

## Helping Patients Benefit From Biotech Drugs

9/30/2013

Why Robust Biopharmaceutical Innovation Is Increasingly Dependent On a Functional Regulatory Path For Quality Biosimilars

By Scott Gottlieb, MD and Gillian Woollett, MA, DPhil

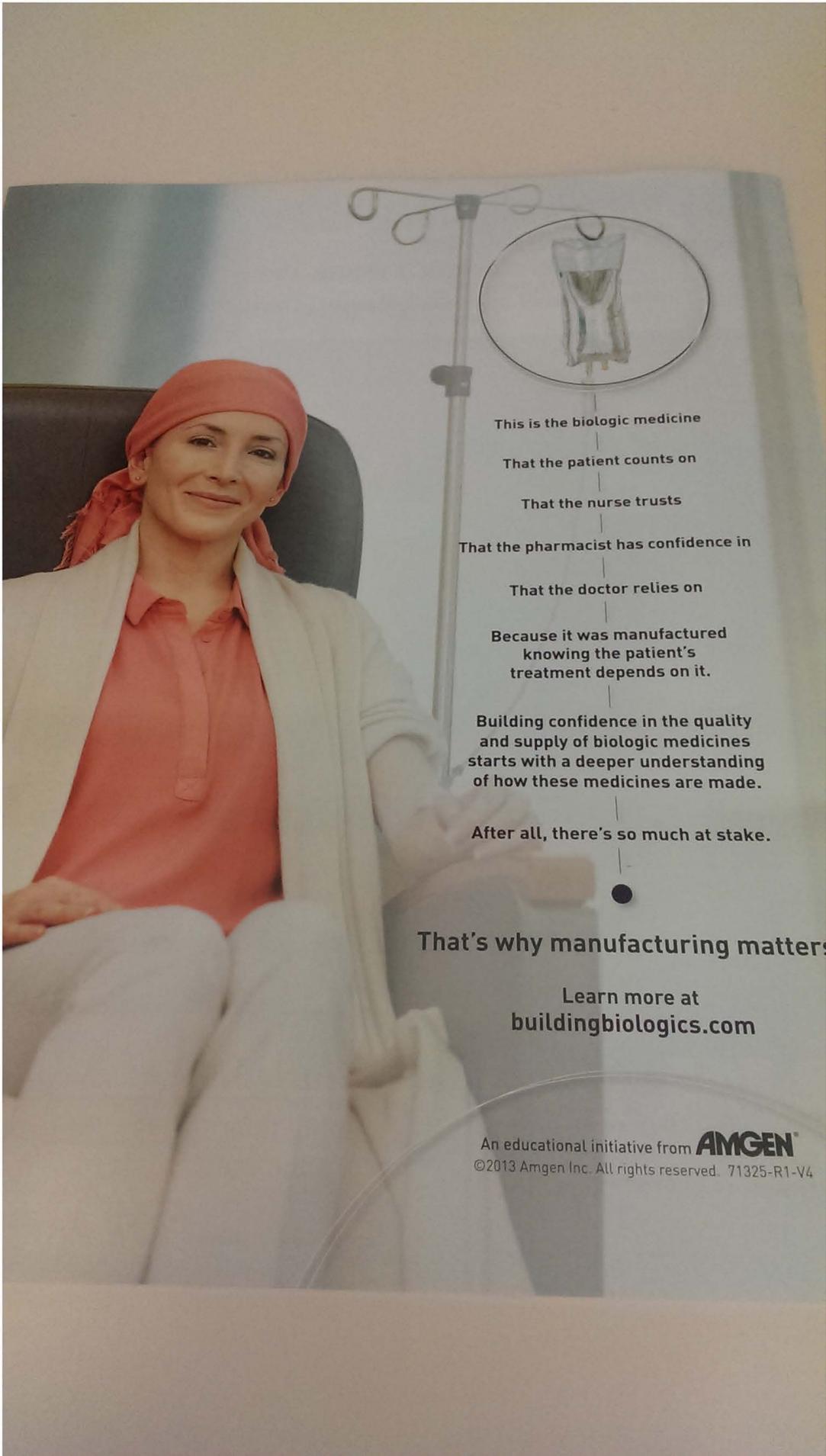
Leading up to passage of the landmark 2010 legislation creating a regulatory path for the approval of biosimilars (the Biologics Price Competition and Innovation Act), both proponents of such a policy and its critics seemed to coalesce around one point in support of the law. The development of a biosimilars framework should serve as sustainable compromise between access and innovation at a time when prescription drug costs were an increasing political focus. The biosimilars policy was viewed as a preferable alternative to other legislative ideas that sought to put explicit government controls on the pricing and prescribing of higher cost drugs.

