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The End Of Drug Innovation In Diabetes?

by Melanie Senior

Lacking revolutionary new treatment mechanisms in type 2 diabetes, pharma is relying on combinations, convenience, and beyond-the-pill services. As prices are squeezed, the winners will be those who can deliver the best-value outcomes, not necessarily those with a best-in-class drug.

- Recent advances in type 2 diabetes have been incremental, relying on longer-acting dosage forms and/or combinations of existing drug classes.
- As prices are squeezed in an increasingly competitive field, several pharmas are shifting their focus beyond pills and injections, onto related services and adherence solutions that can improve outcomes.
- This shift requires new approaches, new partners, and, for most, a new way of doing business, whose sustainability remains unclear.
- The winners in diabetes will be those who can convince budget-strained payors that they offer the best-value outcomes – with or without beyond-the-pill services.
- Diabetes isn't the only health care arena being transformed by the trifecta of shift-to-outcomes, pricing pressure, and novel technologies. But its prevalence, and commercial significance, mean it's where the pressures are most urgently felt.

No pharmaceutical executive with a stake in the $45 billion diabetes therapy market is going to say that drug innovation has come to an end. But there's little doubt that the medications currently available for the disease – and there are plenty – haven't done enough to prevent what the World Health Organization and many others now label as a global epidemic, affecting 350 million people worldwide. "It's not the end of the drug…but if you want to help with outcomes…you need to bring something else," says Pierre Chancel, VP, diabetes at *Sanofi*.

That "something else" is fundamentally about increasing treatment adherence, thereby improving outcomes and reducing overall system costs. Diabetes currently costs the world's health care systems $584 billion globally, according to the International Diabetes Federation.

And of the nearly 400 million diabetics straining the systems today – expected to reach 500 million by 2035 – as many as half aren't adequately controlling their blood sugar levels, even with medication, according to a 2013 study in the *Journal of the American Medical Association*. Another 50% of sufferers remain undiagnosed.

The top diabetes players' strategies to improve outcomes vary as a function of their portfolios and commercial pressures. Sanofi is dangerously dependent on market-leading long-acting insulin *Lantus* (glargine), whose almost $8 billion annual sales will soon face generic competition. With an unremarkable follow-on insulin in *Toujeo*, a higher-concentration, depot-formulation of Lantus, Sanofi has launched headlong into the "beyond the pill" culture to shore up its franchise. Thus the focus of its June 2014 deal with device giant Medtronic Inc. is on building convenient drug-device pairings and customized support programs around its insulins. *[See Deal]* These patient-centric "integrated care solutions" require new, far more patient-focused ways of thinking – and new kinds of expertise.

Eli Lilly & Co. is pursuing a less risky strategy. It's sticking with drugs, but going for breadth and payor convenience. Lacking any outstanding individual product, it has quietly built out an end-to-end portfolio across oral and injectable diabetes therapies. The idea is to provide a one-stop shop, and, with a biosimilar version of Lantus in the mix, one in which value is driven largely by competitive pricing. *AstraZeneca PLC*, meanwhile, aspiring to become a top-three diabetes player by revenue by 2020, is doing a bit of both: offering a comprehensive range of convenient oral combination treatments, complemented by around-the-pill services (but no devices). "If we want to deliver on our ambition to be a leader…our strategy has to be a beyond-the-product offering," emphasizes VP, global product portfolio strategy for cardiovascular and metabolism Fouzia Laghrissi-Thode, MD.

As for diabetes-focused *Novo Nordisk AS*, the world's biggest producer of insulin, its beyond-the-drug efforts include "helping deliver demographic solutions," explains chief scientific officer Mads Krogsgaard Thomsen, PhD. With overburdened health systems at the risk of collapse, "we have to be seen as delivering more than just the drugs," he says. So Novo has teamed up with *University College London* and city authorities across the globe to try to figure out the sociological and anthropomorphic reasons for diabetes' spread in urban environments. Meanwhile, Thomsen is – naturally enough, given Novo's recognized leadership in diabetes therapies – the most vehement in insisting that drug innovation in type 2 diabetes is "absolutely not" at an end. "Five of the most significant drugs in the company's recent history will be launched in the next five years," he contends.

