GLP-1 Packaging: A Closer Look at the Landscape for Elastomeric Components, Containment, and Drug Delivery Devices (45-Minute Teleconference)

Competitor | Moderated Call | Moderator: Shane Sullivan | September 18, 2023 | 35 Min Read

Relevant Companies: WST | STVN | ATR | Datwyler Ag | Schott Pharmaceutical Packaging, Inc. | BDX | EMBC | GXI:GR | 8086:JP | GLW | LLY | NOVOB:DC

Ashraf Zaman, VP of Global Sales for the Injectables Division - AptarGroup, Inc.

KEY QUESTIONS

- What is the competitive landscape in GLP-1 containment between Stevanato, BD, Schott, and Gerresheimer?
- Do you envision the status quo staying as is for contract manufactured pens and autoinjectors used for GLP-1s?
- Is West's technical moat with NovaPure and similar offerings relevant to GLP-1s?
- How are capacity investments playing out for GLP-1s? Is there enough capacity to satisfy demand?

HIGHLIGHTS

> On GLP-1 packaging requirements: "In fact, their packaging requirement, we found are not actually that high, let's say. So a standard syringe is fine, you don't need fancy expensive coatings. In terms of the rubber components, again, unfortunately for us, standard rubber works fine."
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> On primary and secondary supplier considerations for GLP-1s: "Traditionally, 80/20 would have been the target. What I'm seeing more for GLP-1 is more 50/50. My thinking is the following, that if you only give 20% to one company, they're only going to reserve a certain amount of capacity for you. If you suddenly go up, they're unlikely to have that surge capacity."

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Shane Sullivan: Hello everyone. Good morning or good afternoon wherever you are. Thanks for joining us on today's call concerning GLP-1 packaging. Before we get started here, just one reminder for those in the audience listening in: If you have any questions that you would like me to relay anonymously to the advisor on your behalf, feel free to email us at Ask@Guidepoint.com and I would be glad to do so.

With that, Ashraf, I'd like to thank you once again for joining us today. Should be a very interesting discussion, I think. To begin, would you mind introducing yourself and providing us with an overview of your background, please?

Ashraf Zaman: Sure. Shane, Thank you. Thank you for that quick introduction. My name is Ashraf. I'm working currently with Aptar. Aptar is the global leader in terms of supplying elastomer components to the prefilled syringe industry, and they also supply elastomer components to vials. I've been here 3 years as the vice president of global sales. Prior to this, I was with Stevanato Group for 5.5 years. I was heading a product management and key account management for Stevanato Group just before the IPO.

Before that, I was with Becton Dickinson, BD for 8 years in various commercial roles, including Sales Director in North America. Before that, I was 5 years with Catalent, one of the leading CDMOs in the world. In total about 20 years' experience in primary packaging glass container space.

Shane Sullivan: Awesome. Sounds very relevant to what we'll be discussing. Let's start out at a high level. Could you describe the primary systems, meaning the combination of the elastomeric components, containers, and delivery devices that are used to package the major GLP-1 brands?

Ashraf Zaman: Sure, sure. I'm going to focus on the injectables version. There is an oral tablet, but I'm not sure how relevant that is, but we can come on to that later. In terms of injectables, I would try and imagine three different dosage formats. The most lucrative, the most profitable is what we call the prefilled syringe in an autoinjector. For example, Trulicity, Mounjaro, Wegovy; these are all available in autoinjectors which contain a prefilled syringe inside. Trulicity is by far the most profitable and the one that all the companies want to sell in. This is usually a weekly injection.

Another format would be a cartridge which goes into a pen. It's not an autoinjector, it's called a pen. It's a cartridge, and this tends to be multiple dose, so you can titrate the dosage, give yourself a dose. Again, it's a weekly dose, but usually in one pen, you have four doses, so it's like a monthly pen that you take for your four doses. Finally, it's the vials. Vials is less common right now, but what you do start to see is the vials is being used in the private market. You have compounding pharmacies, especially in the US, that are selling semaglutide, for example, to weight loss clinics as a compounding pharmacy, and they're using vials for this particular application.

