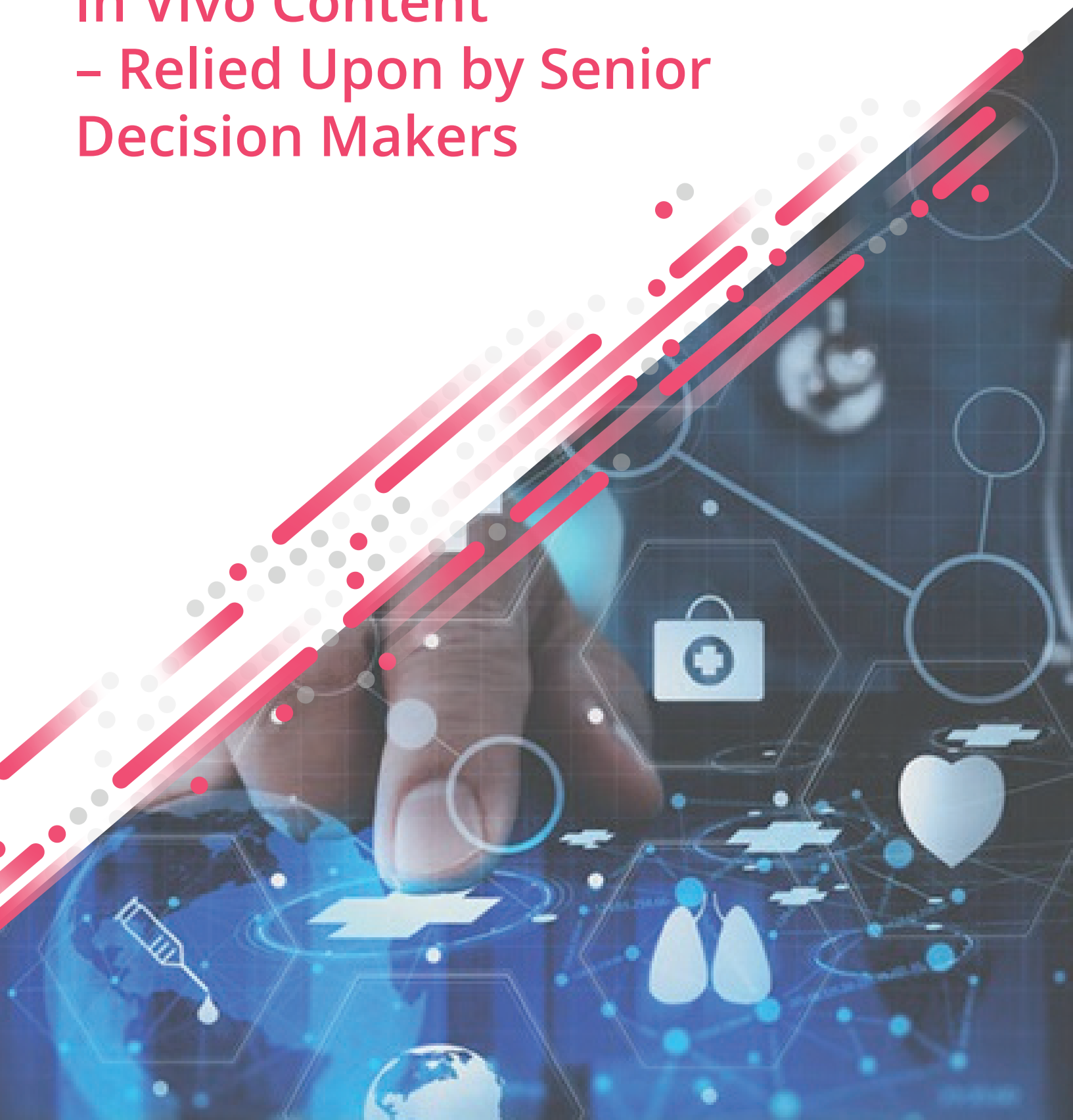
In Vivo
Informa Pharma Intelligence

In Vivo Content – Relied Upon by Senior Decision Makers



The Knowledge Within: An Interview With Merck KGaA's R&D Chief

Executive Summary

Luciano Rossetti, head of global research and development at Merck KGaA, believes the mid-sized pharma is well on its way to becoming a global immuno-oncology specialist. He discusses in-house innovation, the company's recent IO alliance with GSK and the next wave of success that is beginning to swell across the cancer drug development community.

Merck KGaA's Luciano Rossetti talks to In Vivo about the German pharma's next wave of immuno-oncology products that are steadily moving through its pipeline, why GlaxoSmithKline PLC was an ideal IO partner in a very competitive cancer drug development arena and the company's wider deal-making strategy when it comes to pipeline advancement.

In February 2019, Merck entered a global strategic alliance with GSK to jointly develop and commercialize its pipeline cancer therapy M7824 (bintrafusp alfa*). M7824 is an investigational bifunctional fusion protein immunotherapy that is currently in clinical development, including potential registrational studies, for multiple difficult-to-treat cancers. This includes a Phase II trial to investigate M7824 compared with Merck & Co. Inc.'s Keytruda (pembrolizumab) as a first-line treatment in patients with programmed cell death ligand-1 (PD-L1) expressing advanced non-small cell lung cancer (NSCLC).

Merck received an upfront payment of €300m ($340m) from GSK and is eligible for potential development milestone payments of up to €500m triggered by data from the M7824 lung cancer program. Merck will also be eligible for further payments upon successfully achieving future approval and commercial milestones of up to €2.9bn – resulting in a total potential deal value of up to €3.7bn.

"Among our pipeline assets, perhaps the most innovative with the greatest potential is M7824, a bifunctional fusion protein immunotherapy that acts in a single molecule," said Rossetti, head of global research and development at Merck. The compound is designed to simultaneously target two immuno-suppressive pathways: transforming growth factor-β (TGF-β) and an anti-PD-L1. Bifunctional antibodies aim to increase efficacy above and beyond that achieved with individual therapies or combinations of individual therapies. In addition to use as a single agent, M7824 is also being considered for use in combination with other assets from the pipelines of both Merck and GSK under their agreement. (Also see "GSK Makes I-O Move With Merck KGaA Deal Worth Up To €3.7bn" - Scrip, 5 Feb, 2019.)

Despite Merck's commitment to IO development, GSK initially appeared as an odd partner of choice. The UK big pharma is not a key player in the IO space and has spent recent months bulking out its cancer pipeline through acquisitions and deals. During GSK's fourth quarter earnings call in February 2019, GSK's CEO Emma Walmsley said its oncology pipeline has doubled in size since July 2018 to include 16 assets in the clinic. As well as its deal with Merck, in December GSK acquired cancer development company Tesaro Inc. for $5.1bn. (Also see "GSK Embraces PARP Promise With Tesaro Buy" - Scrip, 3 Dec, 2018.)

However, Rossetti said, "We wanted someone very committed to oncology that has a complimentary skillset, but also someone that doesn't have a full commitment to any immuno-oncology lead compounds."

He added that Merck still held discussions with some of the major IO players, but ultimately the company was concerned "in terms of having this new immunotherapy as an anchor for future combinations, for new therapies in certain fields like non-small cell lung cancer, it was not ideal to go for an established player who had already committed enormous resources to a marketed anti-PD-1 or anti-PD-L1, or something in very late-stage." Instead, Merck's main criteria when seeking a partner for M7824 was to have "someone that was truly heavily committed to growth and investment in oncology, but also to be a major player in terms of global reach."

