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A Gloomy Outlook On Macro Trends From Industry CEOs

by Jessica Merrill

Pfizer CEO Albert Bourla, Eli Lilly CEO David Ricks and Seagen CEO David Epstein discussed pressing issues facing the pharmaceutical industry at the recent Galien Forum.

Global tensions and US drug pricing pressure are growing risks to the pharmaceutical sector that could have long-lasting implications, according to some of the industry's top CEOs, who participated in a panel discussion at the Galien Forum in New York City on 26 October. *Pfizer Inc.* CEO Albert Bourla, *Eli Lilly and Company* CEO David Ricks and *Seagen Inc.* CEO David Epstein discussed pressing issues for the pharmaceutical industry in the post-COVID era.

A new war in the Middle East, coming on top of the ongoing war between Ukraine and Russia, and mounting tensions between nations like the US, China and India, could disrupt business and present new risks to the sector's supply chains, commercial efforts and R&D, the CEOs agreed.

"The first thing of course is that people are losing their lives," CEO Albert Bourla said. "But clearly there are implications on everyone."

"We are heavily interconnected to the supply chain and every time you have these types of risks you feel threatened that these can be disruptive, and disruption in our case means that medicines cannot be given to people," he said.

The industry's supply chains were put to the test during the early stages of the COVID-19 pandemic, when many countries sought to stockpile medicines or ingredients, underscoring how quickly the global system can be disrupted and emphasizing the biopharma industry's reliance on manufacturing outside the US.

Given the industry's investment and expansion into China, any changes to the relationship between China and the US are also a concern, Bourla added.

“All these tensions create tension in China that will disfavor us compared to others,” he said. “China also is emerging as a major science power. I think they are not at the level of the US or UK, at that stage, but they are catching up very, very quickly, so I think in four or five years we will see innovation from Chinese laboratories becoming global innovations, and that will become now even more tension.”

Lilly’s Ricks also pointed to revenue risk if access to certain commercial markets is restricted, though thus far, he said the impact has been small. “Russia/Ukraine at least are much smaller than China, but even with that, China is what, 6%-7% of our global industry in revenue. Most of the Chinese pharmaceutical market is domestic, which is interesting.”

“Probably the biggest risk I worry about is more of a long-term one, which is adding risk to the already incredibly risky operation of R&D,” Ricks said. The US and much of the Western world have come to agree to a large extent on regulatory standards and intellectual property enforcement for drugs, and even generally on the value of medicines, he said.

“Probably that gets worse over the next 10 years,” he predicted. “So, imagine a small company or a large company having to conduct different development programs for different regulatory regimes. Again, we’ve gotten used to doing it once for the world. You could see that regressing, and I think that’s a consequence of the terrible wars and conflicts and diffusion of the world.”

Epstein, who leads Seagen, a company that is awaiting regulatory clearance to be acquired by Pfizer, took a smaller biopharma company’s viewpoint.

“As a medium-sized company … one of the decisions we would have been making if we were a standalone company in the future would have been which other markets to enter, where you take risks and build up commercial infrastructure, drug development infrastructure, where you put manufacturing plants,” he said. “It’s already pretty difficult for a small-to-medium company to find the capital to do that. It’s a big choice, and now, if you overlap on top of that, a country’s borders might be closed or that my people might get attacked, it adds a level of risk that most small companies just simply won’t be able to do things.”

Geopolitical tensions also create another uncertainty to the already challenging environment for raising capital from venture capital, he added, reflecting on his experience working at Flagship Pioneering for six years before joining Seagen last year. (Also see "*Seagen Taps Epstein As New CEO After A Tumultuous Year*" - Scrip, 10 Nov, 2022.)

“Geopolitical risk is adding to the already horrific financial problem,” he said. “It’s hard to raise capital. You add geopolitical risk on top of that and then you add on top of that … reimbursement risk, whether it be in the US now with the [Inflation Reduction Act (IRA)] or some of the different rules the German government has put in place … it really changes the possibility

of there being, I think, a small company growth engine that companies like a Lilly or a Pfizer could one day bring in [to] accelerate their portfolios."