When the concept of a pathway for so-called “generic” biologics first began to take shape back in 2003 it arose out of concerns about the high price of many biological drugs and the burdens that cost sharing could impose on patients. The creation of a viable pathway for follow on biologics (after legitimate IP had lapsed on the branded alternatives) was held out as the appropriate compromise to address concerns about access, and a superior alternative to calls for more blunt measures like drug price controls, which would put investment and innovation at risk.

If a viable path existed for biosimilars, it was argued, consumers would be assured access and affordability through competitive pricing after a reasonable period of IP protection had lapsed. Both sides compromised around 12 years of exclusivity (to run in parallel to patents). It was a period of time that was supported by economic studies showing that this interval would strike the right balance between providing proper incentives for innovation and investment while enabling timely access.

Meanwhile, branded drug makers would have a continued incentive to innovate on their products to develop better, next generation medicines aimed at new and existing targets that could supplant older, “generic” versions.

That implicit tradeoff, one that accepts market-based pricing on innovative drugs in exchange for very competitive pricing once IP has lapsed, has been the cornerstone of innovation in the small molecule space for almost 30 years. Among high tech industries, it represents the most successful modern policy compromise struck between the sometimes-competing desires to



This is the biologic medicine

That the patient counts on

That the nurse trusts

That the pharmacist has confidence in

That the doctor relies on

Because it was manufactured  
knowing the patient's  
treatment depends on it.

Building confidence in the quality  
and supply of biologic medicines  
starts with a deeper understanding  
of how these medicines are made.

After all, there's so much at stake.

That's why manufacturing matters.

Learn more at  
[buildingbiologics.com](http://buildingbiologics.com)

An educational initiative from **AMGEN**<sup>®</sup>  
©2013 Amgen Inc. All rights reserved. 71325-R1-V4

stimulate robust innovation in an area of high-cost-of-innovation science, while maximizing value to consumers.

When it comes to biological drugs, the importance of these policy compromises is more tangible today than at any time. The increasing proportion of more effective biological drugs targeted to vexing, unmet medical needs is clear. More than 50 percent of the U.S. prescription drug budget expected to be biologics by 2018 (it was 0.5% in 1989). Yet the biggest challenges to this construct may not be scientific, nor the ability of sponsors to make safe and effective biosimilars and FDA to review and approve those applications. It is the result of policy failings if we abdicate, if not outright abandon, the compromise that underpinned this original pact.

As we look to the future, showing that this policy compromise works is going to be the most powerful argument we have against continued calls for policy measures that seek to impose direct government limits on access and pricing of new drugs in the name of cost control — and put at risk continued investment and innovation.

The stakes couldn't be higher. Advances in science are demonstrating that a viable pathway for biosimilars can be a spark to not only more value, but also greater innovation.

The science for developing all biologics, including biosimilars, has advanced notably in recent years. Sophisticated drug developers trying to make copy drugs have a better ability to evaluate the characteristics of marketed biologics and understand how variations in these qualities can manifest as clinically important differences.

This scientific understanding, in turn, has translated into much more reliable methods for developing similar copies, as well as for manufacturing them more efficiently, making it easier to sell the products as lower cost alternatives.

Meanwhile, the clinical advances being made over the existing crop of biological drugs, to develop wholly new and better medicines, are in some cases spectacular.

These new medicines hold the potential for significant gains in our ability to combat diseases from cancer to many rheumatologic ailments. Completely new drugs that offer significant advances over some of the most widely used biological drugs — from new biological drugs that target the HER2/NEU receptor in breast cancer, the CD20 receptor in blood tumors, or Tumor Necrosis Factor in rheumatologic disease — offer the potential for major clinical advances and better patient outcomes.

