The year 2012 is coming to an end, and it’s been a big year for generic drugs.

It’s the year that the most lucrative drug of all time, Pfizer’s cholesterol-lowering medication Lipitor (atorvastatin calcium), went from being worth more than $7 billion in annual sales to becoming commoditized. The drug had lost patent protection in November 2011, when Ranbaxy Labs became the sole company legally authorized to market the generic version of the drug. Ranbaxy itself lost market exclusivity in May 2012. It’s also the biggest year of the so-called patent cliff, the period during which numerous top-selling branded drugs are expected to lose patent protection and face generic competition.

It’s the year that Watson bought Swiss generic drug maker Actavis for $5.6 billion, becoming the world’s third-largest generic drug maker after Israel-based Teva Pharmaceutical Industries and U.S.-based Mylan. As a condition for the merger, Watson and Actavis had to divest rights to nearly two dozen drugs, selling most of them to Par Pharmaceutical Cos. and Sandoz, the generics arm of Swiss drug maker Novartis.

And it’s the year the Food and Drug Administration released draft guidance for biosimilars regulations. The Patient Protection and Affordable Care Act mandated the creation of a regulatory approval pathway for biosimilars — a long-awaited prize for generic drug makers and a few brand drug makers as well — but it will likely be some time before the regulations are actually put into place, and even longer before the market becomes fully mature.

All of these events speak to some of the most important trends in the world of generics, trends that are often interrelated.

“The profitability of the generic industry is driven by first-to-file and exclusivity periods,” IMS Health VP industry relations Doug Long told Drug Store News. “Those periods are the most profitable before [drugs] become multi-source — when you have more players, the price gets lower.” This means that the generic drug company that is the first to win approval from the FDA for a drug has the most to gain because, under FDA regulations, it is entitled to 180 days in which to compete exclusively against the branded version, notwithstanding the possibility of the branded drug’s manufacturer making a contract with another company to market the branded drug at a discount, known as an authorized generic; an example would be Watson Pharmaceuticals’ marketing of authorized generic atorvastatin calcium while Ranbaxy was marketing the generic version and Pfizer marketed the branded version. After those 180 days, the generic exclusivity period ends and any company that passes muster can market a generic version. It’s been pretty smooth sailing, as top-selling drugs ranging from Lipitor to Bristol-Myers Squibb’s and Sanofi’s blood-thinning drug Plavix (clopidogrel bisulfate) and Takeda’s Type 2 diabetes drug Actos (pioglitazone) have lost patent protection, providing generic drug makers with ample opportunities.

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Differentiation

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to rake in huge profits. But in the next few years, that supply of expiring patents will start to dry up, causing greater commoditization in the marketplace.

This, Long said, is likely to lead to a lot of merger and acquisition activity among generic drug makers. The Watson-Actavis merger is only the largest one in recent memory. Others have included the $1.9 billion purchase of Par Pharmaceutical Cos. by investment firm TPG, which also owns IMS. Another notable one was Sandoz’s acquisition of Melville, N.Y.-based Fougera for $1.5 billion, a purchase that Long attributed to Sandoz’ desire for Fougera’s expertise in dermatological drugs like creams and ointments. That same motivation is also behind India-based Sun Pharmaceutical Industries’ efforts to acquire Israel-based Taro Pharmaceutical Industries for $1.5 billion, a purchase that Long attributed to Sandoz’ desire for Fougera’s expertise in dermatological drugs like creams and ointments.

“Generic companies have been moving up the value chain, and moving up the value chain means moving out of or reducing your exposure to the oral solids and oral liquids,” Long said. “So they’re moving up the value chain and trying to get into places that are less crowded and that have higher barriers of entry.” In other words, it is a game of differentiation. Injectables are another kind of drug that can be hard to make, and companies like Hospira and Sagent Pharmaceuticals have worked to gain leadership in that market, as their most recent drug launches show. But mergers and acquisitions are likely to continue for the foreseeable future, Long said.

