BIOPHARMADIVE

5 questions facing pharma in 2024

Many drugmakers hope to compete with Novo and Lilly in obesity, while others seek to win oncology's next era. Meanwhile, a contentious drug pricing law looms.

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Jonathan Gardner
Senior Reporter


Ned Pagliarulo
Lead Editor

Eli Lilly's headquarters in Indianapolis is seen in November 2021. jetcityimage via Getty Images

The arrival of powerful new drugs for obesity has reshaped the pharmaceutical industry, transforming Eli Lilly and Novo Nordisk into the sector's most valuable companies and sending others scrambling to catch up.

Analysts predict that so-called GLP-1 drugs like Lilly's Zepbound and Novo's Ozempic will become some of the most lucrative products ever sold. Their benefits appear to extend beyond weight loss and blood sugar control, too, raising the possibility they may also change how obesity is treated.

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This year should help answer whether any other companies can break Lilly and Novo's duopoly. A similar dynamic is playing out in oncology, where drugmakers are competing against Merck & Co.'s and Bristol Myers Squibb's recent dominance.

Other storylines in drug pricing, Alzheimer's and next-generation manufacturing figure to be important as well. Read on for five of

the most important questions facing pharma in 2024:

Can anyone challenge Novo and Lilly in obesity?

Nordisk and Lilly had a big head start developing drugs based around the gut hormone GLP-1 for diabetes and, later, weight loss. Ozempic, Novo's weekly GLP-1 for blood sugar control used off-label in obesity, has become a popular culture shorthand for weight loss treatment. Lilly, meanwhile, has an answer to Novo with its newly approved Zepbound, which also targets another hormone receptor called GIP.

With the GLP-1 drug market expected to reach as high as $90 billion a year, other companies are eager to compete and perhaps even surpass the two leaders. Among them are large pharmaceutical companies like Pfizer, Amgen and Boehringer Ingelheim, as well as smaller biotechs like Zealand Pharma and Kallyope. To have a chance, aspiring developers will need to improve on the weaknesses of Ozempic — sold as Wegvoy for weight loss — and Zepbound.

Chief among them is the drugs' under-the-skin injection method of delivery. Novo has a GLP-1 diabetes pill called Rybelsus, which has also shown it can deliver weight loss in non-diabetic people who are obese. Lilly has sped development of a drug called orforglipron, while Pfizer has stumbled developing two rival pills.

Another way to best the incumbents could be by reducing side effects like nausea and vomiting, which are substantial. In the SELECT trial that showed Wegovy can protect heart health, 17% of participants stopped taking it because of adverse events, twice as many as the dropout rate in the control group.

A third approach to beating the on-market GLP-1s may involve preserving lean body mass like muscle. Patients in Wegovy's clinical trials lost healthy lean body mass as well as fat. A drug that

helps people retain muscle tissue could improve their metabolic health and prevent complications like diabetes.

Outperforming on cardiovascular benefits would be the surest, but most time-consuming and expensive strategy. While GLP-1 drugs have sparked a shift in how obesity is treated, insurers are still focused on whether treatment can prevent hospitalization or heart complications. Wegovy has set the benchmark by reducing the relative risk of heart attacks, stroke and death by 20%. Lilly could have data later this year.

With the recent rush of R&D investment, many would-be competitors could soon hit key mid- and late-stage trial milestones that determine whether their drugs work and have a chance commercially. A shakeout of obesity projects wouldn't be surprising as the year progresses. — *Jonathan Gardner*

Merck and Bristol Myers have dominated cancer immunotherapy. Who wins oncology's next era?

Merck's Keytruda and Bristol Myers' Opdivo have dominated the cancer treatment conversation for a decade. Both will reach the end of their patent-protected monopolies as soon as 2028 in the U.S., pushing the two drugmakers to explore commonly used ways of extending market exclusivity, like combination treatment and formulation changes.

But drugmakers are also working hard to find what comes next. Researchers have struggled to develop successor medicines that stimulate immune attacks on tumor cells as Keytruda and Opdivo do, with Bristol Myers' combination drug Opdualag an exception to the rule.

The flurry of dealmaking around antibody-drug conjugates in 2023, headlined by Pfizer's $43 billion acquisition of Seagen, is a sure sign big pharma sees these targeted therapies as a significant

new opportunity. Radiopharmaceuticals, which deliver radiation directly to tumor cells, are also drawing significant investment.

Bispecific antibodies, which help immune cells find and destroy tumor cells, have proven successful in treating blood cancers like multiple myeloma and lymphoma. They've had less success in solid tumors, although they are still being tested in prostate and lung cancer.

