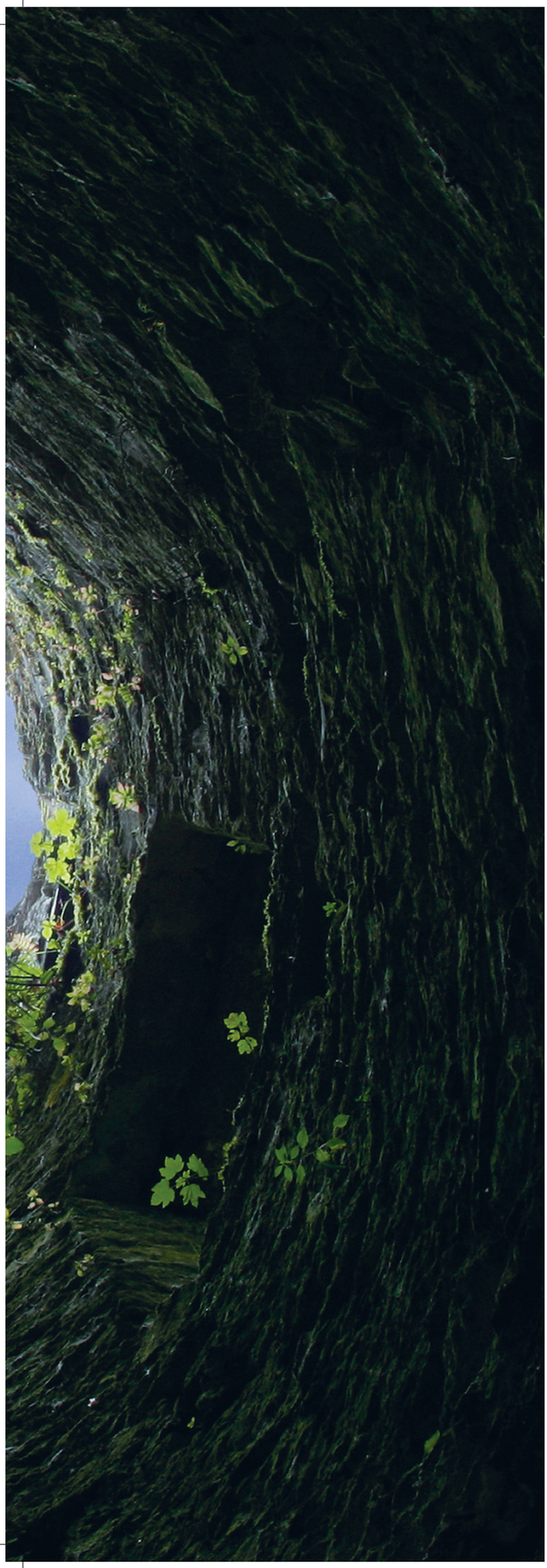
Brian Sweet, AstraZeneca executive director, health alliances (left), with Marcus Wilson, president, HealthCore



DEEP IS THE NEW BIG

Meeting pharma's value-based reimbursement challenge: **Marc Iskowitz** looks at how companies, driven by payer and provider pressure, are leveraging Big Data across the product lifecycle

As patients move through the healthcare system, massive databases track them at population scale. Each doctor visit, prescription refill and lab test forms a digital trail from which researchers study resource utilization, which has traditionally been a proxy for health outcome. That was yesteryear's class of data.

Today, petabytes are piling up—and not just within the big managed-care claims databases. New sources of clinical data, like electronic health records and patient registries, are enabling a deeper view of the inputs to treatment decisions and also their result. Researchers are layering the two to study, in de-identified aggregate fashion, the comparative effectiveness and safety of medicines.

Deep Data has another big benefit: providing insights to inform how payers and providers evaluate medicines for coverage. For instance, AstraZeneca has leveraged clinical evidence derived from administrative claims and EHRs to look at the effect of formulary decisions on total cost of care for some late-stage commercial products.

"[We] showed that the removal of a branded medicine in our portfolio from the preferred-tier status actually resulted in higher

PHOTO: BILL BERNSTEIN

overall costs, which were related to cost of office and [ER] visits as well as disease-state related tests," reports Brian Sweet, AstraZeneca executive director of health alliances. Considering such study results has helped the company "solidify tier-placement decisions with respect to our medication that are more favorable than what you would expect with a generic market where we have to compete with a late-stage commercial product," he adds.

Since 2010 the company has maintained a strategic initiative with HealthCore—the health outcomes research subsidiary of managed-care company WellPoint—that has helped extract these insights. "There's lots of Big Data out there with not a lot of robust insight," says Marcus Wilson, president, HealthCore. "There's a limit to what you can get from it without it being effectively integrated."