Convenience, Not Novelty

The near-term drugs in Novo's pipeline nicely illustrate where most activity in type 2 diabetes therapy is focused: on longer-acting versions, and combinations, of existing treatments. *Tresiba* (degludec) is an "ultra"-long-acting basal insulin already approved in the EU and Japan and

awaiting FDA go-ahead. (Novo also has an ultra-rapid-acting insulin in Phase III.) *Xultophy* (IDegLira) is a combination of insulin and Novo's top-selling glucagon-like peptide-1 (GLP-1) analog *Victoza* (liraglutide), also available in the EU. Phase III semaglutide is a once-weekly GLP-1 analog. This injectable class works by stimulating insulin secretion, and Victoza, which sold $2 billion in 2013, has attractive weight loss effects. Indeed, a higher-dose version of the drug, *Saxenda*, was approved by FDA in December 2014 for obesity. Further out is an oral long-acting GLP-1 analog.

Over at AstraZeneca, the latest US diabetes approval was in October 2014, for *Xigduo XR*, which combines liflozin (*Forxiga/Farxiga*), a sodium-glucose cotransporter 2 (SGLT2) inhibitor, with metformin in a once-daily tablet. Xigduo twice-daily was approved in Europe in January. SGLT2 inhibitors are the newest class of diabetes drugs, pioneered in Europe with Forxiga in late 2012, and in the US by *Johnson & Johnson*'s *Invokana* (canagliflozin) in 2013. Their driving force: oral administration, and potential weight loss – both compelling reasons to try them before insulin (though there are some safety concerns, too, including around urinary tract infections). Next in line at AZ is a soon-to-be-filed duo of dapagliflozin and saxagliptin, a dipeptidyl peptidase-4 inhibitor already sold as *Onglyza* (and which already exists as part of *Kombiglyze XR*, with metformin). And after that: a trio of dapagliflozin, saxagliptin, and metformin in one pill.

Meanwhile, at *Merck & Co. Inc.*, as its $4 billion-a-year daily *Januvia* (sitagliptin) star begins to fade (along with its *Janumet* combination, with metformin), hope rests on once-weekly omarigliptin – but perhaps more importantly, on a future combination with ertugliflozin, an SGLT2 contender accessed in 2013 from Pfizer for $60 million. *[See Deal]*

Significant science goes into sustained-release (and more rapid-acting) formulations of these drugs, and into making them more convenient and more likely to help patients maintain good glycemic control. The ultra-rapid-acting insulins, for instance, may offer more flexibility in injection timing around mealtimes. But since Forxiga's European launch in 2012, the underlying mechanisms aren't new. Insulin was discovered nearly 100 years ago. And the market's crowding in all categories: several others besides Novo have more rapid-acting insulins in development (Lilly just signed a deal with France's *Adocia SAS* for an ultra-rapid version of its *Humalog* [lispro].)*[See Deal] Boehringer Ingelheim GMBH* and Lilly's SGLT2 inhibitor, *Jardiance* (empagliflozin), was approved on both sides of the Atlantic during 2014; there are multiple development-stage SGLT2s and combinations. (*See Exhibit 1*.)

Exhibit 1

Big Pharma's Diabetes Portfolios

Company	Marketed Products	Pipeline
AstraZeneca	Byetta (exanatide); Bydureon (XR exanatide);	Bydureon weekly;

	Forxiga/Farxiga (dapagliflozin); Onglyza (saxagliptin); Komboglyze/Kombiglyze XR (saxa-metformin); Xigduo; Xigduo XR (dapa-metformin)	saxagliptin-dapagliflozin combo (both due to file in 2015)
Boehringer Ingelheim*	Trajenta/Tradjenta; Jentadueto/Trajenta Duo (linagliptin-metformin); Jardiance (empagliflozin); Abasria/Basaglar (glargine biosimilar)**	Empagliflozin-linagliptin (PIII); empagliflozin-metformin (PIII)
Eli Lilly	As for BI, plus: Glucagon; Humalog (lispro); Humulin (insulin, various mixes and strengths); Trulicity (dulaglutide)	Basal insulin (peglispro) (PIII); Glucagon receptor antagonist (PII); GLP-1/glucagon receptor co-agonist (PII); three "new biologic entities" (PI)
Johnson & Johnson	Invokana (canagliflozin); Invokamet/Vokanamet (canagliflozin-metformin)	
Merck & Co.	Januvia (sitagliptin); Janumet (sita-metformin); Janumet XR	Ertugliflozin (PIII); insulin glargine (PIII); omarigliptin (weekly DPP-IV inhibitor [PIII])
Novo Nordisk	Victoza (liraglutide); Tresiba (insulin degludec) (not US); Xultophy (IDegLira, degludec-liraglutide) (not US); Ryzodeg (degludec-aspart) (not US); Levemir (insulin detemir); Novolog (insulin aspart); Novolog Mix; Prandin (repaglinide); GlucaGen Hypokit (glucagon)	Ultra-rapid aspart (PIII); semaglutide (weekly GLP-1) (PIII); long-acting oral GLP-1 tablet (PII); weekly basal insulin (PI)
Sanofi	Lantus (glargine); Apidra (insulin glulisine); Insuman (rapid-intermediate mixes); Lyxumia (lixisenatide) (EU); Amaryl (glimepiride)	Toujeo (high conc. glargine) (reg.); Lyxumia (PIII, US); LixiLan (glargine-lixi) (PIII)

