IN brief

Amylin's three-party good-bye

The buyout of Amylin Pharmaceuticals by Bristol-Myers Squibb (BMS) completed in August called for BMS to pay $31 per share and gather up ownership of Amylin for about $5.3 billion. But the uniquely structured deal also brought in a third party (London-based AstraZeneca) and added a $1.7-billion payout by BMS to cover both Amylin debt and a contractual obligation to Eli Lilly, putting the total deal value at $7 billion.

New York–based BMS immediately packaged Amylin's products together into a new collaboration with AstraZeneca, in which the latter pays the now wholly-owned subsidiary Amylin $3.4 billion, and any forthcoming profits and losses are split equally between AstraZeneca and BMS. The assets in the collaboration are Amylin's GLP-1 agonists, Byetta (exenatide) and Bydureon (exenatide extended release); metreleptin, being reviewed by the FDA for diabetes and/or hypertriglyceridemia in rare forms of inherited or acquired lipodystrophy; and Symlin (pramlintide acetate), approved for type 1 and 2 diabetes in patients with inadequate glycemic control already taking meal-time insulin. The three approved products combined to sell about $830 million worldwide in 2011.

The side payments to Indianapolis-based Eli Lilly in the buyout stem from Amylin's initial development and commercialization partnership for Byetta with Eli Lilly, signed in 2002, with a total potential value of $300 million. But in May 2011, Amylin sued Lilly for engaging in anticompetitive acts and for breaching that original 2002 agreement, as Lilly earlier in the year had formed a collaboration with Boehringer Ingelheim in Ingelheim, Germany. The two companies were to jointly develop and commercialize two oral diabetes agents, Boehringer Ingelheim's linagliptin and BI10773, and Lilly's two basal insulin analogs, LY2605541 and LY2963016, with an option to co-develop and co-commercialize Lilly's anti-TGF-β monoclonal antibody. Lilly planned to use the same sales force to sell both exenatide and the direct competitor Boehringer Ingelheim's linagliptin, and this is the detail that caused Amylin to file suit. The issue was resolved when Lilly and Amylin ended the alliance and Amylin regained rights to exenatide. Having full rights made Amylin an attractive acquisition target, except that the breakup called for Amylin to, among other things, pay 15% of global sales of exenatide until the sum reached $1.2 billion, plus interest. Any potential suitor needed to take on that long-term financial commitment, and thus, BMS's multiparty buyout deal, with money flowing in three directions. *Brady Huggett*

Industry cautiously welcomes Supreme Court decision on healthcare overhaul

This summer's ruling by the US Supreme Court to uphold President Barack Obama's healthcare reform law has been welcomed by the drug industry. Industry executives say The Patient Protection and Affordable Care Act (PPACA), which requires most Americans to obtain health insurance and includes a handful of provisions that affect drug development, isn't perfect and may not ultimately benefit biotechs' bottom line, but the ruling at least ends a highly fractionalized and protracted battle. "The biggest enemy of the economy and our industry is uncertainty," says Ron Cohen, founder of Acorda Therapeutics in Ardsley, New York. "It's good that we have closure." At the same time, companies are scrambling to ensure that they will be compliant with the law's provisions on reporting physician payments.

Associated Press, Getty Images

Although the general population remains generally split on the healthcare reform, most in biotech industry view it as a positive.

The PPACA legislation was enacted in 2010, but was promptly challenged by 26 states and a trade group for small businesses. In a 5–4 decision on June 28 this year, the Supreme Court deemed the law constitutional, upholding it almost in its entirety. The court based its decision on the US Congress's power to impose taxes. The law requires individuals to obtain health insurance by 2014 or pay a penalty, and that financial penalty "may reasonably be characterized as a tax," Chief Justice John Roberts wrote in the majority opinion. "Because the Constitution permits such a tax, it is not our role to forbid it, or to pass upon its wisdom or fairness," he wrote.

A few key provisions stand out for innovative biotech companies. Most notably, drug makers' markets should expand as more Americans become insured and gain access to medicines. Small companies developing therapeutics also receive grants and tax credits for their projects, which may prove crucial for cash-starved startups (**Box 1**). What's more, innovative drugs will receive 12 years of exclusivity against competition from biosimilars. The language demarcating extra exclusivity for biologics should provide innovative companies, and the investors who place their money in them, with more certainty, say industry executives. At the same time, PPACA now at least provides a legal framework for the US Food and Drug Administration (FDA) to come up with a pathway for biosimilars manufacturers.

How much the drug market will expand in 2014 when PPACA comes into force is unclear. More than 53 million Americans are uninsured, and the healthcare reform law aims to cover more than half of them. To that end, the law expands Medicaid to include people at or below 133% of the federal poverty level. This bodes well for companies like GlycoMimetics in Gaithersburg, Maryland, which is developing a small-molecule drug to treat vasoocclusive crisis of sickle cell disease. Most people with the disease access treatment through Medicaid and Medicare, says Rachel King, CEO of GlycoMimetics. An expansion of Medicaid would be a way to give more people access to the company's drug candidate, if it is approved.

But although the Medicaid expansion was initially mandatory for states, the Supreme Court in its decision deemed the provision overly coercive, and effectively made the program voluntary for states. Kings says she is concerned that if states opt out, that will limit patients' access. Indeed, several state governors have already said publicly they would not participate in the expansion, even though the federal government would pay for 100% of the additional costs through 2020. The US Congressional Budget Office in July estimated that in 2022, 3 million fewer people would be insured due to state opt-outs.