The collaboration quotient

Real-world data and research partnerships can potentially accomplish such integration. Pharma-payer collaborations run the gamut, from helping a company position its early-stage commercial products to reflect actual clinical practice, to helping it understand how a marketed medicine is performing outside of controlled clinical trials.

By linking sources of real-world health information, companies and payers say, they can meet providers' expectations of pharma value, improve adherence and boost outcomes. In a PricewaterhouseCoopers Health Research Institute survey, 43% of insurers agreed that they would benefit from data-sharing partnerships with pharma.

The trend reflects a growing need for drug makers to prove the cost-efficiency of their products to cash-strapped governments.

AstraZeneca knows this first-hand: in February the UK's National Institute for Health and Clinical Excellence (NICE) cost-effectiveness watchdog issued a no-go on its new drug Forxiga, which it co-markets with Bristol-Myers Squibb, although the diabetes pill was approved in November for sale in the EU. Apparently the gatekeeper was unconvinced that Forxiga works any better as an add-on therapy than existing drugs.

"A lot of the discussion in Europe the last several years has been around discouraging the rapid uptake of a lot of very innovative products, and a higher reliance on existing products," says Jon Resnick, VP of real-world evidence solutions, IMS Health, which works with AstraZeneca to mine and analyze data in EU markets.

That's been a concern for industry. "[Purchasers are saying], 'Come to us with evidence to show the drug works, but most importantly, the drug works in the real world, outside of the controlled clinical trial setting,'" adds Siva Narayanan, SVP, evidence generation, value and access at marketing research agency Ipsos Healthcare.

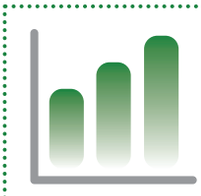
Some physician KOLs are also playing a more influential role in terms of coverage decisions. Memorial Sloan-Kettering Cancer Center recently refused to pay for new colorectal cancer drug Zaltrap, citing data that it performed no better than a similar medicine at less than half the cost. Sanofi gave in, lowering the price to that of the competing therapy barely two months after launch.

Bolstering the infrastructure

To meet the demand, companies are bolstering their Big Data infrastructure. "If there is this foundation of information that can be created into an evidence base," Resnick says, "it can allow for greater efficiency and value." Some companies, says Narayanan, are moving toward having one central source of integrated real-world data, housed in the company, that marketing and other departments can tap into to understand the current real-world landscape. "That's where the ROI comes," he says.

The science behind this new form of analysis is evolving. "It's really early days for the role of real-world evidence in our research programs and in clinical practice," says Sachin Jain, MD, chief medical information and innovation officer at Merck. There's still work to do, Jain says, on refining the methodology as well as in collecting the evidence and getting access to it.

We're talking about a different animal compared to the gold standard of research—the randomized controlled clinical trial. "Anyone who works in the space will tell you that data and analytics from real-



43% of insurers say that they would benefit from a data-sharing partnership with pharma Source: PwC HRI payer value survey 2012

Drug-development insights sought from social media

Administrative claims databases and electronic health records are the tip of the iceberg in terms of data sources fueling the current paradigm of real-world evidence. Social networks, where patients gather to discuss their illnesses, have become research platforms in their own right, with some advantages over traditional data streams.

"It's a surprise to no one that as an industry, we've really lagged behind in terms of engaging with end users of our medicines and patients, so social media creates new kinds of opportunities for us to understand, from the patient perspective, what the relative value of our medicines are in the real world," says Sachin Jain, MD, chief medical information and innovation officer at Merck.

For certain chronic and rare diseases, especially those of the central nervous system like ALS, MS and Parkinson's, subjective feedback can give the best indication of patients' response to treatment. Claims databases traditionally don't measure patient-reported outcomes, and while EHRs are beginning to incorporate symptom reporting, it's still the exception.

Merck's partnership with online patient network and research platform PatientsLikeMe shows one way drug makers are trying to fill the gap. The two are working together to evaluate the impact of psoriasis on patients (Merck has a psoriasis agent in Phase IIb testing).

PatientsLikeMe collects data on how patients' real-world experiences with disease, symptoms and drug side-effects impact them. ("Those insights can help with our drug development," says Jain.) As well, that data show what happens when patients use its system—PatientsLikeMe has already published studies showing that patients, in HIV and depression, improve in real-world outcomes just by being members.

"We feel that the science behind patient-reported outcomes and the access to them, both for individual patients and then for clinicians and for clinical researchers, is just not good enough," says Ben Heywood, PLM president and co-founder, "and we're working to enhance our platform to make it much broader across more diseases."

A UCB-funded study involving epilepsy patients is ongoing, and Heywood says the network is about to announce a new partnership with the Robert Wood Johnson Foundation to build out these capabilities further.

world data are hypothesis-generating rather than hypothesis-testing," says Jain, adding that new directions of inquiry do emerge.