Another tactic in this game of differentiation is biosimilars. Notwithstanding the lack of a real regulatory structure for biosimilars, it’s hard to tell whether they constitute another tactic or another game altogether. Long noted that while it costs about $1 million to $2 million to bring a generic pharmaceutical drug to market, the cost for a biosimilar is going to be about $100 million to $200 million, due to the added requirements of things like clinical trials, which aren’t needed for generic drugs. This will likely restrict biosimilars to a small handful of companies. That will include established players like Teva Pharmaceutical Industries, Sandoz and Hospira, which make biosimilars for the European market; companies like Watson, which has a deal with Amgen; and Mylan. Some Indian companies are looking to get in on the action as well, and Long mentioned Dr. Reddy’s and Ranbaxy as possible players, as well as South Korea’s Samsung, which has been developing a biosimilar version of Genentech’s and Biogen Idec’s cancer drug Rituxan (rituximab).

And it would be neglectful not to mention the Generic Drug User Fee Amendments to the reauthorization of the Prescription Drug User Fee Act. GDUFA, as the amendments are called, create a system of user fees expected to raise about $299 million per year from the generics industry, which will allow the Food and Drug Administration to clear out a backlog of more than 2,000 generic drug regulatory applications currently awaiting approval.

“Generic companies have been moving up the value chain, and moving up the value chain means moving out of or reducing your exposure to the oral solids and oral liquids.”

Doug Long,
IMS Health VP industry relations

<table>
<thead>
<tr>
<th>Top 10 generics companies</th>
<th>U.S. SALES</th>
<th>% MARKET SHARE</th>
<th>% GROWTH</th>
</tr>
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<tbody>
<tr>
<td>U.S. Industry</td>
<td>$48,059</td>
<td>15.0%</td>
<td>13.9%</td>
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<tr>
<td>Teva</td>
<td>6,437</td>
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<td>Mylan Labs</td>
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<tr>
<td>Watson Pharma</td>
<td>4,750</td>
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<tr>
<td>Sandoz (Novartis)</td>
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<td>Par Pharma</td>
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<td>Ranbaxy Labs Limit</td>
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<td>Actavis U.S.</td>
<td>1,109</td>
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<td>31.8</td>
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</table>

*In millions
Source: IMS Health, National Sales Perspectives, year to date June 2012

Source: IMS Health, National Sales Perspectives, June 2012, National Prescription Audit, June 2012, Branded generics disaggregated.
Branded generics transform the old into the new

In the classic Arabian Nights tale “Aladdin and the Magic Lamp,” the sorcerer who sold Aladdin the lamp containing the genie attempts to get it back by walking through the town where Aladdin and his wife live disguised as a merchant, trading “new lamps for old.”

Rubbing pill bottles isn’t likely to bring forth any genies ready to grant three wishes, but the idea of inputting something old and outputting something shiny and new is sort of the gist behind branded generics.

According to IMS Health VP industry relations Doug Long, “branded generics” has multiple meanings. One refers simply to generic drugs given brand names, such as a number of generic contraceptives on the market that carry brand names because calling them by their full generic names would be too cumbersome. Another kind of branded generic consists of a drug that has lost patent protection for which a drug maker develops a novel method of delivery to create a new drug. Last month, EffRx and Mission Pharmacal launched Binosto, which takes the generic osteoporosis drug alendronate sodium and reformulates it as an effervescent tablet that dissolves in water, a similar drug-delivery method to Alka-Seltzer.

The top-selling and probably best-known branded generic is Perdue Pharma’s OxyContin, an extended-release formulation of the generic opioid painkiller oxycodone. OxyContin itself is scheduled to start losing patent protection in April 2013.

Another use for off-patent molecules, Long said, is to pair them with another molecule to create a branded drug. Vintage Pharmaceuticals, for example, markets Percocet, which combines oxycodone and acetaminophen. Endo Pharmaceuticals is also developing generic versions of branded generics or branded generics.

Generics target specialty pharmacy with biosimilars

Perhaps the iconic scene at the end of Ridley Scott’s 1991 movie “Thelma & Louise” — with Gina Davis’ and Susan Sarandon’s characters hurdling into the Grand Canyon in a green convertible — is a good metaphor for what’s happening in the generic drug industry these days.

All right, maybe that’s a little too dramatic, but the so-called “patent cliff” is here. But unlike Thelma and Louise, it’s not too late for drug makers to adapt to an environment in which the supply of top-selling primary-care drugs with expiring patents begins to dwindle, leaving entire disease-state categories commoditized.