It is a reasonable bet that, on some level, the competitive threat that biosimilars would emerge to an earlier generation of drugs that address these targets helped galvanize the investment in the new advances. This competition for new science and IP was a basic premise of the biosimilar law. It is already a key part of the economic model for small molecule drugs. Indeed it is a model for how competitive market forces can foster both innovation and value throughout the U.S. economy.

But these opportunities — for safe, effective, and lower cost biosimilars to the existing generation of drugs, coupled with a new generation of advances to these medicines — are by no means a sure thing. The biggest challenges to these opportunities rest not with science but policy as we flout from the compact between access and innovation that the pathway was predicated upon.

For one thing, there was the basic thesis that a robust pathway for biosimilars and the price competition that they offer is the best answer to those who would try otherwise to empower government agencies to control the price and utilization of new drugs. The compact offered by the biosimilars compromise seems to be getting shorter shrift in today's policy debates over price and access. Backing away from this essential construct could undermine the careful balance between access and innovation that has formed the basis for drug competition for decades.

It could also undermine the biosimilars pathway before that framework has even been fully implemented by excising a key premise that helped underpin that careful compromise. The entire construct would become something that innovators no longer see offering any policy benefit. Large constituencies would more vigorously resist the pathway, rather than share a stake in its successful implementation.

The policy compromise that helped support the creation of this legislative pathway is also not helped by the seemingly continual debate over the "optimal" number of years an innovator should enjoy protection of their data and IP. This is another compromise that would have seemed to be settled by the original law. At the least, it would not appear to be a point that would need constant revisiting in the absence of any scientific or economic development having emerged since the law's recent passage. It is also not what is currently limiting the use of the new pathway given the number of biologics for which the 12 exclusivity has already long expired.

Then there is the practical work of implementation, and the issues that emerge as the rubber meets the road at the Food and Drug Administration.

The cost of developing a quality biosimilar product can reach \$250 million (a small molecule generic drug is typically \$1-5 million). While this is typically lower than the investment needed to develop an innovator product (often estimated at \$1.4 billion), it is still a significant investment. The capital needed to develop a biosimilar is made higher, and the public health and economic benefits potentially reduced, by the measured pace by which a regulatory path for these drugs has emerged. The difficulty in enrolling patients in trials for biosimilars, when those patients don't perceive any practical benefit, is also slowing down the process.

A lot of FDA's deliberation surely owes to the complexity of the underlying science. Despite some early hyperbole leading up to passage of the biosimilars legislation about how easy it would be to copy biologics and prove their similarity or sameness in abridged trials, the fact remains that this is not a uniformly trivial endeavor.

But the science for doing these things is continuing to advance at a brisk pace. So is the sophistication of regulators. Some of the slowness is the result of policy choices. European drug authorities have approved biosimilar versions of complex proteins, including monoclonal antibody drugs, through an abridged regulatory process that creates genuine savings. This has translated into lower drug costs as well as increased market competition among multiple entrants.

Here in the U.S., the FDA still has to make key regulatory decisions about how the agency will approach some pivotal questions when it comes to these drugs. Among them: how much clinical data will be required to confirm similarity; whether biosimilars will need to prove non-inferiority or equivalence; what the requirements will be for proving two biological drugs can be used interchangeably; and whether a biosimilar drug that demonstrates its utility for one or a few of

the accepted indications can gain a label indication for some or all of the other indications where the comparator biologic is already approved. Other key questions remain about how FDA treats these issues as a matter of both science and regulation as the reference product and the biosimilar change over time (often through the normal course of routine manufacturing changes).

How FDA addresses these questions will have a big influence on how viable the market for biosimilars becomes in the U.S. Whether policy makers give this carefully struck compact between access and innovation a chance to take shape will ultimately govern the success of this market. Everyone has a stake in the outcome.

Paradoxically, this may be especially true for the branded drug companies. They have demonstrated the capacity to innovate even today's crop of biologics with brand new drugs that in some cases are watershed improvements over the existing medicines. This innovation could quite literally change the course of some diseases. There are presently 1,000 biotech-based medicines in clinical development – the highest number ever. The collective as well as individual impact for patients from biologic breakthroughs, from orphan diseases to common ones, is significant.