Rossetti said there was an immediate alignment with the GSK team at the highest level. "There was immediate alignment on the philosophy and the principles on how to develop this exciting novel drug and bring it to the patients with difficult-to-treat cancers." Investors are intrigued by the opportunity

M7824 represents, because of the potential of its dual mechanism it could potentially overcome some of the hurdles that limit the number of patients that respond to PD-1/L1 treatment. The drug represents an enormous commercial opportunity in cancer.

Other Pipeline Developments

Merck's R&D chief also noted that the company has at least six clinical-stage compounds in development that are reaching critical steps in terms of registrational or late-stage trials. "Our clinical-stage pipeline over the last few years has developed very rapidly and with great success," he noted, adding that this busy pipeline is what pushed Merck to seek a strategic partnership for M7824 "to maximize the value of this asset and to better balance the risk management of our extremely rich pipeline."

Outside of oncology, Rossetti highlighted evobrutinib as being at a critical development stage for Merck. The compound is expected to move into Phase III trials in the third quarter of this year for the treatment of multiple sclerosis (MS). The company is also awaiting Phase IIb data for evobrutinib in rheumatoid arthritis and lupus. Merck has also submitted a new drug application (NDA) for its oral drug Mavenclad (cladribine tablets) as a potential treatment for relapsing forms of MS, with a decision from the US Food and Drug Administration (FDA) expected in the second quarter.

Also, in its IO portfolio, Merck's PD-L1 inhibitor, Bavencio (avelumab), which is partnered with Pfizer Inc., recently reported further trial results in renal cell carcinoma (RCC). And on February 11, the US Food and Drug Administration (FDA) accepted for priority review the supplemental biologics license application (sBLA) for Bavencio in combination with Pfizer's Inlyta (axitinib) for patients with advanced RCC. Inlyta, an oral therapy designed to inhibit tyrosine kinases, including vascular endothelial growth factor (VEGF) receptors 1, 2 and 3, is already approved in the US and Europe to treat RCC.

"It makes sense for us to find strategic partners to fully maximize some assets, particularly ones like M7824; which, if it hits and confirms some of the initial signals, will require a very rapid escalation of our planning soon," Rossetti said.

IO Deal-Making

Rossetti sees only more IO partnerships across the industry in the near-term. "There are some big players in oncology that have relatively dry internal pipelines and they are heavily investing and looking for partnerships or for licensing deals," he said. Merck, however is in the situation where it has an organic road ahead coming largely from products developed in-house, but it needs partners to maximize the potential of certain compounds, he noted.

Rossetti expects a heavy level of activity in the field of oncology in terms of the degree of collaborations, partnerships and acquisitions. "That's what seems to be happening and it makes sense."

"We're just at the beginning of a new era in which we are basically able to reawaken the immune system and activate it to attack tumor cells," Rossetti said, when considering the next moves for the IO drug development community. "We're just scratching the surface," he said. "Only a small minority of patients are dramatically benefitting from these great new therapies, while the potential exists to expand the number of patients as well as the durability of these responses. Looking back at the last couple of years, a lot of promise has been made in terms of immunotherapies, but there has also been a lot of disappointments relative to the enormous number of clinical trials that have been initiated all over the world to investigate these innovative therapies."

Merck is familiar with setbacks in cancer drug development. In November 2018, Merck and Pfizer lost an opportunity to crack the ovarian cancer market early when Bavencio failed as a monotherapy and in combination with chemotherapy in the Phase III JAVELIN Ovarian 200 study of tough-to-treat platinum-resistant or refractory disease. The companies announced in a November 19, 2018, top-line release that the drug missed progression-free survival (PFS) and overall (OS) endpoints when tested alone or with pegylated liposomal doxorubicin (PLD) chemotherapy against PLD alone in the three-arm study of 556 women with cancer resistant or refractory to platinum chemotherapy. Bavencio is one of the more advanced checkpoint inhibitors in development for ovarian cancer and the companies were hoping to be the first in the PD-1/L1 class approved for this indication. (Also see "Merck KGAA/Pfizer's Anti-PD-L1 Bavencio Loses An Opportunity In Ovarian Cancer" - Scrip, 19 Nov, 2018.)

The Next Wave

Rossetti believes the industry is now ready for more data-driven decisions on what to take forward in pipelines. This earlier and better-informed decision making will spark another "wave of innovation around immunotherapy," he said. He expects M7824 to play a role in this next movement in cancer treatment.

"It's an early product, with about 700 patients treated to date. In general, these are small cohorts but we have impressive signals that need to be fully confirmed during the next stages," he highlighted. If the early signals are confirmed, M7824 could lead to transformational effects in non-small cell lung cancer,

biliary tract cancer, HPV-associated tumors, and other areas, Rossetti said.

In the coming years, there will be "more and more demand to find the right patients for the right therapies or the right therapies for the right patients," Rossetti said. "Immuno-oncology is particularly challenging. We do believe in PD-L1 as a good driver but cancer is tremendously complex and a number of patients do not respond to these therapies, or acquire resistance to them, leaving them with limited treatment options."

"The next challenge is going to be fully understanding the drivers for specific tumors, whether it be targeted oncology or immuno-oncology," Rossetti said. "We need to be able to identify these drivers earlier and treat them with very specific biologics or small molecules. That's where big investment is required to realize the full potential of precision medicine and that's where we as a company are focusing most for our future."

When it comes to precision medicine, Merck wants to use more evidence and analysis derived from digital databases. "We're putting some effort in digital pathology but also in gene sequencing and expression analysis, which is the most important genetic factor underpinning tumors, before we even start designing our first-in-human studies. Investments are prompt in some of those novel types of analyses in the clinic."

In-House Versus Acquired

Rossetti regularly promotes Merck's in-house discoveries and developments. "For many years, we have been very strong in drug discovery with laboratories producing extremely good ideas and promising approaches. But in many ways, we were not fully materializing our clinical pipeline," he said.

However, the company is focused now on investing in translational medicine across its development program, in alignment with marketing colleagues. As such, there was a unifying intent to develop internal programs, he said. "We feel, in the last few years, that we have enhanced our productivity within the organization and in advancing innovative therapies. By having a very focused discovery strategy as well as a complete end-to-end organization, we can successfully develop our products all the way through registration to launch."

Rossetti added that to have a strategy based on how may acquisitions and licensing agreements can be done, a company must have substantial resources. "In the rare cases in which clinical-stage, well-validated or highly promising assets are available, it takes a huge amount of resource to step in." He said Merck has "more and more trust in the ability of our own internal lab to produce truly breakthrough innovation, and M7824 is an example of this." Whereas externally feeding the pipeline would be "incredibly costly and highly competitive." This was why Merck chose to focus on maximizing the output of its discovery units, Rossetti noted.

"I think we're being clear that there's still the possibility for us to do smaller deals for something to complement our pipeline, but the general philosophy is to stick with the internal and organic growth of the pipeline," he said. To balance that pipeline and manage where its R&D dollars go, Merck, in 2013-2014, narrowed its R&D focus to very specific core areas. "We focus on multiple sclerosis and leveraging immunology," Rossetti highlighted, adding that one example of where Merck has pulled back its R&D efforts is in neuroscience. "We made the decision that in terms of true innovation in the lab, we were less competitive in neuroscience, where there are specific scientific areas within oncology and immunology where we believe we can be very competitive. In terms of disease areas we are prioritizing specific tumor types and are also very committed to multiple sclerosis." He also noted that in autoimmune diseases, Merck has a particular focus on systemic lupus erythematosus. "These are really narrow areas and a major focus of our scientific efforts."