But it may be a cheaper alternative. "One of the reasons pharma is investing in all of this is that the cost of trials has just become incredibly burdensome," observes Ben Heywood, president and co-founder of social-network-turned-research-platform PatientsLikeMe. "If you're in Phase IV and you're spending as much as you spent in Phase III to learn about the drugs, the numbers don't add up."

Merck and UCB are among about 40 life science customers with whom PatientsLikeMe works to monitor how drugs are impacting patients (see sidebar).

While the new analytics are not about to replace trials, experts say the research holds the potential to go beyond the insight derived in clinical studies. For instance, a five-year partnership formed by Humana and Pfizer, now in its second year, has the two researching ways to improve healthcare for the elderly.

The Humana data set serves "as a real-world laboratory to provide insight to improve patient health outcomes, quality of care, and costs," says Steve Chick, VP, Humana competitive health analytics leader.

The focus initially was on three chronic conditions: pain, cardiovascular disease and Alzheimer's disease. The partners jointly examine specific groups of patients and subgroups who are the target population for a treatment in development. "We then use real-world data to examine patient preferences and behavior…and other critical variables," says Chick. "The emphasis here is getting the right medicine to the right patient."

As Marc Berger, MD, Pfizer VP, real-world data and analytics, explains, "Real-world evidence supplements clinical trial data by providing insight into the impact of interventions in real-world populations, such as real-world adherence patterns and comparisons of outcomes from therapies that may not be captured in randomized controlled trials."

45% of insurers say they expect to see clear cost savings from pharma for formulary placement Source: PwC HRI payer value survey 2012

AstraZeneca's Sweet says multiple-mix-style trial designs incorporating randomized clinical trial data with prospective observational or sub-study heath economic data sets give pharma the best of both worlds. "There are various ways we can build real-world data endpoints into the clinical trial process," he says, "and that we think is very valuable to the organization because it provides data at launch for our products that payers, providers and patients are asking for."

In one case, Sweet says AZ engaged and listened to payers around the onset of a study for an early-stage commercial product and incorporated their requirements for data into the trial's design to help it better reflect clinical practice. "We're currently using these real-world results in payer discussions and have successfully influenced formulary placement on many occasions with that information."

What do payers get out of such deals? Humana's Chick outlines several benefits of its Pfizer alliance: joint learning to improve population health, leveraging real-world evidence to make benefit and drug-placement decisions, among others.

For purchasers, it's not just about slashing costs, insists HealthCore's Wilson. "[Payers] want to be very responsible on how they're actually improving cost and, first and foremost, improving quality," he explains. "To do that, you really have to have a deep view."

Adds Chick, "We at Humana and a manufacturer want the same thing—a patient or member whose health is well-managed. Coming to a common ground on this is not that difficult, but we have traditionally taken very different approaches to get there. It will be essential for insurers and payers and pharma manufacturers to come to agreement more readily and robustly on taking a collaborative approach to solving the value of Big Data."

60% of insurers expect clear relative clinical benefit from pharma for formulary placement Source: PwC HRI payer value survey 2012

Arriving at a common ground may be everyone's objective, but "Getting there will take a lot of trust and collaboration, allowing technologies to talk to each other and data pockets to speak to each other," says IMS Health's Resnick.

Resnick envisions evidentiary data powering sales force discussions with physicians on how different patient segments in their disease population respond to different types of treatment; fueling interactions with managed care to show how pharma can add value to a contract and to the care continuum; and facilitating dialogue with regulators as they seek to reconcile the efficacy-safety tradeoff.

Beyond the pill

The new data sources can "allow people to share responsibility and financial risk. It's going beyond the pill," adds Steve Davis, VP of life sciences for clinical data firm Humedica, which has a real-world evidence pact with Pfizer focusing in the US.

"If different partnerships can form on objective sources of data that are clinically rich, that are across the continuum of care," Davis posits, "think about the opportunity to reimburse pharma or providers of care based on wellness and therapeutic benefit rather than paying them for the pill regardless if it works."

As health plans and the federal government move away from unit-based payment models and toward the outcomes-driven kind, these will start to affect prescribing patterns, analysts predict. Physician incentives in the US are being geared around quality management and how well clinicians treat disease.

Merck's Jain, a Harvard-trained internist and MBA who worked in the Office of the National Coordinator of Heath IT and was part of the launch team at CMS for the Center for Medicare and Medicaid Innovation, sees parallels between the emergence of real-world analysis and the nation's adoption of healthcare IT. Both, he says, have inspired a deep interest in all quarters.

"Particularly as costs increase and there's increasing scrutiny applied to the quality of care being applied to patients," Jain says, "every sector of the healthcare industry is interested in getting a clear view of what's happening to patients in the real world, so there's a great deal of alignment that's going to drive the kind of connectivity necessary to form that more complete view." ■