If I go through each of these those three dosage formats, first for an autoinjector, of course, you've got the plastic device on the outside. Inside, you've got a syringe which is usually made out of glass, you've got the needle, and then you've got two pieces of rubber. One rubber is covering up the needle shield and the other rubber is what we call the plunger, which goes into the fat end of the syringe. That's the plunger that pushes the drug out of the syringe.

When you think about cartridge, again, you have two pieces of rubber, one which we call the plunger, again; exactly the same size and diameter as the syringe plunger. Again, it's responsible for pushing the drug out of the cartridge. Then you've got the tip of the cartridge, which is more of a cap, which is almost with an aluminum seal around it. This is where you attach the needle in order to inject the drug. The last format is the vials. Pretty straightforward; you've got the glass vial and you've got a rubber bung which sits on top.

Shane Sullivan: Excellent, very thorough description. Can we draw a line between GLP-1s used for obesity versus those used for diabetes in terms of format one, prefilled syringe with auto injector and format two, cartridge with pen? Meaning, are there preferences for one delivery system over the other, depending on the indication and the dosing administration requirements that such indication requires?

Ashraf Zaman: I would say, look, I'd say it's more of a branding thing than a packaging thing. What do I mean by that? Sometimes the drug inside, let's take semaglutide, it's still semaglutide inside, but it's branded as Wegovy for weight loss, or it's branded with a different drug name for, let's say, diabetes. It would extract different values by the pharmaceutical companies, but essentially, it's the same inside. Autoinjectors are used both for diabetes and for weight loss, for obesity. Pens are used for both, vials are used for both.

If I had to really, really push to give you a more definitive answer, I would say, look, the diabetic patients, they're more familiar with injecting themselves. There's less of an educational step to take. They're fine with vials, withdrawing drugs out of the vial, injecting themselves because they're used to doing that with insulin. They're used to operating a pen cartridge where they have to adjust the dose by twisting the end of the pen, injecting themselves. They're ok with the, let's say, these two types of dosage format.

The obesity patients tend to be the ones that are more new to injecting themselves. They obviously prefer the autoinjectors. I would say, look, if I had to choose, I would say Autoinjectors is probably preferred by obesity patients, whereas pens and vials can be used by diabetes. But again, it's more of a branding. There's not a definitive line you can say that, all autoinjectors go for obesity, all pens go for diabetes. You cannot draw such a definitive line.

Shane Sullivan: What are the nuances of GLP-1s when it comes to the technical specifications of the primary packaging? What I mean by that is, from a containment standpoint, it's primarily glass. Why is that? What type of glass? Are they using the highest-end glass?

Ashraf Zaman: Sure. It's all type 1 borosilicate glass. It's a high-standard glass. This is, let's say, the universal standard for syringes, cartridges, vials. Everyone, no matter who the supplier has to use a type 1 borosilicate glass. That's by default, the standard. What is interesting, you come back onto the technical specifications, the drug itself, these GLP-1s, they're not so sensitive; they're not like the high-end monoclonal antibodies. They're

just proteins, peptides, they're not mRNA vaccines.

In fact, their packaging requirement, we found is not actually that high, let's say. So a standard syringe is fine, you don't need fancy expensive coatings. In terms of the rubber components, again, unfortunately for us, standard rubber works fine. You don't need a special-coated, Teflon-coated or Novo Pure standard, let's say, rubber components to supply this market. The proteins are actually very, very stable.

Shane Sullivan: Interesting. Why glass as opposed to plastic? Could they be packaged in plastic conceptually?

Ashraf Zaman: Sure, sure. There's nothing specific to GLP-1. There's a question out there amongst the pharma companies in primary packaging suppliers, glass beats plastics. Historically, glass has dominated the market. Glass is more than 95% of the prefilled syringe market. More than 95% of the cartridge market is glass. For historic reasons, glass is very inert. What makes glass beautiful is that it's not permeable to oxygen, whereas most forms of polymer or plastic is permeable to oxygen.

