning about the power (and limitations) of the early application of technologies underpinning personalized medicine. In translational medicine labs across the globe new insights are being harvested, giving us a smarter future perspective of where the 'technology can go' even if it is not there yet.

2. Investment in personalized medicine experimentation
As recent investment analyses illustrate[8] personalized medicine is benefiting from an ever higher profile among professional investors as well as industry leaders. This in turn is triggering higher levels of clinical and industrial experimentation incorporating everything from supercomputers[9] to next generation sequencing[10]. Nor is such experimentation limited to technology. Involvement in, for example, social media and smart phone applications in patients' personalized health care empowerment is a significant force for change and is symbolic of the disparate stakeholders aligning around the personalized medicine concept.

3. Systems integration in personalized medicine
Perhaps a little more opaque, but nonetheless recent publications have started to argue that personalized medicine lends itself to a systems integration approach, as Ginsberg *et al* argued in a recent *JAMA* paper, " … to minimize health care cost increases, genomic approaches must replace existing inefficient technologies and reduce the use of downstream resource"[11]. Our own research into the transformative capabilities of personalized medicine, suggests a significant clinical dividend is available, but only when personalized medicine is introduced as part of a total system in a disease. Specifically, to replicate a PM2.0 world we have modelled the combined impact of a systems integration in melanoma derived from better early diagnostics, prognostic testing and responder testing alongside new first line targeted therapies aimed at reducing second line surgery and the burden of five-year surveillance, both of which conspire to drive up the cost of melanoma[12]. Figure 1 illustrates marginal and transformative clinical impact of a systems integration model applied in one disease area (melanoma). We have replicated these models in infectious and metabolic disease and see similar profound impact.

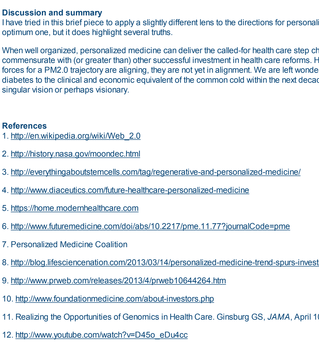

Figure 1: Melanoma PM2.0 clinical impact analysis.

4. Greater transparency of the significant (versus moderate) returns available from PM2.0
Within pharma there are already the whispers (to be fair Roche has been promoting the investor benefits of personalized medicine for some years now) that personalized medicine might make economic good sense. In a reversal of the widely held perspective that treating small patient groups meant financial suicide for large pharma, the triple benefits of accelerated regulatory approval, smaller clinical trials and significant clinical impact for patient subgroups have already delivered early revenue and time to peak sales opportunities versus the 'one size fits all' model. Using our intervention-based business models we have tried to elucidate better the potential future impact on pharma and payer profits of a shift to a PM2.0. paradigm. What these models point to is that a systems integration approach in personalized medicine could also provide significantly more revenue for pharma and significant cost reduction for payers than their current business models. Figure 2 describes the increases and decreases in costs in our Melanoma 2.0 model. We note that both industrial groups (pharma and payers) obtain a significant economic dividend from a PM2.0 aligned program.

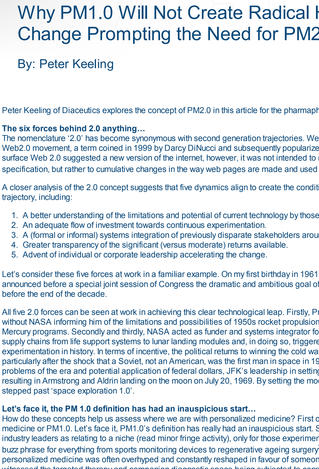

Figure 2: Melanoma PM2.0 economic impact analysis: Melanoma transformational model shown only.

5. Advent of individual or corporate leadership accelerating PM2.0 change
One of the major gaps, in my view, mitigating against a PM2.0 drive to date has been lack of 'C suite' leadership from pharma and payers. I acknowledge that many CEOs and R&D heads now list personalized medicine as a pillar of growth for their business but that is not the same as organizing a business model shift towards personalized medicine. Nor do I subscribe to the academic view from the likes of Christenson that personalized medicine will ultimately disrupt (threaten) the pharma and payer business models in the same way that the PC changed forever the mainstream computer business in the 1980s.[13] One of the strengths of the pharma model has been to manage and spread risk in a long cycle business. Take GSK as an example. Andrew Witty has met the challenge of declining R&D productivity not only with new internal innovation process but by promising shareholders that China (and developing countries) is an area for significant growth. Given that only 3 per cent of GSK's revenues in 2012 emanated from China there are decades of opportunity to offset the risks of long cycle therapeutic discovery. GSK's model is well configured to survive without a compulsion to lead personalized medicine into a new trajectory. At the other end of the spectrum, Severin Schwan's embrace of personalized medicine as integral to Roche's future is either prescient or an outlier to his peers in the industry. The arrival on the disease management scene of a new entrant called Calico, backed by Google and led by a personalized medicine veteran in Art Levinson, has the potential to increase the competitive pressure on large industry incumbents but will not competitively impact in the short term without the bold purchase of, say, Astra Zeneca or one of the other recently troubled Pharmacos. The bottom line, however, is that at the minute personalized medicine does not seem to have its Bill Gates or JFK.

Discussion and summary
I have tried in this brief piece to apply a slightly different lens to the directions for personalized medicine. It is neither the only lens nor the optimum one, but it does highlight several truths.

When well organized, personalized medicine can deliver the called-for health care step change and provide the industrial rewards commensurate with (or greater than) other successful investment in health care reforms. However, despite our perspective that the five forces for a PM2.0 trajectory are aligning, they are not yet in alignment. We are left wondering if the goal, for example, to consign diabetes to the clinical and economic equivalent of the common cold within the next decade is impossible, or simply the absence of a singular vision or perhaps visionary.

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