*In collaboration with Eli Lilly.

**Basaglar has tentative FDA approval but Sanofi litigation has delayed launch.

SOURCES: Company web sites and news reports; FDA; EMA

Combination treatment can help – especially those assembling some of the newer drug classes. The weight loss effects of dapagliflozin, for example, plus the convenience of the pill form, make the forthcoming triple from AstraZeneca “a pretty persuasive offering,” according to Andrew Baum, MD, global head of health care research at Citi in London. Meanwhile, Phase III data for even the dapa-saxa duo, presented at the American Diabetes Association meeting in June 2014, suggested it helped 40% of patients get to goal blood sugar, twice as many as on either treatment alone.

But just as remarkable as the improvement seen with dapa-saxa is the low success rate for the predecessor drugs – just one-fifth of patients getting to goal. Even that may be better than average, given that trial outcomes rarely reflect what's going on in the real world. Treatment compliance and poor outcomes remain a real issue in diabetes – one that the drugs and combinations currently available haven't, apparently, done a great job of addressing.

The next generation of incremental improvements may yet help reverse the tide of diabetes more convincingly. Indeed, the dearth of new tricks makes getting the existing ones to work better even more important. AstraZeneca is very explicit not just about its combination-treatment approach, but also about encouraging earlier treatment. "The current treatment paradigm is doing too little, too late," says Laghrissi-Thode. The tendency is to treat to failure: to offer one particular drug, say, cheap metformin, until that fails to control blood sugar adequately, at which point the patient is switched to the next therapy, a gliptin for instance. Unfortunately, diabetes is progressive: uncontrolled blood sugar causes damage in the meantime: damage that can and often does lead to far more serious, and more costly, downstream complications. Laghrissi-Thode argues that combinations like AZ's offer the opportunity to treat patients earlier, in a more comprehensive manner, to achieve their blood sugar targets.

Lacking Proof Of Outcomes, Drug Prices Crater

They have to prove it. The difficulties pharmas have faced to date in convincingly proving their drugs' value – both in absolute outcomes and relative to the very similar competitors – has created enormous pressure on pricing. European payors are pushing back on higher-priced, new drugs in favor of older, cheaper ones. Cost watchdog the National Institute of Health and Care Excellence (NICE) still recommends that insulin treatment in England and Wales start with human NPH (neutral protamine hagedorn) insulin, for example. Germany pegged analog insulin prices to human insulins, claiming they were no better; authorities there in 2013 claimed data submitted around Forxiga showed no added benefit either over existing standard therapy, thereby restricting the product's price. In the US, payors are playing off the competitors against each other, leading to higher rebates. "Pharmacy benefit managers have already extracted significant cost savings, and crudely speaking, they can smell blood," says Baum.

Drug firms are feeling the pinch: in October 2014, Sanofi's then-CEO Chris Viehbacher warned that this "more challenging US diabetes price environment" would impact 2015 sales; soon after that, he was sacked. There has since been further upheaval within the top ranks of Sanofi's US diabetes business. The French group had already been forced to discount Lantus in 2014 (admittedly, though, there was some froth to get out of the system: from 2007 to 2013, Lantus' price rose by 160%, according to Bloomberg). *Express Scripts Holding Co.*, a large PBM, barred Novo's Victoza and mealtime insulin *NovoLog* (aspart) from its formulary in 2014, in favor of cheaper alternatives (though the impact on Novo's sales growth was less than expected). "Prices are literally cratering…on a class-by-class basis," comments a senior managed care executive at one Big Pharma. "First it was in cardiovascular disease; in the last 18 months the pressure has hit

diabetes."