Now, there are newer polymer syringes out there, COC, COP syringes, which have addressed the issue of permeability of oxygen because most drugs don't like oxygen. However, the price point is still very, very high. A polymer syringe today is still more expensive than a glass syringe. There might become a tipping point where there's enough critical mass to produce polymer syringes in such a high amount that you can actually produce it at a lower cost. But right now, as it stands, there's no incentive for you to go to a polymer syringe if a glass syringe works.

Shane Sullivan: It seems like the technical specifications here are not quite rigorous. They use standard glass, they don't require fancy coatings for the rubber. What do you think is informing these pharmaceutical companies choice of primary packaging vendors? Because it seems, at least to me, that multiple suppliers can meet the baseline technical requirements.

Ashraf Zaman: Sure, sure. There aren't many suppliers. I'll go through one-by-one case example. The first real blockbuster GLP-1 was Trulicity by Lilly. At the time, Lilly put out a tender and they had no idea this was going to be a blockbuster. They chose. BD. They chose BD because BD at the time was the number one supplier of syringes in the world, and BD had multiple factories around the world. They knew by having one supplier and mono sourcing, they were able to basically, instead of validating 3 or 4 different suppliers, you can have one supplier with six factories, was an effective way to go. They went at the time, and it was close to 15 years ago when they launched with BD as a single source.

After that, things got a bit different because the volumes went through the roof. Trulicity became a true blockbuster even before we started getting into weight loss use. Now with Mounjaro, with Wegovy, it's a slightly different model. Now, Novo Lilly, they're working a slightly different way. They put out an RFQ, so they reach out to - there's only five syringe manufacturers in the world, so they reach out to all five, and then they shortlist, they call them in for interviews, and then they do what's called a technical study. They'll put the syringe on stability, do compatibility, do some technical testing, and then finally, they'll narrow it down to maybe 2 or 3. That allows for competitive pricing. Then they'll start to negotiate.

When they negotiate, it's not just the pricing. They're also looking at your business continuity plan. They're looking at basically your sustainability profile. What do you have to say about ESG? What does your supply chain look ? What is your lead time? How much safety stock are you prepared to hold for me? After that, they're narrowing it down to two. For example, it's not yet public information, but we know which are the two vendors Lilly has chosen for Mounjaro. We also know which are the two vendors Novo has chosen for Wegovy.

Then you've got other companies like Boehringer Ingelheim, which has got a drug in Pipeline, and they've actually, recently just finished their selection process. They went through a similar selection process as Lilly and Novo, but they're a bit more price-sensitive, but they've also narrowed it down to two syringe suppliers that they're now going to go with for the drug that's in their pipeline launching in 2026. All of that was with Aptar rubber, which is good news for us. But the syringe suppliers, each of them have chosen two.

Just to summarize, originally, people like Lilly just chose one. It was sufficient. But right now, we see a trend that they're choosing two; one as a primary supplier, one as a secondary supplier, and the things they're taking into consideration are of course the technical fit, price sustainability profile, lead time, and your business continuity, your risk-mitigation plan.

Shane Sullivan: I want to talk about a few things. Are these components typically purchased as an all-in-one system, or are they mixed and matched? We know that - I can't remember if it was Lilly or Novo; actually, I think it was Lilly. They're outsourcing both API manufacturing and fill-and-finish. Does the fill-and-finish vendor typically have any sway on the decision in terms of making recommendations or anything of that sort?

Ashraf Zaman: At that level, no. Let me answer that; at that level, no. When it's a reputable pharma company, they know what drug they've got, and they'll come and tell you, we want this and this syringe supplier. Where the CMO's have some influence is if it's a startup, if it's a biotech, small biotech, two men and a molecule, they really don't know, they haven't got the time, and they haven't got the leverage to negotiate a good deal. Then yes, then they go to the CDMO, and they get a whole package from the CDMO, where the will buy the primary packaging.