After years of disappointment, cancer vaccines are finally making gains, too. The messenger RNA technology employed by Moderna, BioNTech and others can be used to create personalized treatments that stimulate an immune response to patients' tumor cells. Key data from Phase 3 trials of Moderna's Merck-partnered vaccine in melanoma and lung cancer could come in the next couple of years. — *Jonathan Gardner*

How will the industry's challenge to the IRA pan out?

The Inflation Reduction Act is perhaps the biggest overhang on drugmakers in 2024, potentially suppressing revenue for certain top-selling drugs starting in 2026 and dampening investors' enthusiasm for funding pharmaceutical research and development. This is true even if companies' drugs aren't one of the first 10 medicines selected for price negotiation in the Medicare program.

That list will be widened over time; up to 20 new drugs a year are set to be added to the negotiation list beginning in 2029. A half-dozen drugmakers have therefore sued the government to block the law from taking effect. The progress of those lawsuits will be closely watched as the clock ticks down to Medicare's publication of the first 10 drugs' "maximum fair price," which is due on Sept. 1.

The lawsuits claim, in various ways, that the drug pricing provisions are an unconstitutional violation of the Fifth Amendment's ban on taking private property for public use without compensation. AstraZeneca has also argued the

government's implementation of the law breaches the Administrative Procedures Act.

A Jan. 31 hearing on AstraZeneca's lawsuit in a Delaware federal district court could give drugmakers a better idea of whether their litigation will succeed.

Some legal scholars argue they won't because companies don't have a constitutionally protected right to sell drugs to the government. However, those experts note that "some courts have deployed certain legal doctrines in unprecedented fashion," a trend that could yield a victory against the IRA. — *Jonathan Gardner*

Will new Alzheimer's drugs find a market?

Aduhelm, the Alzheimer's disease drug approved in mid-2021, was supposed to be a blockbuster. As the first new Alzheimer's treatment in decades, it was initially viewed as likely to become an important tool for slowing the disease.

That never happened. Doubts over whether the drug actually helped patients, along with controversy over the price set by its developer, Biogen, muted uptake. Prominent treatment centers declined to adopt it, while Medicare, which covers many of those with Alzheimer's in the U.S., refused coverage. Biogen has since all but withdrawn Aduhelm from the market.

Expectations are higher for Leqembi, a similar but more clearly effective drug developed by Eisai and Biogen that won full U.S. approval last year. At the J.P. Morgan Healthcare Conference Tuesday, Biogen CEO Chris Viehbacher pointed to signs of growing market adoption, helped along by more favorable Medicare coverage decisions.

Leqembi could soon be joined by a rival drug from Lilly called donanemab. The Food and Drug Administration is reviewing it and should soon make a decision on approval. Analysts view it as more

effective, potentially helping convince doctors of the utility of this class of drugs, which target a protein called amyloid.

But there are still significant challenges. Treatment involves a special kind of testing for amyloid and the drugs have notable safety risks that need monitoring. Biogen has suggested demand could eventually outstrip the availability of neurologists to prescribe treatment.

“There’s a lot of work to do to convince the healthcare system to rearrange itself to treat people with Alzheimer’s versus ignore them and warehouse them, which is kind of what happens now,” said Lilly CEO David Ricks during a JPM presentation Tuesday.

This year could offer early signs of how well — or whether — that shift is happening. — *Ned Pagliarulo*

Complex drugs are here. Which companies will get manufacturing right?

The pharmaceutical industry is very good at mass producing chemical pills. Over the past four decades, it’s also mastered churning out the protein drugs that are among the most widely used products today.

New types of therapies are breaking those production molds. The genetics revolution has ushered in drugs that can silence genes as well as treatments that can deliver them. Cells, rather than proteins or chemical compounds, are more and more commonly the “unit” of medicine for certain cancers and inherited conditions.

Drugmakers are also getting skilled at tying antibodies to radioactive isotopes or chemical toxins, both useful for attacking tumors in a targeted way that can spare healthy tissue. Others are tweaking the structure of antibodies, adapting them to bind to multiple proteins at once.

These innovations are flowing from biotech into big pharma. Some, like Novartis, have made it their core strategy. A good number of the largest deals in recent years were motivated by pharmas seeking to acquire technologies like gene therapy, RNA interference, CAR-T, radiopharmaceuticals or antibody-drug conjugates.

But getting these new drugs to patients is no easy task. Manufacturing gene and cell therapies requires mass production of engineered viruses and nucleic acids as well as bespoke supply chains. Radiopharmaceuticals need a steady source of medical isotopes.

The companies that get manufacturing right will be the companies that control the market. Already this has played out in CAR-T, where Bristol Myers has struggled to make sufficient quantities of its multiple myeloma therapy.

Novartis, an early adopter of radiopharmaceuticals, initially had trouble keeping up with production of a prostate cancer therapy. Now, as more rivals invest in the field, the company is pointing to its early start as a competitive edge. — *Ned Pagliarulo*