“Eventually, that patent cliff will not be there,” IMS Health VP industry relations Doug Long told Drug Store News. “When you have a brand innovation drought, particularly in primary care or pill forms, eventually that will create a generic small molecule opportunity drought, and that’s likely to happen at the end of the decade.”

The response for both generic and branded drug makers has been to move up the value chain, Long said, which includes moving into specialty drugs for diseases like cancer and autoimmune disorders.

According to IMS Health, the specialty drug market was worth $42.8 billion during the 12-month period ended in June, and according to Medco Health Solutions, now part of Express Scripts, specialty pharmacy costs could account for 40% of drug spending by 2020. So it should come as no surprise that a huge number of drug makers, retailers and others hope to grab a piece of it.

One of the ways generic drug makers hope to do this is with biosimilars. The Patient Protection and Affordable Care Act included a mandate for the Food and Drug Administration to create an abbreviated regulatory approval pathway for biosimilars, similar to the one for generic pharmaceuticals that the Hatch-Waxman Act created 28 years ago.
Branded
CONTINUED FROM PAGE 32

cals, meanwhile, markets Percodan, a cross between oxycodone and aspirin.

In the meantime, branded drug makers will continue finding ways to get the most out of the drugs they’ve developed.

A long-standing practice has been what Long calls “incremental improvements,” like launching an extended-release formulation of an existing drug, but these efforts have been getting less successful, he said. Perhaps a similar approach is to extend-release formulation of an existing drug, but these efforts have been what Long calls “incremental improvements,” like launching an extended-release formulation of a drug, but questions remain that preclude approval.

Biosimilars
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The regulations aren’t in place yet, but some drug makers aren’t content to wait — and some are seeking approval for biosimilars using the pathway for novel biologics already in place. At the end of August, the FDA approved Teva Pharmaceutical Industries’ tbo-filgrastim for treating neutropenia, a condition in which the number of white blood cells is decreased, making patients more susceptible to life-threatening bacterial infections. The company sought approval using a biologics license application, or BLA, the same approval pathway used for novel biotech drugs because while the

NewsBYTES

FDA approves Par leukemia drug
WOODCLIFF LAKE, N.J. — The Food and Drug Administration has approved a generic drug for leukemia made by a subsidiary of Par Pharmaceutical Cos.

Par said Oct. 25 that the FDA had approved Anchen Pharmaceuticals’ tretinoin capsules in the 10-mg strength.

The drug is a generic version of Roche’s Vesanoid, various versions of which have annual sales of about $29 million, according to IMS Health.

Federal court orders FDA to allow Watson diabetes drug launch; Mylan challenges ruling
PARSIPPANY, N.J. — A federal court has ordered the Food and Drug Administration to approve a generic diabetes drug made by Watson Pharmaceuticals, the drug maker said.

Watson said the U.S. District Court for the District of Columbia granted summary judgment in favor of Watson, ruling that the FDA would have to approve its generic version of Takeda’s Actos (pioglitazone hydrochloride) tablets in the 15-mg, 30-mg and 45-mg strengths. Mylan is challenging the decision.

Mylan, the world’s second-largest generic drug maker, filed a motion to stay the court’s order.

“Mylan is disappointed in [the] ruling regarding pioglitazone, and we believe the court erred in its decision by directly contravening the Hatch-Waxman Act,” Mylan CEO Heather Bresch said, referring to the 1984 law that created an abbreviated approval pathway for generic pharmaceutical drugs.

“Mylan does not believe Watson is entitled to participate in Mylan’s 180-day exclusivity period in relation to this product, and we intend to pursue this case vigorously, including seeking expedited relief from the appellate court if necessary.”

Watson filed suit against the FDA in August 2012, alleging that an agency decision to deny Watson’s claim to shared exclusivity in marketing a generic version of Actos would improperly delay its launch of the drug.

Actos had sales of about $2.7 billion during the 12-month period ended in May, according to IMS Health.

FDA approves generic Lupin contraceptive
MUMBAI, India — The Food and Drug Administration has approved a generic contraceptive made by Indian drug maker Lupin, the company said on Oct. 18.