To be competitive in these areas, Merck is getting even more niche. "In terms of our scientific focus, even within immuno-oncology, we are creating a center of excellence in bispecific and bifunctional proteins to really leverage the ability of having a single molecule with more than one mechanism." He added, "We also want to do more to direct these mechanisms to the antibody component of bispecific and bifunctional compounds as well as to specific areas within the tumor environment. This is one area that we have invested a lot in."

Merck is also advancing its activities within DNA damage repair (DDR) research and development. "As we think long-term, there will be some synergies between inhibiting the mechanism for DDR that we believe can amplify the efficacy of current therapies, in particular the autoimmune checkpoints," Rossetti said.

"We have ambitious view about the pipeline," Rossetti noted, adding that over the last 12 to 18 months the company's confidence in its R&D offering has grown. He cited M7824 and evobrutinib as prime examples that have made the company feel as though "we are on the right path." What Rossetti seeks now is "to see big success in our launches and even more regulatory success to confirm this progress."

**Bintrafusp alfa is the proposed International Nonproprietary Name (INN) for the bifunctional immunotherapy M7824.*

Innovations In Market Access: The Will, But Not The Way?

Executive Summary

In this In Vivo executive roundtable, an informal working group of biopharma leaders in market access reviews the current state of play with regulators, patients and payers. Contacts with the first two stakeholders are clear-eyed and surprisingly productive, but the payer remains the tie that grinds – an inscrutable partner of necessity in moving complex, costly innovations toward acceptance in the marketplace.

With the Boston Consulting Group (BCG) as convener, market access functional leads from 20 major R&D-based companies in the US, Europe and Japan have joined to offer a forum for discussion of global-level challenges to drug access.

Over the past several years, the group has initiated specific projects covering alternative drug financing options in Europe, a global policy framework for value assessment, and key functional competencies and performance metrics in market access. (Also see "Access To Medicines Innovation: Seven Points To A Sustainable System" - In Vivo, 2 Aug, 2017.)

So what? Payer calculations in valuing new medicines currently represent a 20th century approach to leading-edge, 21st century science. Patient access depends on payers too getting out front to work with industry and test what is possible in innovative pricing and reimbursement (P&R). The basic vanilla volume discount is behind the times.

Q: In Vivo: Market access has established its importance as a key function in biopharma. But how it relates to an increasingly disruptive external environment remains a work in progress. To provide practical context to today's discussion, what's the one question that comes up most frequently in your day-to-day interactions on market access strategy with colleagues in the business or from stakeholders outside the company?

A: Martin Walter, VP, head global market access, Boehringer Ingelheim GMBH: The question that comes to me most frequently is how to address changes and disruptions in the market environment, such as the vertical integration of payers and pharmacy benefit managers (PBMs) in the US, while finding novel ways to demonstrate value to payers so that patients can access our products. Another is how digital technologies will impact evidence generation and advance our value proposition. Facing up to the challenge from online sellers like Amazon.com entering health care and improving the customer experience is relevant to us as well. Combined, these trends raise larger strategic questions about changing our approach to developing and commercializing products and services that fight disease and advance health for patients. It is my task to help address and resolve those questions.

A: Peter Vanovertveld, senior VP, head global pricing and market access, Vifor Pharma Group: As a relatively small player in biopharma, Vifor Pharma is seeking to better access the patient population while improving our price performance. How to achieve that goal is the question I face every day. We want to transition from a singular focus on maximizing prices to a more integrated approach, one where market access is part of a broad customer-focused plan involving regular productive contact with patients, providers and policy makers. To leverage our limited resources, we have adopted a cross-functional matrix structure on market access. We believe this is essential to compete with the big pharma leaders.

A: Sachin Kamal-Bahl, health services researcher and former VP and head, center for health systems innovation and leadership, Pfizer Inc.: I have a unique position, one where I can work on reforms at a very interesting time in the evolution of the health care ecosystem. As a thought leader in this space, and having just left a senior policy and practice role at Pfizer, I work with an increasing range of stakeholders on new options in financing the cost of novel medical treatments. I am also considering different ways value should be defined in the context of the major shifts taking place in the structure of health systems – that the two are interconnected is the premise by which I approach this important issue. Our internal colleagues in the business want innovative, forward-looking guidance on access solutions that help the patients most likely to benefit from our medicines. My current efforts are largely aimed at working toward these solutions.

A: Jens Grueger, head, global access, Roche: Our global

mission at Roche transcends the notion of market access – we are all about patient access. Every outcome we project for our products is geared to increasing patient access first. In fact, one of the key questions I work on with colleagues at Roche is identifying the hurdles that restrict patient access to our medicines and to address them proactively with strategies to address affordability, demonstrate value and build support for medicines innovation at the societal level. The questions I receive most frequently are the future of the US pricing blueprint; the trends in health technology assessment in Europe (particularly the consequences of a more harmonized effectiveness review versus continued duplication among 27 separate processes, which obscures the overall positive impact of our outcomes), and how to pursue access to our innovations globally, given the gaps in infrastructure that exist in Africa and other developing regions.

A: Christophe Segalini, head, global market and pricing, Gilead Sciences Inc.: The top-of-mind issue for my group is aligning perceptions of value in our contacts with an increasing number of stakeholders, in business and across geographies. Access to the patient is a never-ending quest. Just when you think you are about to seize the opportunity to bring in a new drug to fill an unmet medical need, the rules of engagement change, often in such way as to raise the bar on the value you must demonstrate to payers. This, combined with the fact that the P&R vetting process is not always transparent and creates uncertainty, adds to the risks inherent in a long and expensive pathway to market. Internally, we spend a lot of time persuading our colleagues in the business to see the market access function as an enterprise-wide responsibility. It's a mindset – a shared cultural attribute – that cannot be delegated or deferred to others.

A: Indranil Bagchi, senior VP, global value and access, Novartis Oncology: My role focuses on oncology, where generating data that establishes progression-free as well as overall survival, improving patient-reported outcomes and advancing the standard of care is critical to meeting the requirements of regulators and payers. Developing a clinical trial protocol that will anticipate their evidentiary needs, often years in advance of a decision on approval, is one of our biggest challenges. We have also helped to devise new payment models appropriate to the novel therapies Novartis is bringing to market. An additional item on our agenda is positioning oncology around the commitment our CEO has made to global access for all our medicines. How to make this work for complex, high-cost cancer therapies in resource-constrained settings is the kind of question that keeps us up at night.

A: Les Funtleyder, chief financial officer, Applied Therapeutics Inc.: My work focuses on preparing the company for potential launch and approval of a number of drugs; each has a distinct therapeutic profile and thus variable implications for market access. Several address diabetic complications, where we must develop a value proposition centered on the fact that patients will likely have to take the drug as a treatment, not a cure, and most likely for the remainder of their life, in addition to other diabetes treatments. In my opinion, our most exciting asset is an orphan drug geared for pediatric use, and where the outcome will be demonstrable to payers very early on. As a company that is currently private, we intend to consider ethical aspects when determining a price. How to do this in a way that also supplies a return on the investment is the question that preoccupies us right now.

Travails Of A Decade

Q: In Vivo: What has changed in the way you and your companies approach market access? What external environmental factors require you to perform differently in your organization today, compared to when you first entered this space?

A: Grueger: In the past, market access was primarily a technical exercise, focused on health economics and policy, pricing and reimbursement. Today, we operate within a broader framework: securing patient access to new medicines. It's a more strategic orientation, combining scientific expertise with stakeholder outreach and a sensitivity to competitive commercial realities. The approach is integrative and expansive as opposed to being narrow and academic.