But for Lilly Novo, where they're buying such big volumes, they'll come to you, they'll come to Catalent, they'll come to Thermo Fisher and they'll say, "This is where you buy your syringe from. I've already negotiated the price and here it is. Tell me back to your first question. Are they sold separately or as a system? It's a good question. I'll say both. For example, for the plunger, if you remember the plunger, which is the fat end of the syringe or the cartridge, usually, this is sourced directly. Novo, Lilly will directly negotiate with us at Aptar or Datwyler, or West to get the price. Will either buy them directly to be shipped to their filling facility in North Carolina, or Italy, or wherever their filling facility is, or directly to their CDMO. That's for the plunger.

For the other end, which is the needle shield or the tip cap of the cartridge, this one, they negotiate the prices directly with Aptar, or Datwyler, or West, but this product is shipped to the syringe manufacturer or the cartridge manufacturer because what they have to do when they make the syringe of the cartridge, they have to assemble the rubber, of course, onto the end of the syringe or cartridge before then shipping it to the CDMO or the pharma company. So, both.

Shane Sullivan: Is there a geographic element here, meaning, certain suppluers have more manufacturing concentration in Europe, or the United States, or even India or China? How is that weighing on those decisions?

Ashraf Zaman: You mean Lilly, Novo, these people, or do you mean the primary packaging suppliers, their locations?

Shane Sullivan: The primary packaging suppliers.

Ashraf Zaman: Sure. I'll go through them one by one. Obviously, BD is the market leader for syringes. They have six sites. They have their headquarters in France, in Grenoble, they've got a site in Tatabanya in Hungary, they've got the site in Columbus, in Nebraska, in the US, they've got a site in Cuautitlan in Mexico, they've got a site in Japan, in Fukushima, and they've got a small site in China. They're also building a seventh, let's say, site in Zaragoza in Spain. BD, a large industrial footprint, selling 2.6 billion syringes per year. They're by far the biggest market leader.

Number two in the world right now is Stevanato Group. They manufacture in Italy, and they've launched a second site in Indianapolis. So, not by coincidence, right next to the headquarters of Lilly. They've got a third site which is in Zhangjiagang in Shanghai, in China, which hasn't started yet on syringes, but will soon start syringes. I think it's public information. After that you've got Schott producing in Switzerland in Saint Gallen. They're also expanding into Hungary.

You've got Gerresheimer producing in Germany and expanding into North Macedonia. You've got Nipro producing in Germany. You've also got a Chinese player which is not so big in the GLP-1 market today, but you've got a Chinese player called Shandong Weigao, which as the name suggests, is based in Shandong in China. That's the geographic location. In terms of how what that means, what the influence is in terms of supply, I would say, look, no is the answer; it doesn't. But if you speak to the pharma companies, they would of course prefer that your factory is as close as possible to their filling location.

A lot of people got scared during COVID-19. If you remember, there was a period where countries got very protective, put up barriers about, "We're going to keep these things for ourselves." That scared a few companies and they went up a little bit. If you have multiple factories in multiple locations, it's an advantageous, and I think Novo included that in their RFQ that it would be advantageous if you have multiple, let's say, sites. But in the end, when the rubber meets the road, they didn't really allow it to influence them. I can confirm that the people that chose some of them only have one site. It was a theoretical, let's say, request, but in practical terms, it didn't matter. As long as you have safety stock you agree to store in different parts of your supply chain, you can mitigate the risk of only having one factory.

Shane Sullivan: I want to be careful. Could you talk a bit about the competitive landscape in containment right now between Stevanato, BD or Embecta; I'm actually not sure which one it is - and Gerresheimer, in terms of how you view their prospects? We know BD is a leader in syringes. Stevanato has touted themselves as a leader in cartridges. Gerresheimer has had some issues.

