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Beyond Pills: Designing a Winning Drug Delivery Strategy for the New Era of Biologics

With the rise of biologics, the days of simply popping a pill for a cure are waning. Increasing numbers of better, more-targeted therapies are working their way through companies' research-and-development pipelines that will need to be injected, infused or delivered in other non-traditional ways.

Drug delivery may not sound sexy, but at least three factors – increased competition from biosimilars, formulation challenges of therapies in the pipeline, and an expansion of both disease areas and patients served by biologics – have come together to make it a critical issue for drug companies. Innovative drug-delivery methods can improve the patient experience and increase these new therapies' efficacy and safety, while helping drug makers gain higher sales and increased market share.

Coming up with a strategy for drug delivery isn't easy and many companies are still taking a fragmented approach, resulting in delayed (or suboptimal) product launches. The problem is that it's extremely difficult, if not impossible, to fix drug delivery challenges after the fact. The development of the therapy, and the development of a novel and workable way to deliver it need to happen simultaneously, early in the R&D process. In fact, formulation challenges must be ironed out in Phase 1, with devices figured out by late-Phase 2. Otherwise, drug makers may find themselves with an FDA-approved therapy that patients either refuse to accept or won't stay on.

Beyond Pills

When patients think of drugs that they take at home, they generally think of pills, and the technology for small-molecule drugs has advanced enough that most can be turned into oral therapies. But proteins – whether stable, small proteins like insulin or more tricky ones like monoclonal antibodies (mAbs) – are too large. They simply cannot be administered orally, and will require alternative delivery methods.

The use of mAbs (as well as larger engineered proteins) is expanding. While mAbs historically were used mainly to treat autoimmune diseases or cancer (think Humira for rheumatoid arthritis or Herceptin for breast cancer), today there are many treatments for new therapeutic areas in development. Already, there have been introductions of mAbs to treat asthma (Xolair), while mAbs to treat hypercholesterolemia (PCSK9s), and migraines (CGRPs) are in late-stage trials. Therapies for many other disease areas, from diabetes to Alzheimer's, are under development.

The Rise and Spread of Monoclonal Antibodies

Therapies using mAbs originally focused on oncology and immunology, but mAbs in development are expanding to

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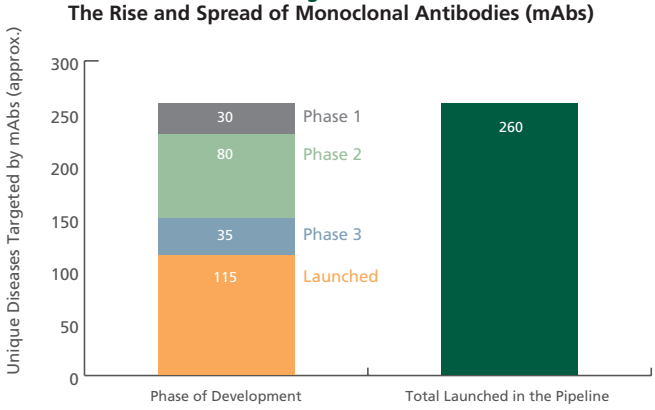
cardiovascular, gastrointestinal, respiratory and infectious diseases. That expansion – which could increase the number of unique diseases targeted from 115 today to 260 – will significantly diversify the patient population taking these self-administered biologics (see Figure 1).

Figure 1
The Rise and Spread of Monoclonal Antibodies (mAbs)



Source: L.E.K. Consulting research

At the same time, many of the drugs in the pipeline have technical difficulties that will require new thinking on drug delivery. These new therapies are fragile, they stick to containers, they're too viscous for standard, spring-based autoinjectors, they have low concentrations and high volumes, and they degrade rapidly. Call it the end of the days of the well-behaved antibody.

We believe that 15-20% of all proteins in development today have some kind of formulation challenge. In the earlier phases of development, we believe that number is likely to be even higher. Drug companies that face these formulation challenges must think about drug delivery early in the R&D process – even as early as molecular engineering – or they could wind up with a drug that receives FDA approval, yet isn't commercially optimal.

Equally important, as the range of targeted diseases expands, drug makers are trying to get these substances to places in the body — such as the lungs — that are extremely difficult to reach, as well as developing drugs that will need to cross the blood-brain barrier. This is currently a significant deterrent to the use of biologics in treating psychiatric illnesses and neurological diseases. Recently, for example, ArmaGen signed a deal with Shire to get enzyme replacement therapy across the blood-brain barrier to treat the progressive neurological complications of Hunter syndrome. There also has been significant activity in nanoparticle development. For example, Pfizer, Roche, Merck and other pharmaceutical companies have signed deals with Bind Therapeutics to develop medicines using the biotech startup's nanotechnology platform for targeted delivery.

Pharmaceutical companies that introduce novel technologies for drug delivery can gain in multiple ways. One, their drugs have a better chance of hitting their intended biological targets. Two, the delivery methods can make it easier for the patient to self-administer the medicine. Three, because the drugs are easier to take, patient acceptance should improve. And lastly, persistence and adherence to the drug regimen also should increase.