A: Walter: A decade ago our efforts centered almost entirely on securing regulatory marketing authorization, which in most cases guaranteed entry to the market and access for patients. Today, there is no such assurance, requiring us to devote substantial resources to understanding what payers want from a product and from us, which in turn demands sophisticated evidence documenting how it will create health and economic value for the patient and the health system. There is a strong budgeting aspect to access that was significantly less pronounced before.

A: Bagchi: In the 1990s we were an "enabling" function. Today, market access has been institutionally transformed, with a key role in C-suite strategy and clinical candidate development. There is a clear awareness in companies today that all our efforts in developing and commercializing a medicine will not go anywhere unless, payers, policymakers and other stakeholders make our products accessible to patients who need them the most. This is why some of us here today created the Market Access Roundtable with the Boston Consulting Group (BCG) to raise the profile of market access as a vital stand-alone activity in biopharma, and to educate our colleagues in the companies to recognize and accept the diverse capabilities that we bring to the table.

Market Access: Meet Market Launch

Q: In Vivo: It is well known that many new drug launches today fail to meet growth expectations. Are market access people expected to take the lead in fixing problems in the launch cycle?

A: Vanovertveld: It depends. Many of the challenges in launching a product today are systemic and cannot be attributed to a single set of actions. Reimbursement rules are extraordinarily complex and are revised frequently. It's now common practice for my company, as well as others, to start devising a specific compound launch strategy early on. By the time you get to Phase III, there will be a carefully drafted blueprint designed to anticipate provider and patient behavior, attract new scrips and deflect the rearguard actions of competitors seeking to retain market share. There is no doubt that my group is part of the solution when a new product's market performance falls below expectations.

A: Segalini: The pathway to market access is inconsistent and unique to the circumstances of each product. Despite the extensive planning that accompanies a launch, the environment is unpredictable and thus hard to anticipate. We now have a seat at the decision-making table with the commercial and clinical development teams, which gives us the opportunity to use our networks and extend the perspective necessary to cope with uncertainty on take-up of a new drug. However, it will take time for the market access function to achieve perfect vision in aligning to a new world of payers. This is partly because payers lack such vision themselves.

A: Grueger: Regarding the launch cycle, we succeed when we direct internal priorities toward access for the patient – the "market" is an abstract if no patients are getting the drug. Uptake of the product is what counts. Here, there are a growing number of barriers, ranging from fiscal and budget issues around affordability to gaps in delivery infrastructure. We can have in place an extensive distribution network, service "hubs" to help patients comply with treatment, and companion diagnostics to ensure patients are getting the right drug, at the right time, for the right condition – and still we cannot be sure every patient who can benefit has access. What we can do is convince the organization to focus on the only metric that matters: how many real patients are benefiting from our product today? The whole organization must come together to make this happen, with the market access team as the facilitator.

A: Kamal-Bahl: To keep launch plans on track, companies need to tighten the link between access and quality. An impediment to quality is the bureaucracy involved in insurers allowing a patient on therapy – what's increasingly commonplace is a 20-plus page application, where the responsibility is most often placed on overworked physicians because the patient is incapable of making their own case. It's a big drag on access. It can be an impediment causing new product launches to falter unless there is irrefutable evidence that the product represents a big improvement against current standard of care.

Funding Pathways: New Ways To Pay

Q: In Vivo: Many biopharma companies are evaluating alternative financing arrangements like annuities or debt financing to support the high pricing for new gene-based therapies. Are any such novel financing schemes likely to gain traction, or is it still a theoretical exercise?

A: Kamal-Bahl: Premium pricing for products at launch combined with invoicing for the full net cost per patient upfront is clearly an issue for payers. The message that comes through loud and clear is the products are too expensive for the value they provide. And if the industry is replacing an incremental benefit from that regular 30-day supply of medicine with a quick, one-shot cure delivered by gene therapy, then criticism of the higher expense will grow more intense – ultimately, it's unsustainable. If we don't address such price escalation it could be read as a great disservice to the payer community, to providers and patients, and to the health system itself. Clearly, payers are now

willing to experiment as more gene or cell-based therapies come on stream. The states of Louisiana and Oklahoma were last year granted waivers by the federal Centers for Medicare and Medicaid Services (CMS) to pilot prospective payment tools for these high-cost drugs. We will see more examples as the health care system grapples with these game-changing treatments in the next few years.

A: Bagchi: Novartis has introduced a novel payment model for Kymriah, our lead CAR-T cell therapy. For the pediatric and young adult B-cell acute lymphoblastic leukemia indication in the US, we offer a voluntary outcomes-based contract to certified treatment centers that provide Kymriah. If a treatment center opts in, the contract only allows for payment when patients respond to the drug. We now have extended various forms of this value-based model to other countries where Kymriah is available and where we find payers and reimbursement authorities are interested in such an approach.

A: Segalini: The resources industry is putting on the table to support patient access are significant. It ought to be recognized, as we strive to meet the requirements of payers working within a much narrower budget window. It's already evident the burden of proof will be raised higher in delivering value to patients. The surprising thing to me is that the health system – including payers – does not match the industry in coming up with new ideas to pay for our medicines. We tend to be the source of new thinking maybe 80% of the time. We present our calculations and suggest a few fresh options, and the response is too often "OK, let's just find a classic volume-based discount agreement." This creativity deficit is widely ignored yet it has implications for the future stability of the health system. If decision-makers lack the vision to change and just follow the familiar course of reducing their drug procurement overhead at 3% each year, then don't expect anything further than that – certainly not more innovation for the patient. What is required is action by all parties in the biopharma business to break the mold and experiment with pilot programs that help move access and reimbursement to a better place. To continue the progress of science over the past 20 years into the next decade, innovation in the P&R system is necessary too. Health systems must combat the uncertainty that comes from arbitrary cost containment goals imposed without consultation and for objectives that are non-transparent and unexplained. How do we calculate the long-term damage to the incentive to innovate as biopharma companies struggle on how react to payer policies they can't plan for?

A: Walter: Another systemic problem that complicates medicines access is the drug payment models we have today ignore problems that originate elsewhere in the health sector. My company is committed to demonstrating the broader value of our products, and to show payers that drugs can be cost-effective against other health interventions like hospital care. At present, gene therapy in isolation appears prohibitively costly, but with time those therapies will create ample rewards for patients and society in curing or preventing illness, disability or premature death. With the increasing vertical integration in the US, perhaps we will see bigger players in the health system embrace this broader perspective on the value of drugs. But the financial incentives to facilitate this change currently do not exist.

Envisioning Value

Q: In Vivo: Can we foresee the various parts of the health system coalescing around some basic methodological consensus on how to calculate or measure value? Is the quality adjusted life year (QALY) a way to re-position biopharma away from its current isolated state in a health system marked by pervasive silo thinking?

A: Grueger: The QALY is a well-established methodology but addresses a very small component of value, focused on the duration and quality of functional life. It's a lot like the Dow Jones stock index, in that it provides some basic understanding of what is meant by value but still leaves a lot out of the picture. QALY is often applied under a "willingness to pay" threshold for assessing value, usually in concert with fixed budgetary caps on drug spending. This interpretation of the QALY is endorsed in the UK, Australia and Canada. In the US, the Institute for Clinical and Economic Review (ICER), a non-profit NGO that conducts cost-effectiveness evaluations on drugs, uses QALY but incorporates additional measurements based on the perceived clinical experiences of different groups of patients. Finally, QALY can be misused in comparing a novel gene therapy with a generic that has been on the market for decades, with the price of the latter as the benchmark. Nor should it serve as a therapy straight jacket, where an Alzheimer's treatment is evaluated solely on a theoretical patient experience, taking no account of the disease's broader family or societal impact. You get an entirely different measure of value when you include this latter element in a

QALY calculation. This explains why it's difficult for biopharma companies to endorse QALY as the basis in determining a drug's value.