Ashraf Zaman: Sure. Embecta, by the way, is the spinoff of BD for diabetes care. So, we'll talk about BD, Stevanato, Schott, Gerresheimer, and Nipro are the main players, let's say. In terms of syringes, I would say that BD is definitely the market leader. Strong position. They're losing market share, but the market is growing organically 8%-9%. Even if they're losing market share, they're still growing by 200 million syringes every year, and they're quite happy with that. They're trying to focus more on biologics like they all are, and less on the lower value part of the market, the antithrombotic market. Stevanato are saying yes to everybody. They've had a culture of just saying yes to everything, take the business, we make money, and they continue to have, let's say, profitable growth by saying yes to everybody.

They compete heavily with Schott, and Schott, competes heavily, also with Gerresheimer. The syringe market is competitive, especially when it comes to new business. When it comes to going after this Novo RFQ, the Boehringer ingelheim RFQ, I can tell you it got very, very tense, very heated, even discussions with us because they wanted to get the rubber from us, they wanted to secure their supply chain, and squeezing us for pricing as well, because it's part of the total package they were negotiating. It got very competitive.

Nipro, for example, is the only one that's a bit sleeping, I would say. They're the only ones with excess capacity. Everybody else is full of orders. When it comes to syringes, Nipro is the one, for some reason, their go-to-market isn't quite so strong at the moment. That's the dynamics for syringes, especially with GLP-1s. There are other of course, non-GLP-1 applications like the Moderna vaccine for mRNA. That has a slightly different scope because that's more polymer-based. But at least for GLP-1, that's the landscape.

In terms of cartridges, yes, I confirm Stevanato is the number one, followed probably by Schott, and then Gerresheimer. The three of them are the three leading suppliers of cartridges in the world. There are basically three main consumers of cartridges in the world, and these are the three companies that buy insulin; Novo, Lilly and Sanofi are the three biggest suppliers of insulin, the three biggest consumers of cartridges. These six of them, the three suppliers and the three customers, every year, they rotate a little bit, the market share and pricing. But in the end, they have approximately a third each of the market.

When it comes to vials, it's very interesting. Traditionally, it was, let's say, not so competitive. People were growing organically. But what happened in the last 2 years, 3 years since COVID, a lot of customers, pharma companies over-ordered their vials, so there's a lot of excess stock. At the same time, a lot of these glass manufacturers, they increase their capacity, so there's a lot of increased capacity. What I'm hearing from some of my customers is not only are they buying less rubber next year, but they're almost buying zero vials because they have so much stock and they have a 5-year shelf life, these bulk vials. Some of these pharma companies have got so much vials, they're refusing to buy any more.

It's getting very competitive in terms of vials. I've had some crazy prices being offered because the glass manufacturers want to continue running their lines. They don't want to stop their lines. But yes, I think the pricing for the vials is going to become an interesting thing to watch over the next couple of years.

Shane Sullivan: What about the contract manufactured pens and autoinjectors? Which players are active in that category right now? It's usually the case that Eli, Novo owns the IP, right?

Ashraf Zaman: Right. Especially for Eli, they invented this pen themselves. The autoinjector was developed in-house, they're very proud of that, the team. They use the same for Trulicity, they use the same for Mounjaro, but of course, they don't manufacture the pen. They have CDMOs to do that. For example, West, Gerresheimer are the type of CDMOs that they would use to build that. Novo uses more SHL, also Gerresheimer, Rexam, and Nemera to do their - after their CDMO to manufacture the pens.

Here, it's quite interesting because Gerresheimer, for example, produces the pen, but they don't actually sell any of the syringes. I don't know if it's a risk mitigation strategy from Novo where they don't get their syringes from Gerresheimer, but they get the pens.

Shane Sullivan: Do you envision that status quo staying as is? My understanding is that the contract manufactured pens and autoinjectors business is a bit lower margin, and mayne not quite as sticky. I don't know if you can comment on that. But players with proprietary higher-margin pen systems, is there an opportunity in the GLP-1 category?