US Price Policy Is Bad For Business

The three CEOs also used the Galien stage as an opportunity to underscore some of the potential serious and unintended consequences of new US drug pricing policy stemming from the IRA that will pave the way for the Centers for Medicare & Medicaid Services (CMS) to negotiate drug prices for certain big-selling drugs beginning in 2026. SC148966 (Also see "*Patent Cliff Likely Accelerated By Two Years For Most Drugs On Medicare Price Negotiation List*" - Scrip, 29 Aug, 2023.)

Much of the focus was on one of industry's standard talking points since the legislation was first passed in 2022: unintended consequences stemming from the shorter nine-year life cycle granted to small molecule drugs before facing negotiation versus the 13 years granted to biologics.

Ricks speculated the result of the negotiation policies will mean there will be less investment in small molecules, less investment in medium-sized indications and less investment in drugs for older patients.

"The way the law works, they negotiate top sellers. What you don't want to do is be caught being negotiated but never really gotten a return on your capital, so I think we'll try to guess niche markets which may still go forward versus big markets," he said. "Big markets/small molecules will still go forward, but perhaps in a different way ... but I think a number of diseases which end up being sort of medium size will be underserved."

Lilly, Ricks said, has already changed more than half a dozen research programs to adapt to the law. In some cases that could mean accelerating new indications to run programs in parallel because the time clock for a drug starts when it first reaches the market.

"I think that's probably good for big companies because we have the capital to do it, bad for small companies, but maybe also bad for the industry because inherently those programs will have more risk because you're doing things in parallel, so that is a risk premium someone will have to pay somewhere along the line," he said.

Another consequence of the time clock could be that drug makers choose to launch a drug outside the US first before launching in the US, something that does not often happen today. A company may choose to hold off on a US launch to debut with multiple indications at once.

"I've heard a couple of CEOs talking about this, which could happen, is that if you can't parallel process and you're convinced you have to go serially, we may now enter an age where the US

doesn't launch first," he said. "That may shift [so] smaller indications launch in Europe first, where we don't have this clock starting effect, and then later in the US."

Epstein said a company the size of Seagen would face serious challenges running clinical trials in parallel.

"As a small or medium company, how would it be possible that we could do three or four Phase III pivotal trials in parallel? Where is that capital going to come from? And, if we get it wrong, the company is gone," Epstein said.

"There will never be a drug like that again"

He also highlighted a provision for orphan drugs that exempts them from negotiations as long as they are only approved for only one indication. The exemption would be removed if a second indication is approved, something that is common with drugs for rare diseases as a way to make them commercially viable. That's the case with Seagen's Adcetris (brentuximab vedotin), for example, which is approved for seven orphan indications.

"There will never be a drug like that again," Epstein said, unless lobbying efforts under way to change the language in the bill are successful. "It will be one indication. You will stop, and then if you thought the other indications had some value, you might bring another molecule with all the inherent costs and risk associated with it," he said.

Another implication that has been discussed frequently by industry is less investment late in a drug's life cycle, when a company's investment might not be recouped. Epstein said the issue is already coming up with Seagen's own antibody-drug conjugate Padcev (enfortumab vedotin), which was a breakout star at the European Society for Medical Oncology meeting (ESMO) this year on the strength of positive Phase III data, including in combination with *Merck & Co., Inc.*'s Keytruda in first-line urothelial carcinoma. (Also see "*ESMO 23: Madrid Meeting Hails Padcev/Keytruda Combo As New Bladder Cancer Standard Of Care*" - Scrip, 23 Oct, 2023.)

Seagen and its partner *Astellas Pharma, Inc.* are also studying Padcev in earlier-stage muscle invasive disease, where an indication could be approved in 2025 or 2026.

The drug also has potential in non-muscle invasive disease, a new program, he said. "Why should we do it? It will come so late in the life cycle that there'll be no economic return from doing so. We're obviously talking to our partner, Astellas, on that indication and we'll make the right decision, but there's no way anybody could economically justify it," he said.

Pfizer's Bourla said the Medicare price negotiation program is more about politics than drug pricing.

“The thing that upsets me is that none of these consequences were intended,” Bourla said. “When they voted for this bill, they didn’t want to do any of these things, but they were so furious to vote something that would be against pharma because they’re thinking this is their main political win.”