A: Segalini: Bear in mind that health economics as a discipline applied to medicine is rooted in research developed more than two decades ago, when the possibilities for a secure life free of a disabling condition were not as prevalent as today. Yet it makes an enormous difference if a medicine gives 20 years of life back to someone who in a previous generation would have had no such option.

A: Walter: Finding the ultimate measure of value to satisfy everyone is difficult, if not impossible. The right course is to identify and then build a consensus on the factors that help define value around the perspective of the individual patient, their condition and course of treatment. With such a framework you can openly discuss which value factors will be considered by a certain stakeholder and which ones will not. Its critical all the key stakeholders in health care engage in this discussion, transparently.

A: Kamal-Bahl: Steve Pearson, the founder and president of ICER, agrees about the need to elevate the debate on how to measure pharmaceutical value. Despite that, ICER's approach to measurement is constricted and not very transparent. I've looked at their model – and it's hard to determine what underpins their assumptions, how to import the methodology to the product, and then replicate the numbers they come up with. The effort to incorporate a patient perspective in the evaluations has a pro forma, "check the box" aspect that only adds to the uncertainty. Another institutional player in this space is the Innovation and Value Initiative (IVI), which is looking at the medicines value question from a different angle. It has developed a measurement model that, while following well-established economic principles, introduces criteria focused not only on the clinical benefit to patients but on the broader impacts on the family, care-givers, employers and society as well. The model is more flexible than QALY. Most important, it is fully transparent – the software, the assumptions, the mathematics, all the inputs to the model are out there for people to look at on the IVI website. IVI lacks the prominence of ICER, with its record of more than 20 detailed evaluative reports on big ticket therapies, but their model is worth examining. We believe it is in the industry's best interest to have a diversity of options to work with on the value front.

A: Bagchi: Numerical calculations and thresholds geared to establishing value within a single identifiable range are here – and they are not going away. As we are all aware, there are multiple different value frameworks available now to specifically address value assessments within oncology, including the ASCO, ESMO and NCCN frameworks. The proliferation of these highlight the current lack of consensus among stakeholders on how value assessments should be done.

A: Grueger: Economics and politics need to be clear in their incentives to industry when it comes to investing in a cure instead of a chronic care drug that alleviates symptoms or keeps the condition stable – the cure versus control dilemma. Under the current incentive system, the potential ROI from a cure is difficult to assess because affordability remains an opaque concept for stakeholders, with no clear pathway to consensus. And many payers, particularly commercial insurers here in the US, will never derive the reduction in liability exposure from the extended years of disease-free life that accompanies a cure. That's because their numbers on covered lives fluctuate on a yearly basis – people come and go. We believe that cure is better than chronic treatment, but at the moment payers do not seem to be willing to reward the patient and recognize the societal benefit that a cure delivers, to the same extent that they do for chronic treatment.

The New Tech: Impact on Market Access

Q: In Vivo: Do digital technologies and other advances in information processing and analytics offer new opportunities to empower your work on market access?

A: Kamal-Bahl: Artificial intelligence and other emerging technology tools show promise in making clinical trials more relevant to the requirements of regulators and improving the efficiency of trial recruitment and protocol design. This is also opening the door to acceptance of real-world evidence as a part of the registration dossier. This trend is critical in improving on our basic value proposition beyond what we can furnish in the framework of the traditional randomized clinical trial.

A: Grueger: We need more regulatory guidance throughout the spectrum of evidence generation. Flexibility on the type of evidence we can provide in areas of high unmet medical need is important – there are examples like spinal muscular atrophy where you don't need to run a control trial for

the first time when data shows infants sitting up unaided after the administration of an investigational candidate drug. In such cases, speed to market – getting patients with no alternative options treated – is abetted when different strands of evidence are incorporated. We in market access roles should encourage this trend, extending the reach of acceptable data into the real world without, of course, impinging on the integrity of the RCT gold standard.

A: Segalini: Data technology gives market access the possibility to shape decisions in three distinct areas: value communication, evidence generation and transaction confirmation and transparency. In the latter case, the Netherlands and Switzerland are pursuing projects with the industry and providers using the blockchain to improve the safety and reliability of cash flow activity. Digital analytics are also being applied to assess disease states and monitor compliance, particularly for conditions like hemophilia and schizophrenia, with difficult to treat patient populations. It adds more to our value armamentarium, being available in real time for evaluation by the provider, pharmacist and other stakeholders. It creates a broader constituency of support for the treatment.

A: Bagchi: Care coordination through digital analytics is another big boost to market access. Technology that raises the efficiency of a health intervention will underscore what medicines do to reduce costs in other parts of the system. There is so much waste and low value activity in health care today. If data helps reveal this and leads to higher productivity gains elsewhere, it will free up more dollars for investment in the areas written into our professional DNA, like prevention, disease management and quality of life.

Regulators: The Search for Stasis

Q: In Vivo: What is the current state of the relationship between the R&D industry and the major regulatory bodies like the FDA and EMA. Are initiatives like the EMA's adaptive pathway pilots helping to make a better value case for the novel – and expensive – therapies that companies are bringing forward today?

A: Bagchi: In principle, much progress is being achieved through these programs. Whether it succeeds at the base line level is still a question, given the persistent challenge we have with oncology drugs in harvesting the hard-to-procure survival data regulators want as the condition for marketing approval and reimbursement. Even when companies obtain regulatory approval, there are requests for additional data for which they need access to appropriate patients. And finding these patients – the right patients – is hard. But the agencies are very willing to work with us to find common ground. They are aware that as the science of drug discovery moves into the complex specialty and gene therapy space, regulatory science has to change too. Those long and large Phase III trials for the new, precisely targeted therapies are increasingly difficult to pull off. Data requirements will simply have to evolve.

A: Kamal-Bahl: The precedents are being set in the context of progress – it's a positive for the industry. A medium seems to have been established where you can conduct a small trial around a cohort of qualified patients, which does take time to arrange, and then follow that with an extended look at the full patient population further along, after a provisional acceptance.

A: Grueger: The European regulatory context involves a separation between evidence assessment and the ultimate agreement to reimburse. But I see an opportunity in the discussion of a harmonized European-level evidence review, combining a clinical scientific and relative effectiveness assessment. It a major political issue right now, particularly as a replacement for the country-specific process. We believe there is a case for change, given the complex new technologies coming to market: few countries in Europe have the resources and capabilities necessary to assess these.

Paying For Innovation: A Transatlantic Free Lunch?

Q: In Vivo: Europe also continues to experiment in different approaches to P&R. Tendering and bulk procurement of drugs linked to volume purchasing appears to be an emerging theme.

A: Vanovertveld: Some countries are indeed experimenting in this area. The concept itself is not a red flag, and companies involved in the supply of goods to public institutions have a social obligation to contribute to procurement. What is still not clear is how these systems will actually operate – the terms of engagement raise many questions. There is always the prospect that these systems will simply lead to a commoditization of the market.

A: Funtleyder: Here in the US, the Trump Administration has proposed an International Price Index (IPI) for selected high-cost drugs administered in the clinic and reimbursed under the Medicare Part B program. It is basically a framework for a reference price structure where prices will be pegged against those in several European countries, such as the Czech Republic. If the price index is put in place, any tendering and bulk procurement scheme in Europe could lead to significantly lower prices for index-eligible medicines in the US, particularly if the concept is permanently embedded by a new, more progressive Administration after 2020.