Ashraf Zaman: That's a good question. I think, first of all, it's not as sticky because it's a secondary packaging, so it's not in contact with the drug. It's still considered secondary active, so you can't just be blasé about changing it. You have to make sure it works well with your syringe, or cartridge, and you've got to do human factor studies. So, it is easier to change that than a primary packaging. In terms of whether SHL, Ypsomed, Owen Mumford is proprietary, I think with Lilly and Novo, no. I think Lilly are again very proud of their autoinjector. Novo is happy with theirs; I don't think they're looking to change.

Where I think there's a value play for them is with all the generics that are coming out with the likes of Boehringer Ingelheim. Because what they might do is they might say, "My delivery device, my auto injector, my pen, this is going to be my differentiator. My drug is better than Lilly or Novo, but not only that, for my delivery system, it's easier to administer, especially for obesity, where people aren't familiar with injections." If you have something that's more discreet or easier to use, just one step, not two steps or three steps, then that's definitely what I would push if I was Ypsomed or Owen Mumford.

Shane Sullivan: Thanks for opining on that. In rubber, I won't ask about Aptar, but it sounds like West's technical mode with NovaPure and similar things doesn't really matter in GLP-1. Is that a fair encapsulation?

Ashraf Zaman: It's correct, yes. Studies have been done. It's just a pretty simple protein. Right now, there's no suggestion to need NovaPure or even FluroTec; these advanced coatings. Your standard plunger is doing the job.

Shane Sullivan: What is the all-in revenue opportunity for the primary and secondary packaging used in GLP-1s? I heard one person throw out $20. Could it be higher, lower? I think it would be a good place to start.

Ashraf Zaman: You talking about primary packaging or all the packaging for one?

Shane Sullivan: The primary packaging and the pen or autoinjector together.

Ashraf Zaman: Do you want to include the CDMO activity or is it just the raw materials, the components?

Shane Sullivan: Just the components.

Ashraf Zaman: Let's go through them one by one. If I take the syringe and plus the rubber which goes on the end, let's assume here it's $0.35. We've got the plunger. Let's assume here is $0.10 and you've got the autoinjector. It can go for, say, $2. Then you've got the plastic holder. The pen, may be $0.50. You've got the cartoon, the printing. If I just look at that, you're basically at around for $4-$5 mark, so $20 would be great. But I think the whole device sells for a good price.

Shane Sullivan: You said that the prefilled syringe and autoinjector versus cartridge and pen format is more profitable, correct?

Ashraf Zaman: Absolutely, yes. There are many reasons for that. First of all, you need four of those, not one, because a pen would be only one dose. Sorry, a pen has four doses, so you only sell one of those a month. With the autoinjector, you'd have to sell four of those. This is more - it's better for everyone concerned.

Shane Sullivan: I want to talk a bit about capacities in this space. Do you think recent demand for GLP-1s for obesity has come as a surprise to suppliers? I've been hearing about glass shortages, for example, not even counting the CDMO-related bottlenecks. How is that shaping up? How are capacity investments playing out?

Ashraf Zaman: I've been caught by surprise. I would say no, I don't think anybody was surprised. We knew this was on the horizon. I think COVID threw a curveball. But if it wasn't for COVID, it probably would have been maybe 1 or 2 years more in advance. We knew it was coming, some investments were made. We probably didn't anticipate the off-label use. Apart from the supply chain issue, one of the reasons why there's not enough in the world is because there's a huge off-label use in the private market, especially in the US, for obesity as a lifestyle drug as well. That's the bit I think people didn't understand and we didn't anticipate there'd be such a media hype, I'd be doing calls this, for example. That's the bit that we didn't quite understand the impact that that would have.

It was more of a lack of understanding of the market requirement, but we knew that - Trulicity has been around for ages, it was a blockbuster. We knew it was happening. The Wall Street Journal made it very clear they thought that Mounjaro is going to become the number one-selling drug in the world. The signs were there. So, no excuse there. I think in terms of primary packaging, there is enough capacity, There's definitely enough rubber capacity, I can confirm. There's enough syringe capacity. Between everybody, there's enough syringe capacity where we've been caught short and Wegovy, for example, for Novo was caught short because of Catalent, because Catalent had this FDA warning letter and they couldn't produce for 6 months. It's not linked to supply. It's just because they had a specific issue at one of their sites at Catalent. That's basically almost like a force majeure.