As a result, AstraZeneca decided the best way to be sure newly approved Farxiga got enough momentum in the US versus the incumbent, Invokana, was to give it away for free, via coupons. (It was also to help detract from the bladder cancer warning on Farxiga's package, which its competition doesn't have.) AstraZeneca senior management claimed at the group's November 2014 investor day that it was simply doing what Johnson & Johnson (Janssen) did with Invokana. How long the freebies might continue is unclear. "We'll wait and see how well SGLT2s are adopted…before deciding how quickly the zero-pay coupons are blended into whatever rebates are offered," said Paul Hudson, EVP, North America.

Short of compelling evidence in favor of one drug's outcomes over another, these dynamics will likely continue. The small differences between the drugs, in terms of efficacy and compliance, "make it hard to persuasively push the value case," says Citi's Baum. Yet, more so than ever, "the onus is on pharmaceutical companies to strengthen their claims that they're creating value for the payors," he sums up.

Lookalike Drugs Shift Focus To Services And Support

Long-term outcomes trials might help: Janssen's CREDENCE trial is assessing whether Invokana has a renal and vascular protective effect in type 2 diabetics (diabetes is known to increase the risk of heart disease). There's a similar study ongoing with AstraZeneca's once-weekly GLP-1 agonist *Bydureon* (exenatide). But such studies are still carried out under controlled conditions (and most such trials are performed, at the behest of regulators, to quell concerns over long-term safety – an outcomes trial of Farxiga is assessing the risk of CV events).

Hence the compulsion for some pharma firms to engage in beyond-the-pill services, delivered in real-world conditions, to better control and demonstrate their drug's value. That value isn't inherent in the drug itself; it's largely a function of how the care around that drug is delivered. As reimbursement in the US shifts from fee-for-service to outcomes, the pressure to control outcomes is being felt across the board, not just in diabetes – though arguably that's where it's most urgent. "We don't want to take the risk of not getting paid for an outcome we don't control," declared *Novartis AG*'s CEO Joseph Jimenez at the *Financial Times Global Pharmaceutical and Biotechnology Conference* in London in November 2014.

Beyond-the-pill experiments ongoing across many chronic disease areas include programs that use consumer-facing digital health technologies to help encourage patients to take their medicines properly (*see* (Also see "*Digital Health Is Changing Health Care. Is it Changing Pharma?*" - In Vivo, 16 Jun, 2014.)); initiatives to streamline care delivery; tools, products, and services to help physicians tailor treatment regimens more appropriately to different patients; and projects to help figure out treatment gaps and the underlying causes of poor treatment outcomes.

"Our strategy is to have a portfolio that allows physicians to select treatment based on patient profile…and to provide a comprehensive offering to payors and providers," says Laghrissi-Thode of AstraZeneca's combination approach. But in diabetes, personalized approaches don't (yet) translate into identifying genetic mutations and selecting the appropriate drug, as in some cancers. Instead it's about lifestyle, diet, behavior, preferences, and a host of non-medical issues that are less easily measurable, and that pharma hasn't, to date, been involved in very much.

That's changing. AstraZeneca in October 2014 launched *Fit2Me*, a free diet and lifestyle support program that offers customized care plans, digital coaching, and gaming-inspired incentives and rewards for diabetic patients taking AZ's medicines. Like other firms, AZ also has joint working initiatives with the UK's National Health Service (NHS) around professional education. Merck & Co. runs an entire subsidiary, Vree Health, that's devoted to health care service and delivery. (*See* (Also see "*Merck's "Beyond The Pill" Bet, Vree Health, Goes Commercial*" - In Vivo, 18 Oct, 2013.).) In June 2014 it also launched a global outcomes registry to identify gaps in type 2 diabetes management. The three-year project, involving 20,000 patients and tracking measures such as glucose control, health resource utilization, adherence, quality of life, and patient satisfaction, is part of a "broader commitment to generate real-world evidence to help advance diabetes care," according to the company.