A: In Vivo: Many of you here today represent companies based in Europe. Do you have a view on the current moves by the US Trump Administration to manage drug prices, reduce patient out of pocket costs and persuade your governments to bear a larger share of the global cost of R&D through increased incentives to innovate?

A: Grueger: European governments have less credibility today in discussions on rewarding innovation. They argue that drug makers are still making profits. We have to remind them that it is not sustainable to simply wait until a new innovation is approved in the US and then slowly pass it on to the European patient, years later and usually at a much lower price. Europe is completely silent on the fundamental question: what is the appropriate contribution of this region of advanced industrial countries to global health care innovation? Everyone knows the contribution of the US market to global biopharma innovation is disproportionately high. It follows that the US is entitled to consider how – or whether – it should embrace price regulation of drugs. But the implications of doing so can be counter-productive. At the ISPOR annual conference in Barcelona last November, a well-known US economist made what to me is an interesting observation: if the US decides to reference its domestic prices to prices in a European country, the consequence will be less access to medicines in Europe. This is turn will lead to more pressure to keep prices high in the US, to compensate for industry revenues foregone in Europe. The point is governments forget that we are a global industry. Companies will always act rationally to accommodate changes in one market with reciprocal actions in another. The result is not always what government policy-makers expect.

A: Segalini: Europeans discount the ancillary benefits from supporting innovation. It's not just big pharma that gains but vendors and CROs and the academic and research institutions that seed basic discoveries in a rich diversity of fields. The rewards do not fall exclusively to us.

A: Kamal-Bahl: Governments like quick fixes, which sometimes don't turn out in the manner intended. It's important for industry to emphasize a long-term view, and to move the conversation back to the relationship between value and affordability. Getting the balance right requires more recognition of the contributions made by innovation. It's a complex problem with no easy answer, especially because solving it is going to take time.

A: Grueger: More value messaging in Europe will not, in my view, shift the debate in favor of innovation. It's still fundamental to ask directly what governments are willing to pay for. If they won't pay for an innovation they should not be entitled to get it a steep discount, compared to the US.

A: Bagchi: Differential pricing between markets based on willingness and ability to pay maximizes the consumer surplus. However, the ability to price medicines differentially continues to be a challenge due to multiple cross-border phenomena such as reference pricing and joint procurement. In the end, mechanisms need to be in place for the industry to allow for differential pricing, leading to as broad access as possible for our medicines while at the same time ensuring continued reward for innovation in what is primarily an intellectual property-based industry.

A: Segalini: Likewise, we need to explain why companies are reluctant to launch new products across geographies. The proactive use of reference-based pricing in Europe has changed the revenue calculation entirely – fifteen years ago, we could take a conditional bet on profit expectations and move forward with multiple launches of the same product. Today, country "A" will automatically reference country "B" and so on, resulting in a race toward the lowest price in Europe, minus an extra 10%. It's a vicious circle with no exit. Can it be a surprise that certain countries don't get access anymore?

A: Walter: An underlying theme that complicates dialogue between the industry and payers is that concerns about affordability tend to bias the value discussion. If budget are tight, the value and

evidence base for the product will be challenged, even if it is highly innovative from a medical and patient perspective. It is necessary to acknowledge these challenges for payers, to be very open about it and find ways to collaborate. We can't push the problem away – it's got to be a straight conversation with payers and policy makers, covering all sides.

A: Funtleyder: The public – the patient – has an easy grasp of the notion of affordability. Politicians respond to that. On value, the industry tends to get esoteric, even incoherent, with a vocabulary centered on things like QALY on which consumers and policy makers are not well versed. As an investor, I see the market access function as necessarily being tasked with communicating value in a more accessible way. It's long overdue.

A: Venovertveld: Smaller European countries such as Denmark are very explicit in funding system-wide solutions focusing on value for patients and the payer. It welcomes initiatives from pharma, diagnostics and device companies to show how their interventions support home care for patients with chronic disease, in particular where such care is cheaper than institutionalization while increasing clinical outcomes or quality of life.

New Influencers On Market Access

Q: In Vivo: Outreach to external stakeholders is a key function of market access in biopharma. What is the state of the dialogue with this constituency? Have the terms of engagement changed? Are new players emerging with influence on how your products get to patients? And are patients still firmly in the mix?

A: Grueger: An important trend is that drug scientific advice is now commonplace in biopharma, which means that our contacts with major HTA bodies like the UK National Institute for Health and Care Excellence (NICE) have become institutionalized. Ten years ago this relationship did not exist but today we are in a mutually reinforcing – and largely positive – dialogue of substance. At Roche, we are also seeing a major upgrade in our ties to the patient community. We are bringing the patient voice directly into our development teams and also leveraging the insights of all our work colleagues who are patients themselves, survivors or care-givers. Our clinical trials have benefited from the patient's perspective; frankly, we have been surprised about how their input has shaped trial design and made the operation of the trials more relevant to the conditions we are seeking to treat.

A: Funtleyder: One emerging constituency that requires attention is the impact investing community, many of whom are young millennials with means. Black Rock Inc., the world's largest asset manager, with more than $6 trillion under management, is a major proponent of impact investing. This group is forcing the biopharma boardroom to embrace socially responsible behaviors, like keeping list price increases more in range with inflation. It will increasingly affect the internal climate in which the market access function promotes its agenda.

Paying It Forward: What To Wish For

Q: In Vivo: As a concluding thought, what might you prioritize as a policy or practice change to increase market access for patients and enhance your function's effectiveness – externally and internally? Will market access survive as a strategic priority through the next decade – or the next business model?

A: Walter: More consensus among stakeholders around a system on the measurement of patient-centric outcomes on health care. A clear standard and common objective of how all stakeholders must perform in improving health for patients. If we can accomplish that, innovation in health care will accelerate, with additional momentum for policy and practice reforms over time.

A: Bagchi: The challenge for the biopharma market access practice is to better align objectives, metrics and outcomes around what we do. The BCG Roundtable was founded for this purpose; many of its members are here today to underscore the point. On the external front, we have observed today that alignment is faring well between our R&D industry and the drug regulatory agencies. We are talking and exchanging ideas. But we have achieved little so far on alignment with the payer, HTA and care delivery communities. The gap in understanding between us and them is still huge. Nevertheless, more patient advocates are welcoming our support for a better health care system that works for patients. If we were able to engage in more dialogue with patients at the community level, that would be a significant step forward. It works in the rare disease space, where patients are concentrated and very active due to the lack of treatment alternatives.It provides an

example of how the industry can better articulate the desire to put patients at the center of everything it does. Isn't this why we come to work every day?

A: Kamal-Bahl: I would like to see the industry working collectively with other stakeholders on system-wide reforms to promote value-based health care. The current discussion is unfocused, piecemeal and perpetuates the view that biopharma is a silo, outside the mainstream. None of the frameworks in place to evaluate the value of medicines looks at the process from a system-wide perspective. We need to contest that.

A: Segalini: Scientific research has advanced to the point that we have the knowledge to diagnose and treat virtually all patients with certain major diseases. I'd like to see more initiative on practice reforms to get us to that practical result, in the most economically advantageous way. That means one thing: the real innovators in the health system must be identified and rewarded. Change starts with a system-wide approach, one that targets the many wasteful, inefficient steps in care delivery and financing that erode the value proposition. The industry also needs to engage for the long haul rather than in episodic bursts. Three words – stability, creativity and visibility – should guide our journey through the disruptive change that characterizes health care today.