But all of this promise will be put at risk if policy makers start to implement blunt measures to restrict the pricing and access to these drugs by policies that reduce the market-based incentives that have attracted capital into these endeavors, and made the U.S. the world's leader in biopharmaceutical innovation. The existence of a path for biosimilars was hailed as the best way to balance access with innovation – creating competition for not only cheaper drugs, but also better medicines. Patients, providers, and product developers alike, all have a lot at stake in the outcome.

*Dr. Gottlieb is a Resident Fellow at the American Enterprise Institute and a Senior Adviser to Avalere Health. Dr. Woollett is a Senior Vice President at Avalere Health.*

---

**This article is available online at:**

**<http://www.forbes.com/sites/scottgottlieb/2013/09/30/helping-patients-benefit-from-biotech-drugs/>**

## Over-Killing Biosimilars

Friday, February 1, 2013

By Michael McCaughan

---

*The biosimilar pathway in the US is about as innovator-friendly as it could be, so much so that innovators are now focusing on state pharmacy laws that won't matter for years to come. But there is a danger in too-complete a victory: if biosimilars don't constrain costs, price-controls may be the only option.*

---

Sometimes a bad headline can be a good warning.

*The New York Times'* January 28 article on state legislation to regulate pharmacy substitution of biosimilars certainly qualifies as bad (if not downright unfair) for innovator companies: "[Biotech Firms, Billions at Risk, Lobby States to Limit Generics.](#)"

If you just read the headline, you would surely conclude that profit hungry biopharma companies are erecting new barriers to block access to generic drugs, preventing consumers from saving billions. A picture of an *Avastin* vial accompanies the story, and you might think that someone is ready to sell a generic of that product today at a much lower cost, but for the lobbying of Genentech.

The facts, of course, are quite different: no one is ready to market "generic" *Avastin*, and indeed there is no pathway to allow for "generic" biologics in the US. Instead (as the story makes clear), there is a slowly emerging pathway to market biosimilars, the first of which will **not** be interchangeable with brands. And no one believes state pharmacy laws can or should allow substitution of those products.

Instead, the state legislation is focusing on the day, years from now, when there are interchangeable biologics approved by FDA. And, indeed, innovator companies are encouraging states to craft laws that may create barriers to substitution by pharmacies when that day comes.

But that is all, to say the least, hypothetical. There are as yet no biosimilar applications pending at FDA, and it will be years after biosimilars are approved before FDA is likely to consider interchangeability. No one is going to be saving "billions" from biosimilars any time soon, no matter what states do.

Still, the flap over the pharmacy laws carries some important messages. First and foremost, it reinforces how complete the innovator industry's victory has been in the biosimilar debate thus far. Innovators won on the highest profile issue: getting 12 years of data exclusivity for new

biologics. But they also won on the far more important issue of how "biosimilars" are envisioned in the regulatory process.

The contrast with generic drugs is remarkable. Literally on the day after the Waxman/Hatch Act took effect in 1984, FDA received a flood of applications for fully-substitutable generic drugs. The biosimilar law took effect in March 2010; almost three years later there are still no applications, and when there are, they will be for non-substitutable quasi-brands. (For more on exactly how slowly the new market is taking shape, start [here](#).)

Having won those fights, innovators are investing in state pharmacy laws, thinking many, many years ahead and shaping the landscape while the opposition is still fighting rear-guard actions on issues like exclusivity and naming conventions. It is certainly understandable that innovators would want to capitalize on their victories so far and gain as much ground as possible.

But the negative headlines are also important. There is also wisdom in knowing when to call off the fight.

As the *Times* headline so amply illustrates, the point of enacting a biosimilar pathway is to deliver significant savings on the cost of biologic therapies; that is what society wants and expects from the new law. The reality may be that those savings will take a long time to materialize, but they better not take too long. After all, if society gets tired of waiting, Congress can always find a way to make biologics cheaper right away. Like with price controls.

That in turn suggests that the state legislation may be a bridge too far for innovators.

The simple reality is that states are unlikely to forgo the savings from biologics that achieve "interchangeability" at FDA, once they actually exist. It is easy for legislators to act in response to advocacy today, but the laws won't last long once the budget impact is real.

In the meantime, by pressing its case at the state level, innovators may draw more attention to exactly how the biosimilar process is and isn't working in the here and now. If that happens, they may find themselves wishing they had simply accepted victory.