In a similar vein, Novo's *Cities Changing Diabetes* initiative aims to map out some of the drivers of urban diabetes scourge, before designing plans to address them. With Copenhagen, Houston, Mexico City, Shanghai, and Tianjin signed up so far, the project is trying to identify, for example, whether poor diagnosis, a lack of doctors, particular demographics, and/or cultural aspects, such as stigma associated with the disease, are the most important contributors to diabetes' spread in the different cities.

The company is realistic about what it can do once the issues are identified. "We can't go and shut down McDonalds, or invest in health and schools from our R&D budget," says Thomsen. But the firm can try to persuade relevant authorities to get together, to help bring about earlier diagnosis and reduce complications. And although none of this directly helps sell more drugs, it doesn't do the company's image any harm, either – including in important emerging economies such as China and Mexico. "It's not about creating access to our drugs, but about building respect, trust, and a strong reputation," sums up Thomsen.

Integrating Drug-Devices: Will It Work This Time?

Sanofi's hoping that its patient-centric, drug-device push will help it lock patients onto Lantus and its successor, via a range of simple, convenient insulin and drug delivery systems developed within the Medtronic tie-up. Tailored patient support is also part of the solution – for instance with titration and adherence to insulin, especially after the first six months, when drop-off rates can be significant. "It's easier to change the way you do things when you have a good position in the market," says Pascale Witz, EVP, global divisions and strategic development.

Sanofi's previous foray into diabetes devices, via the *BGStar* and *iPhone*-compatible *iBGStar* blood glucose monitors launched in 2010, didn't have much impact in a highly competitive market. Nor, as a result, did it appear to do much to progress the company toward a vision it already held of integrated diabetes care.

The experience doubtless provided some lessons, though, and a foundation, of sorts, for the Medtronic deal. But now Sanofi must move fast. Lantus loses patent protection in February 2015 in the US. Sanofi has used a lawsuit to block Lilly's biosimilar from the US until the second half of 2016, and hopes that by then Toujeo will be approved. But it's not a done deal: Toujeo is filed at FDA and the company expects a decision in the first half of 2015, but a panel meeting isn't out of the question, which could delay launch. Novo's Tresiba has been held up at FDA since early 2013; the regulator demanded a cardiovascular outcomes trial.

Toujeo is designed to help address the difficulties new patients have in controlling insulin dosage. For instance, the drug leads to fewer hypoglycemic episodes when dosage is increased, explains Chancel. But, as Witz points out, "it's not just about having the technology and dumping it on the patient. It's about tailoring it to different patients." By having the right range of insulin and delivery modalities, coupled with different support programs for those requiring "low-touch," web-based reminders, versus those "high-touch" patients requiring face-to-face support, Sanofi hopes it can drive better outcomes. According to Chancel, a pilot already performed with Medtronic as part of an earlier deal in type 1 diabetes shows an increase in blood glucose reduction and in insulin dose, and better adherence after three months.

Sanofi's portfolio includes *LixiLan*, a combination of GLP-1 *Lyxumia* (lixisenatide) and Lantus, whose US filing is expected in late 2015. Lyxumia's US submission was pulled in 2013 for an outcomes trial to complete in early 2015; that has to be positive for the once-daily GLP-1 to have a chance against Victoza.The company also has a rapid-acting inhaled insulin, *Affreza*, developed by *MannKind Corp.* and FDA-approved in June 2014. *[See Deal]*

There are practical hurdles to providing tailored treatment and support elements to the many thousands of diabetic patients. Witz talks about algorithms that help quickly triage patients into segments, and adjust their support-type accordingly.

Great For Patients, But Can Services Shore Up Pricing?

All these initiatives are good news for patients. Those with the disease have a growing range of tools on offer to better manage their health and that provide incentives to stick to their increasingly convenient medications. "Companies have learned that if people understand the how and why of what they're doing, and personally benefit, then they will be more compliant," sums up David Kliff, *Diabetic Investor* publisher and president, Healthy Outcomes.

Payors won't pay extra for services, or convenience, without clear proof that they improve

outcomes, though. And even then, they're unlikely to do more than promise to reimburse the sponsors' drug(s) more readily than competitors (though such favorable treatment matters, a lot). AstraZeneca's Laghrissi-Thode says the company doesn't expect to be paid for its beyond-the-pill services; it also knows it can't expect one plus one equals two in pricing its combination treatments. Similarly, Sanofi's Chancel admits that the best it can expect is that Toujeo, a "better insulin," combined with a program to enhance the value of insulin therapy by persuading patients to stay on it, "will generate data to support a relative price premium" as glargine's price falls. "So we could stay at the branded Lantus level, rather than being pulled down by Lilly," he suggests.