A: Vanovertveld: Transparency is the most formidable driver of change. Sunlight is the ultimate disinfectant. We need more openness in pricing and outcomes. Too little is going on to move us closer to this destination. Surprisingly, I think there is more activity in Europe to open up the system than in the US. Either way, it's not enough. Transparency is no cure-all, but it's one of those "force multipliers" that gradually adds to credibility and responsiveness at the institutional level.

How Should Healthcare Make Use of AI? Ask the Patient

A new survey shows patients want doctors involved in AI-linked decisions

Executive Summary

Technology, human ingenuity and deep pools of financial capital are aligned in an important mission: bringing artificial intelligence (AI) to global healthcare. If investor enthusiasm is any gauge, the mission is advancing quickly. No fewer than 300 healthcare AI startups have closed funding deals in the last five years—nearly 45 percent of them first equity rounds by startups just entering the space.

Technology, human ingenuity and deep pools of financial capital are aligned in an important mission: bringing artificial intelligence (AI) to global healthcare. If investor enthusiasm is any gauge, the mission is advancing quickly. No fewer than 300 healthcare AI startups have closed funding deals in the last five years—nearly 45 percent of them first equity rounds by startups just entering the space.1

In several respects, however, the mission is generating too much heat and too little natural intelligence. Technological assets on AI's frontier are often over billed in the media and poorly validated. Our regulatory and legal frameworks aren't prepared for AI's impact. Most importantly, companies trying to reinvent medical practice haven't devoted enough resources to asking patients what they want from healthcare AI.

With a new patient survey of about 800 European and American patients and 200 caregivers, Syneos Health hopes to address this deficit and shift the conversation from what AI means for healthcare providers, product companies and investors to what AI should do for patients. Responding to our wide-ranging questions, large majorities of patients told us they have certain fears about AI's future prominence, and that they want physicians to oversee the development and use of healthcare AI applications.

Patient Power

Having spent most of the past three and a half years in technology development and communications around healthcare AI, and more than a decade in healthcare tech, I believe our survey results (http://bit.ly/InVivoAI) carry an important message about where the "empowered patient" movement may be heading. In the past few years, this movement has begun to disintermediate physicians and professional organizations in some healthcare settings. The sentiments patients expressed in our survey may suggest a pendulum swing in the other direction.

Before turning to the survey results, I'd like to explain the shift in more detail. Prior to the very recent spike in the public's fascination with AI, the rise of "patient power" in tandem with internet ubiquity created a potent disruptive force in healthcare. Tech-savvy consumers were showing up at the doctor's office with detailed information on their health complaints, culled from respected websites like the American Cancer Society, the Mayo Clinic and MedPage Today.

Many were also keeping track of their vital signs, thanks to a dazzling array of personal health devices and apps. These patients were calling their own shots on how, when, and where they receive medical attention—in the process, shifting "point-of-care" to wherever the patient happened to be sitting.

The ripple effects of patient power were swift and consequential, eroding paternalistic attitudes among researchers, practitioners, and medical organizations. The term "patient-centricity" is on the lips of every provider and product supplier because patients placed it there.

The retreat from paternalism sounded a clarion call to outsiders with an eye on the $3.3 trillion2 U.S. healthcare market. Patient power encouraged Alphabet, Google's parent company, to spawn dozens of health initiatives.3 It may also help explain why Amazon.com is testing its Alexa systems in clinical settings such as diabetes4 care, while snapping up retail pharmacy licenses in multiple states.5 Apple similarly seized on the patient power movement, combining its consumer device platform with health-related software and data services. This allowed empowered consumers to participate directly in clinical research and take charge of clinical care delivery.6

I doubt these companies would make forays on such a scale if patients hadn't broadcast their desire to overturn the status quo. Certainly, investors would be more wary about backing risky startups in this space without such strong signals from consumers.

Course Correction

Yet, what our patient survey seems to show is that the advent of healthcare AI has once again shifted the balance of power. The arrival of powerful new technology in the healthcare space triggers, in equal measure, enthusiasm for change and apprehension about risks. In the end, patients told us, they don't wish to see this transformation proceed without the close supervision of medical authorities they trust.

Does this mean vive le status quo? Not at all. Patient power will continue, cross-sector innovation and investment will grow, and disruption from the likes of Google, Amazon and Apple will continue on the current course. Nevertheless, our survey, titled Artificial Intelligence for Authentic Engagement, reveals that there are powerful, new propulsive elements in consumer sentiment—a course correction that providers, technology developers, and their investors would do well to consider.

The lesson could not be more clear: If the tech moguls and financiers pulling the levers behind healthcare AI insist on taking a "we know best" stance, they will simply resurrect paternalism and earn the ire of empowered patients who, in fact, have unquestionable rights as AI co-creators.

From our survey responses, we learned that patient excitement about healthcare AI doesn't match that of investors. The largest cohort of respondents—44 percent in the EU and 37 percent inthe U.S.— were only "somewhat excited," while fewer than one-fifth in total described themselves as "very excited." On the flip side, 42 percent of Europeans and half of the U.S. cohort said they were "somewhat concerned" about current AI healthcare trends. Nearly one-quarter of American respondents said they were "very concerned," as did 15 percent of Europeans.

Who Do You Trust?

In terms of the course correction I described above, the most telling survey response was to our question about which groups or organizations could be trusted to develop an AI-powered "virtual nurse assistant." Should doctors or hospitals play a role? What about insurance companies, drug manufacturers or technology giants? Presented with this choice, the largest cohort of patients (56 percent) said they would trust their doctors. Hospitals came in second at 42 percent, while technology and biopharmaceutical companies trailed far behind.

There are many other takeaways from the survey that may surprise product developers. In recent years, proposals for robot "companions" for the elderly have soaked up much research funding and venture capital. Yet, in our survey, only three percent of respondents over the age of 65 identified "companionship" as a benefit.

The survey results tell me healthcare communicators who believe in AI's positive potential—myself included—have our work cut out for us. To soothe consumer anxieties about the technology, we must first educate patients and providers on the role AI already plays in trusted applications, such as Alexa, Siri and Google Now.

We must also explain more effectively that the status quo in care management is far from ideal. Asked about their concerns regarding virtual nurse assistants, 60 percent of respondents said they worried about machine errors causing harm. I wonder how many respondents realize that human error by care providers accounts for 10 percent of all U.S. deaths.7 Medical error—little of it involving AI—is the third highest cause of death in the U.S., studies show.

Far too many trends in life-altering technology are driven by vendors and inflated by surfeits of media hot air. AI is no exception. The fanfare may be benign in most areas of consumer tech, where vendors praising the latest gadget hurt no one but well-warned investors. In healthcare, best practice in every case is asking empowered consumers what they want, and humbly bringing their desires to the drawing board.

About the Author

AJ Triano is a SVP leading Engagement Strategy for GSW, a Syneos Health company. His 15-year career in healthcare technology and communications, includes a track record of strategic multichannel guidance and innovative technology pilots in healthcare. AJ spent the last two-and-a-half-years working closely with Apple and major academic research institutions and hospital systems to deliver mClincal research using Apple's ResearchKit and remote care programs using Apple's CareKit frameworks. Innovative digital research and complementary service mHealth programs he helped bring to market are fundamentally changing the way healthcare is both researched and delivered in real time.