Also offsetting the benefits of a bigger roster of insured Americans are the $80 billion in rebates and fees drug makers must pay on their commercialized products to help fund the plan. "In that sense, it costs us money. But on

June 2012	October 2012	January 2013	January 2014	January 2015	January 2016
Patient-Centered Outcomes Research Institute issues first grants	The Independent Payment Advisory Board formed aimed at extending the life of Medicare Trust Fund begins operation. PhRMA has stated elimination of board as a top priority	New funding provided to state Medicaid programs that choose to cover preventive services for patients	PPACA in force. US citizens able to buy coverage directly in affordable insurance exchanges offering choice of health plans	One year into implementation biopharma industry gets first indications of how much new business healthcare reform will provide	Federal support to states ends, which may lead certain cash-strapped states to opt out of Medicare

the other hand, bringing additional people into the system is helpful," says Cohen at Acorda, which has two commercialized products. "It may end up being a wash, and that's fine."

Biotechs are continuing to dig through the more obscure sections of the law and finding measures that affect their businesses. Sections 3001 and 3008, for example, includes incentives for hospitals to reduce infections. That's good for S. San Francisco–based KaloBios Pharmaceuticals, which is developing a therapeutic monoclonal antibody to prevent pneumonia, an infection that often occurs in people who are on ventilators in hospitals. "The government is pushing to reduce preventable infections," says David Pritchard, CEO of KaloBios. "And we've got a drug that prevents infection."

Biotech executives working in orphan, or rare, diseases say the law's insurance market reforms are key for them. The law bans insurance companies from putting annual or lifetime limits on individual policies—a boon to people with continually high healthcare costs and, by extension, the companies that make treatments for them. "Patients with rare diseases often hit these caps early in life," says John Maraganore, CEO of Alnylam Pharmaceuticals in Cambridge, Massachusetts, which is developing treatment for rare diseases, such as transthyretin (TTR)-mediated amyloidosis, hemophilia and beta thalassemia. Maraganore says that some biotech companies could expect a market increase of 20% due to the elimination of the caps, but it will vary depending on the type of drug and the age of the patient population.

The law eliminates other caps as well. Insurance companies can't exclude people for having a preexisting condition, nor can they discontinue coverage after someone receives a bad diagnosis. And children can now stay on their parents' policies until they are 26 years old. This is a key reform for companies like Sarepta Therapeutics in Cambridge, Massachusetts, which is developing a therapy for people with Duchenne muscular dystrophy, who suffer the worst effects of the disease in their teens and early twenties, and rarely live to see age 30.

It is not all good news, however. Likely headaches for industry in the law relate to what are known as the 'sunshine provisions'. The Act requires companies to report all payments to doctors and hospitals that are over $10. "It's a huge administrative burden," says Cohen, which hired new people as a result. "Every single time you buy [a doctor] a lunch you have a reporting obligation," and separate reports have to be filed with each state, he says. The measures are meant to help spot improper industry-doctor relationships, but the paperwork could prove challenging for small companies with few resources, Cohen says.

The law's 2.3% tax on revenue for device manufacturers is proving difficult for the smaller companies in that sector, particularly those that have revenues but aren't yet profitable. Congress included the tax in the law to help pay for the expansion of health coverage. But it is unclear yet whether the presumed market expansion will offset that tax, says Samuel Lynch, founder of BioMimetic Therapeutics in Franklin, Tennessee, which makes recombinant human platelet-derived growth factor products that are regulated as devices. Lynch says the tax will likely force him to pass along some of the additional costs to hospitals in the form of higher prices for his products. Lynch's overall impression of the Act: "I'm not a fan."

In one of the more indirect effects of the law, biotech companies should expect the momentum to pick up on comparative effectiveness, the practice of governments and insurance providers judging drugs based on relative health or cost benefits. "The flip side of some of these changes and the removal of the caps is there will be a more active debate around health outcomes and comparative effectiveness," says Maraganore. Companies developing early-stage drugs should not only collect clinical data but also data around the economic benefits of their candidates, he says. The Act established a government vehicle for conducting comparative effectiveness research called the Patient-Centered Outcomes Research Institute, which issued its first grants in June.

Many provisions in the Act will surely be tweaked over time (**Table 1**), and the possibility that parts of the law could be repealed by legislators after the November elections still looms. In the meantime, some small biotechs will wait to see how the larger companies comply with the law. "There's an election coming up and things may change again," says Lynch at Biomimetic. "As a small company you want to wait to the extent that you can to see how these things are being implemented by larger companies so that [you] don't get too far out in front."

Emily Waltz, *Nashville, Tennessee*

Box 1 Where are they now?

As a measure of Obama's PPACA, legislators in 2010 allocated $1 billion for grants and tax credits to small companies developing therapeutic products. But the sum was spread out across nearly 3,000 companies and 4,600 projects, leaving most with awards of less than $1 million. For the larger of these awardees, the grant "might have been a percentage on one month's burn rate," says Glen Giovannetti, global life sciences leader at Ernst & Young.

But for Remedy Pharmaceuticals in New York, the grant money was a godsend. The $733,437 the company received through the program "moved the whole company forward," says co-founder Sven Jacobson. "It came at a time when very little money was flowing around and people were scared to invest." After investors partly matched the award, Jacobson was able to design a small pilot study of his product. According to Jacobson, the results of this pilot helped him raise another $3.7 million from angel investors and to plan a larger study.

The Therapeutic Discovery awards were a one-shot deal, but the Biotechnology Industry Organization is pushing for Congress to extend and expand the program because it turned out to be so popular. If there is a next time, the organization has proposed that the government should grant larger awards to fewer companies. *EW*