Lupin announced the approval of Kurvelo (levonorgestrel and ethinyl estradiol) tablets in the 0.15 mg/0.03 mg strength.

The drug is a generic version of Teva’s branded Nordette. Nordette had sales of about $59 million during the 12-month period ended in June, according to IMS Health.

FDA approves Sandoz dermatology medication
PRINCETON, N.J. — The Food and Drug Administration has approved a drug made by Sandoz for treating symptoms of various skin diseases.

Sandoz, the generics arm of Swiss drug maker Novartis, announced the approval of desoximetasone ointment in the 0.25% strength. The drug is a generic version of Taro Pharmaceutical Industries’ Topi-cort and, according to Sandoz, is the first Fougera dermatology product Sandoz has launched since its $1.5 billion acquisition of the company in May 2012.

Topi-cort and its generic versions had sales of $36.5 million during the 12-month period that ended in August 2012, according to IMS Health.
NABP report: Rogue pharmacies prolific

By AlAric DeArment

At some point in their lives, most people learn the old lesson about things that look too good to be true, sometimes by hearing it from others, and other times from bad experiences.

It should be hoped that nobody learns that lesson the hard way by buying prescription drugs that carry a high risk of being counterfeit, adulterated or otherwise unsafe to use from one of the thousands of rogue websites that sell them. Rogue Internet pharmacies occupy the online equivalent of that dark alley people usually know better than to enter. Luckily, however, some light is being shown on these rogue websites these days.

Last month, a report by the National Association of Boards of Pharmacy indicated that 97% of the more than 10,000 online drug sellers it surveyed are doing business outside the law. The report, “Internet Drug Outlet Identification Program Progress Report for State and Federal Regulators: October 2012,” noted that 9,543 websites appeared to be affiliated with networks that obtain drugs from “questionable sources,” among other findings.

The report concluded that it was important for members of the international pharmacy community to protect patients worldwide from the potential dangers of illegal online drug sellers, noting that the illegal sites provide a way to sell counterfeit drugs, while also highlighting collaborative efforts with organizations and government agencies around the world that have resulted in the exposure and shutdown of thousands of rogue pharmacy sites.

The federal government has stepped in as well. In September, the Food and Drug Administration launched BeSafeRx, an education campaign to discourage purchasing from rogue sites by providing such information as the tactics rogue sites use to appear legitimate. “Buying medicines from rogue online pharmacies can be risky because they may sell fake, expired, contaminated, not-approved-by-the-FDA or otherwise unsafe products that are dangerous to patients,” FDA commissioner Margaret Hamburg said. “Fraudulent and illegal online pharmacies often offer deeply discounted products. If the low prices seem too good to be true, they probably are.”

But according to a report released earlier this year by Portland, Ore.-based LegitScript, a company that verifies online pharmacies, rogue pharmacy operations appear to be highly organized. In March, LegitScript released a report showing that as many as one-third of rogue pharmacies were hosted under one Internet domain registrar, Internet.bs, a company registered in the Bahamas and based in Panama. Internet.bs is one of about 450 domain name registrars accredited by the Internet Corporation for Assigned Names and Numbers and accounts for only 0.2% of total registered domains online, but between 32.9% and 44% of the rogue online pharmacy domains and 20 registrars account for 81% of the rogue sites.

And a problem intricately related to rogue pharmacies remains as well: counterfeit drugs. In May, the FDA warned that counterfeit versions of Teva’s attention deficit hyperactivity disorder drug Adderall were circulating online. This came two months after Congress passed S. 1886, the Counterfeit Drug Penalty Enhancement Act. In September, the same day the FDA announced the launch of BeSafeRx, the agency, the Generic Pharmaceutical Association, the Pharmaceutical Research and Manufacturers of America and others took part in a conference to find ways to stop the spread of counterfeit drugs, sponsored by the Partnership for Safe Medicines. “In an increasingly global society, heightened cooperation and information sharing between stakeholders around the world is an invaluable tool …,” Partnership for Safe Medicines treasurer Tom Kubic said. “And as more allies join our cause, we are better able to spread our message and educate the public at large about the extreme risks of counterfeit medicines and how to protect themselves and their families.”