References

[1] https://www.cbinsights.com/research/healthcare-ai-startup-boomexpert-research/

[2] https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2017.1299

[3] https://www.cnbc.com/2017/04/18/alphabet-health-tech-influencesilicon-valley.html

[4] https://developer.amazon.com/blogs/alexa/post/64589cae-4596-4156-8cdc-e029582c33ac/announcing-the-alexa-diabetes-challengepowered-by-luminary-labs

[5] http://www.stltoday.com/business/local/amazon-gains-wholesalepharmacy-licenses-in-multiple-states/article_4e77a39f-e644-5c22-b5e6-e613a9ed2512.html

[6] https://www.apple.com/researchkit/

[7] https://www.hopkinsmedicine.org/news/media/releases/study_suggests_medical_errors_now_third_leading_cause_of_death_in_the_us

GE Healthcare Sets Out Its Software And AI Ambitions

Executive Summary

GE Healthcare is using its artificial intelligence platform Edison to power a new generation of medical imaging apps and devices. At the annual European Congress of Radiology (ECR), In Vivo met with Mathias Goyen, GE Healthcare's chief medical officer, Europe, to discuss the future of AI in radiology and how technology will transform practice.

Artificial intelligence (AI) was a hot topic at the recent annual European Congress of Radiology (ECR) and GE Healthcare was one of many industry partners that used the congress to showcase technology in the field.

The health care giant has made AI the centerpiece of its digital portfolio, last year launching Edison, an AI platform designed to connect data from millions of medical imaging devices. The integrated, digital platform can be used by clinicians with Edison applications and services, and by technology developers to combine diverse datasets from across modalities, vendors, health care networks and life sciences settings.

At ECR 2019, held in Vienna, GE Healthcare launched new applications built on Edison, including a CT scanner, X-Ray, MRI and ultrasound device that integrate AI tech with cloud connectivity and are designed to enable fast data processing.

Speaking to In Vivo at the congress, Mathias Goyen, GE Healthcare's chief medical officer, Europe, said AI was an opportunity for clinicians to make faster, more informed decisions that can improve patient outcomes. "We must embrace AI as a helping tool that will make our lives easier. We know it can get rid of the boring stuff and easy tasks. As a radiologist, I don't want to see the normal cases, I want to see the cases where its most likely there is a tumor and I want AI to detect this for me and highlight out of a thousand images the 40 images where this diagnosis can be found," he said.

AI A Game Changer For The "Four Eyes Principle"

In countries where the "four eyes principle" that two individuals approve some action before it can be taken, Goyen said AI could be the ultimate game changer. "In Germany for example, every mammogram must be seen by two radiologists because the diagnosis is so important. Now, we are thinking, AI could be the second or first pair of eyes to evaluate the mammogram. So, the big question is, would it be enough to have me as a radiologist make the decision, together with an AI algorithm?"

Although the medical and legal considerations of using AI in this way are still unclear and pose a level of risk, Goyen can foresee a time when patients could sue a hospital for not using AI. "It could be that in a couple of years, for certain indications, AI is the best way to go and patients could sue hospitals for not using the technology instead of the other way around. Everything right now is in flux, AI is developing and unfolding before our eyes and it's an exciting time to be in health care."

However, while clinicians are still wary of AI and see it as a threat, Goyen insisted it will be a tremendous opportunity for the profession. "At the end of the day, care is about people. Radiologists do a lot more than just looking at cases, and for the foreseeable future, I can't see an AI algorithm replacing an interventional radiologist or talking to patients. You don't want to get your diagnosis from a computer, you want the human touch and to talk to a doctor. GE Healthcare's theme is that AI frees up more time so a doctor in the future can do what they are trained to do – take care of the patient. So, we humanize or rehumanize healthcare by applying AI."

Last year, the company announced a major partnership with Roche Diagnostics to develop digital platforms for precision health in oncology and critical care.((Also see "GE And Roche Join Forces In First-Of-Its-Kind Tech Pact" - Medtech Insight, 8 Jan, 2018.)) The oncology platform, will take in vivo data obtained directly from the patient by radiological imaging and monitoring equipment and combine the results with in vitro data from laboratory tests to help clinicians form a diagnosis. The system will also integrate data from electronic medical records, medical best practices and research. Goyen said the partnership was ideal as both companies combined their respective expertise in imaging and in vitro diagnostics. Indeed, this marriage of specialties could be the future of the field, according to Goyen.

"I think in 10 years' time there will not be a residency in radiology, but more like super diagnostics – including pathology and lab science. These specialties grow together, in vivo and in vitro, so maybe there will be a specialty diagnostician role where everything is included to streamline the data and present it in a digestible format."

Code Of Ethics For AI?

At present, AI technology is altering practice at three levels for clinicians – first at the point of care, secondly at a departmental level to streamline workflow and reduce waiting times, and finally at a network level to streamline patient workflow. But while the potential of the technology is exciting, Goyen said there needs to be a conscious effort to implement a code of AI ethics and ensure it does not become uncontrollable. "In all our efforts in developing AI algorithms, we must always keep in mind that AI doesn't take over, so sometimes some good old-fashioned common sense is still needed," he said. "We need to ask is this really good for our patients or ourselves? It's about artificial morality and ethics in AI."

GE Healthcare's priorities in 2019 will be to form partnerships and elevate customer experience. "We need strong partners – whether that's at the university level, private practice, industry partners or tech partners. We have valued partners working with us now and we need more – we cannot do it alone." And although the GE group recently announced the sale of its biopharma business to Danaher for $21.4bn, to help reduce debt burden, the health care division will continue to invest in R&D in the space. (Also see "GE Deals Biopharma Biz To Danaher For $21.4Bn; Planned Healthcare IPO Probably Won't Happen" - Medtech Insight, 25 Feb, 2019.) "The entire contrast agent business that was part of GE's Life Sciences business that we sold is now coming to GE Healthcare and we will make effort to develop more contrast agents for diagnosis," said Goyen.

"Of course, we are still a manufacturer of awesome equipment. But we are moving more and more towards being a software company and building a lot of things around our equipment." Whether build-in, pay-per-use models or cloud-based concept, Goyen says GE Healthcare is really transforming into a software company and embracing these new techniques.

Podcast: Medtech Pressure Points And Opportunities In 2019

The Global View From ZS

Executive Summary

Menacing clouds on the horizon, or opportunity for medtechs large and small in the evolving health care delivery ecosystems? Probably both, and a significant amount of risk, too, for those medtechs who push through the pain barrier to, in some cases, redefine their own roles. Helping patients understand the value being created will also be a major success factor for medtechs. Whatever the outcomes, these are exciting times, says ZS' Brian Chapman, in this future-gazing podcast with In Vivo.

The current, unusually intense, period of regulatory change – in the EU, US and even China – and the ongoing challenges for global business are making companies look hard at their levels of fitness for the future in the evolving medtech ecosystem.

Manufacturers are living in a period of uncertainty, with often misfiring international trade relations, Brexit, and currency developments in emerging markets all contributing to the sense of unpredictability. Change has always been a factor for medtechs, but therein also lie opportunities – now especially for those who can find a meaningful role in the digital transformation agenda.

We are also seeing a return to product and portfolio focus, partly in place of the major M&A seen in recent years, and for the time being, it's "less about scale." What won't change now is the pressure for companies to keep right on top of their evidence strategies, says Brian Chapman, principal and head of medical products and consulting at ZS, speaking to In Vivo about the outlook for global medtechs in 2019.

Click here to listen to the podcast

https://soundcloud.com/pharmaintelligence/medtech-pressure-points-and-opportunities-in-2019-the-global-view-from-zs