In terms of Lilly, what they're telling us, it's more the assembly of the autoinjector. They are exploring other options like cartridges, pens, vials, because they just can't assemble these auto injectors fast enough. There's a lead time for those machines; it's 18 months lead time for the autoinjector assembly machines. But Mounjaro

hasn't been approved yet for a BCT. Mounjaro has only been approved so far for diabetes. It's being used heavily for obesity off-license. But technically speaking, there hasn't been approved yet. They're getting themselves ready. We've got their forecasts, it's very manageable, nothing to be worried about.

They've invested heavily. In fact, they've reached into their own pockets and invested themselves into machinery equipment just to make sure that we're ready. They've done the same with the syringe manufacturers. So, I think with Wegovy, the specific issue, Mounjaro was like they didn't know it was going to work so well. They hadn't anticipated the market demand.

Shane Sullivan: It's interesting. I know there's a report - I think it came out this morning about issues at Novo's plant that makes - what's the drug? Wegovy. The FDA is involved. Again, I can't remember if it's - I think it was Lilly added Patheon on top of Catalent for fill-and-finish, but it seems like this is being CDMO-driven versus packaging supplier-driven. Is that an accurate encapsulation?

Ashraf Zaman: Yes. The funny thing is there's plenty of capacity in the CDMO world. They just need to choose the right one, make sure it's a safe choice, won't have any FDA issues. But right now - excuse me. But the bottleneck will change. It will CDMOs. For novo, it was assembly equipment. For Lily, who knows what would be next? It might be carton packaging, it could be anything in that supply chain. I think here's the interesting point. Because of the value of this drug, Lily has become the number one pharma company in the world by market capitalization. They know it's all in the back of this GLP-1.

So basically, what they're doing now, I've noticed, is they're actually buying parts of their supply chain. You will have noticed a few months ago there was a public announcement that Novo is buying a company called BIOCORP. BIOCORP is a drug delivery device company; has nothing to do with pharma, nothing specific to do with GLP-1. But what I start to read into that is that, so Novo and soon Lilly are looking all the way down the supply chain and saying, "Look, how can I show this up?"

Regarding CDMO, both of them are building in-house capabilities to do their own filling so they won't rely on CDMOs anymore. They are building their own, let's say, assembly equipment sites in North Carolina for Lilly, for example, so they won't rely on CDMOs. It's quite hard to have your own syringe company, but Lilly has their own autoinjector Novo doesn't. But Novo has just bought this company called BIOCORP, which develops autoinjectors, drug devices. What I see is these people are getting nervous saying, "Hey, we don't want our supply chain to be the reason I miss out on sales." I can see them spending some of their hard-earned money on buying up some of these companies that are part of their supply chain. A bit of vertical integration.

Shane Sullivan: Just one correction for my own sake. It was Novo who tapped into Patheon. My next question would be - one thing I forgot to mention, we talked about the revenue opportunity. That $4-$5 applies toboth the autoinjector and pen-based formats?

Ashraf Zaman: It's not a significant difference between the pen - the pen works out a little bit cheaper because you've got a cartridge inside a syringe. The cartridge is a bit cheaper, but not significantly different. It's still between $4-$5.

Shane Sullivan: Thanks. I just wanted to double-check that. Another important theme has been supplier diversification. It seems like that's picking up steam. What do you think is the likely split, just in terms of what you're seeing? Again, I want to be careful, but when pharma companies pick a primary and secondary supplier for their primary packaging and secondary pen-type stuff, is it usually 80/20? Would you say that's a good baseline?