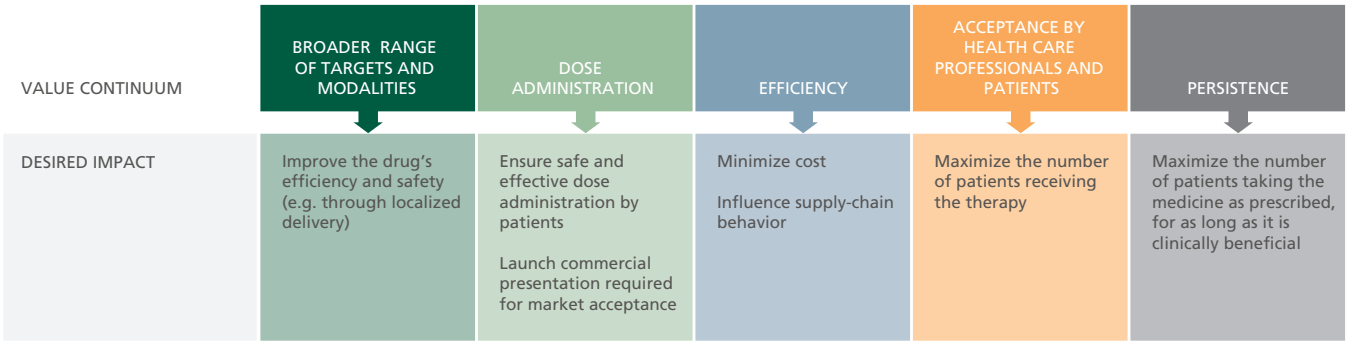
The Benefits of Novel Therapies

Biopharmaceutical companies that introduce a well-thought-out drug-delivery strategy should gain on multiple fronts with more patients, better adherence to prescribed treatment regimens and lower costs (see Figure 2).

The increasing move toward self-administered therapies raises questions about patient acceptance, adherence and compliance. Will patients who are used to popping a pill adhere to a regimen of injecting themselves with a monoclonal antibody? Approximately one quarter of rheumatoid arthritis (RA) patients, for example, refuse or delay biologic therapy in part because of the pain or burden of self-injection. Rejection rates likely would be higher among patients who are suffering from asymptomatic diseases, or patients who are "needle naive" before being offered biologics. Patients with chronic asymptomatic diseases, such as hypercholesterolemia, are likely to be less willing to self-inject than RA patients. There will also be special issues for the elderly, the frail and pediatric patients.

With legislation looming to promote biosimilars and increased pressure from both payers and patients to offer an increased value proposition, we believe innovation in drug delivery will become an increasingly important differentiator. That occurred long ago with insulin, where there's little therapeutic reason to choose one version of insulin over another, and devices have become a significant basis for competition. We believe something

Figure 2
Benefits of Novel Therapies



Source: L.E.K. Consulting analysis

similar — if perhaps less extreme — is likely to evolve in areas where biosimilars are proliferating. Rheumatoid arthritis, an $8 billion market in 2014, offers a case in point where companies such as market leader AbbVie (maker of Humira), as well as Amgen (Enbrel) and newcomers like Janssen Biotech (Simponi) are rolling out new technologies in an effort to appeal to RA patients and their doctors. Similarly, psoriasis and human growth hormone are seeing more device-based competition. Merck Serono, for example, created the easypod — a smart injector that delivers a premeasured dose of Saizen — to gain ground in the treatment of growth hormone deficiency in children.

As self-administered therapies expand to neurologic, cardiovascular and metabolic diseases, addressing compliance will become increasingly important. Innovative designs could be as simple as offering an injectable drug in a premixed or preloaded syringe, or creating a formulation that requires less frequent injections.

A Drug Delivery Strategy

Our experience suggests that pharma and biotech executives need to think as clearly about drug delivery as they do about research and development. An L.E.K. survey of some 20 top global biopharmas put patient acceptance and persistence as the number one challenge that could be addressed by engaging customers with drug delivery technologies. But while these top executives realized they needed a drug-delivery strategy, few knew what to do to create one.

Here are some factors to consider:

1. **Is a drug delivery strategy important to your organization?** If you can answer yes to any of these questions, it is: Do you have self-administered biologics in highly-competitive markets, or have plans to enter those markets? Do you have products used by patients with special requirements such as the elderly, frail, children, or even people who aren't used to injectable therapies? And, do you have biologics in your pipeline that have formulation challenges, such as lyophilization, concentration, shearing or coagulation?

2. **Will a one-off approach suffice or do you need a platform?** The issue here is upfront cost vs. overall payoff. For a company that has only one or two drugs that would benefit from a novel technology, the upfront costs may outweigh the benefits, while for a company with a whole lineup of products, the benefits of scale make it not only viable but worthwhile.

3. **Which technologies matter for the drugs in your pipeline?** Is your pipeline filled with self-administered injectables that would benefit from advanced technologies? Or are most of the drugs under development infused? Can you focus in on one or two technologies that will provide the most benefit to the therapies currently in development at the least upfront cost? How do you ensure the strategy optimizes the needs across the portfolio? What is the best process and governance to enable the strategy?

While some companies that have only one or two products with delivery challenges may find a one-off approach will suffice, many will need a broader strategy for drug delivery. One high-profile example of this is Roche's approach to its oncology therapies. The drug maker has reformulated its cancer treatments to work as microinfusers that patients can take home with them. This drug delivery puts Roche ahead of the competition from biosimilars, while addressing patients' desires to be treated at home rather than having to go to oncology clinics for therapy.

Getting drug delivery right is crucial, but it won't be easy. Biotech executives will need to think about their companies' drug delivery challenges early in the FDA approval process and come up with a strategy that meets the needs of the therapeutics in the pipeline across their portfolio. Those companies that think only about the therapies themselves, without sorting through the challenges of how patients will take them and whether they will adhere to their treatment regimens, risk falling behind. Those that can move to the forefront of new drug-delivery technologies with advanced formulations (such as nanoparticles and microspheres) or advanced devices (like microneedles and microinfusers) will be the ones that will win.