Still, even if compliance-focused solutions serve only to avoid further price depression as generics appear and competition heats up, they will have a business case, of sorts. In certain chronic diseases they may effectively become part of the cost of operating. In diabetes, much will depend on how fast, and how fiercely, the pricing battle evolves.

Lilly won't want to sell its biosimilar glargine too cheaply – even though, with Merck on its heels, it will have to be aggressive (and it's well known for competitive pricing in this domain). But given the extent to which Lantus' price has inflated over the last several years, any data purporting to convince payors to choose branded Toujeo, with added patient support, over a cheaper version would have to be extremely convincing. And if the support-solution does work to improve insulin adherence and titration accuracy, why not import it across with the cheapest insulin? Solutions may prove far easier to copy than drugs. So far, the issue hasn't arisen, because, as Witz acknowledges, "no one has managed to make a huge difference with these solutions." Sanofi's just one of those hoping that will soon change.

What's In Your Bundle?

Sanofi relies more than other diabetes players on non-drug services and devices, given that its portfolio is so narrow. It's betting that bundles of insulin with Medtronic's pumps and glucose monitors and the full surround service will nicely meet providers' growing need for integrated care solutions (and preference for single-source contracts) as they strive to improve performance, as assessed via Healthcare Effectiveness Data and Information Set (HEDIS) measures. By tying up with Medtronic, Sanofi is effectively piggybacking on broader, faster moves within devices toward services and health care delivery. The current sales models (direct to hospitals) and narrowing margins in medtech make it better placed than pharma to make that transition.

But there will be other bundles on offer in diabetes that may make Sanofi's strategy tough to pull off. Besides AstraZeneca's palette of combinations, Lilly will be in a position to offer an end-to-end range of diabetes therapies, from first-line oral drugs to long-acting insulin and GLP-1 analogs. Its once-weekly, single-dose *Trulicity* (dulaglutide) received FDA approval in September 2014 and has shown non-inferiority to once-daily Victoza. Lilly didn't want to comment for this

article. But Kliff reckons they'll hit payors with single-source contracting, offering all the pieces for a competitive price that may potentially lock out not just one competitor, but all of them, from AZ's mostly oral, early-stage treatments, to the likes of Novo focused downstream on insulins. "Lilly's strategy is brilliant. It makes everyone play defense," says Kliff, forcing them to lower their prices. That's why Kliff reckons "the diabetes drug market is going to become a commodity market."

Even if he's right – and there are clear reasons to believe he might be – it won't happen overnight. Indeed, "one could easily write the script that we're going toward [price] capitation in every therapy area, and that the company that has everything, through bundling, will be in a competitive position. The question is, how long will it take to go from here to there [when capitation is the dominant force in delivering health care]?" asks Baum.

The diabetes market is undergoing a huge transformation as payors shift to outcomes, competition heats up, and new tools become available that may help differentiate the real-world impact of largely similar drugs. "Companies are going to struggle with a delicate balancing act between maintaining market share, protecting margins, and fighting off generics," sums up Kliff. In this scenario, scale and portfolio breadth look like a good bet, if only to keep options open as the market evolves. Services and device-drug packages may prove a winning strategy, but the jury's definitely still out. (Many still question whether pharmaceutical firms are the right players to compete in healthcare delivery and consumer-facing services – and indeed in devices.)

The quest for portfolio breadth will also drive more dealmaking. Several companies, including Merck and *GlaxoSmithKline PLC*, for instance, have a handful of diabetes products but lack scale and scope. (GSK's *Tanzeum* (albiglutide), another GLP-1 agonist, was approved at FDA in April 2014.) "A lot of companies will be watching what Lilly is doing, and asking, 'What do we have to do to stay relevant?'" says Kliff. Whereas some may seek to broaden their offerings, others may decide there's less risky money to be made by exiting the space entirely. Carve-out deals or portfolio swaps such as those seen between Novartis and GSK in consumer, vaccines, and oncology earlier this year are two possibilities. *[See Deal]* *[See Deal]* "I think over the next 18 months we'll see some major deals," concludes Kliff.