Ashraf Zaman: I would say, look, traditionally, 80/20 would have been the target. What I'm seeing more for GLP-1 is more 50/50. My thinking is the following, that if you only give 20% to one company, they're only going to reserve a certain amount of capacity for you. If you suddenly go up, they're unlikely to have that surge capacity, and the one that's at 80% is already full. I've seen more of a tendency to go 50/50, but both of you have surged for me, so I can go up to 70 if I want with any one of you. Then they let them fight, saying, "You want more, give me a better price." I'm seeing it more 50/50 based on what I'm supplying to the syringe companies and the forecast I have from them. I can't name, of course, who's giving me what, but I'm seeing it more 50/50 than 80/20 for Novo and for Lilly, is how they're treating their suppliers.

Shane Sullivan: Obviously, there's huge demand for GLP-1s, which translates to huge demand for packaging components, pens, and such. Is there an opportunity for pricing power among the suppliers?

Ashraf Zaman: I would say right now, no, because everybody wants to get on to the GLP-1 bandwagon. Everybody wants to say at their analyst calls, "Hey, I've got high-value products, I am in GLP-1. Because of that, they are prepared to be very competitive with their pricing. At the moment, no. But once the dust settles a bit, once your drug is approved with my syringe, at the next round of negotiations, and this is what's happened historically, you're wedded to me. I'm going to squeeze you a little bit with pricing, it won't be double digit, but it'll be high single digits.

I'd say in the short term, no, I don't think there's much leverage. But certainly, in the next round we're going to negotiations, I expect the syringe companies and suppliers to come back and say, "Hey, look, I need a bit more pricing here. You're capturing a lot of the value. I need a bit more."

Shane Sullivan: I want to move on to some opportunities and risks, just considering the evolution of the GLP-1 category overall. The first thing that comes to mind is oral GLP-1s. I know that there are some hurdles left to clear in terms of manufacturing and such. They require more API given their dosages. But is there an expectation that orals are eventually going to displace injectables, or moreso expand the market? Just trying to think about how transient these tailwinds for suppliers in this space could be.

Ashraf Zaman: I'm not too worried about the orals for a couple of reasons. Number one, there is a precedence and it's in oral anticoagulants. People like me who have followed the market for a while, anticoagulant is the injection that you give to yourself. If you go to hospital, you're lying there for 2 or 3 days. You inject yourself with this drug and then you take it home, maybe inject yourself a couple more days. It's to thin the blood to stop it clotting. These anticoagulants are injected and they have been injected for years. Then orals came out and we were all panicking, because this was the number one use of syringes in the world, was this anticoagulant. We thought, ok, the orals are going to kill the market, but nothing happened. Orals were not as efficacious, not as good at doing the job.

If orals were that good, then there would have been launched as oral in the first place, not as injectables because nobody really likes injecting themselves. That's the first reason, the precedent is not there for any orals to eat into this space of injectables. The second reason is to do with the dosage regimen. The oral GLP-1s for obesity, it's a three-times-a-day dose. Compared to an injectable, which is once a week, and you're treating obesity, and these people tend to have not the best self-control, let's say, or the best adherence. There are other orals available to a weight loss for three times a day, but they just don't work because patients don't stick to the regimen.

What tends to happen if you have to inject yourself once a week on a Sunday evening, you inject yourself. You don't have to make any decisions for the rest of the week. If you have to take a tablet three times a day, you've got a party you're going to, you're having guests over, you're going out for an Indian, you might think, "You know what? I'm going to have good food. I'm not going to take my tablet today." The adherence is low, which means the efficacy is low of the orals. What I do see, potentially, is the orals becoming a gateway drug. Orals as a GLP-1 as a whole is very safe, the safety profile is good.

Eventually, in a few years' time, what might happen is the orals might become something you get over the counter even, so it becomes a gateway drug. You want to lose weight, there's not enough medicine, or syringes, or injections available around the world, you start with the orals. Like with diabetes, the treatment, start with oral, try that for six months. If it works, great. If it doesn't work, then we move on to a pen. If that doesn't work, we move it on to an autoinjector, something like that. That's how, in fact diabetes is treated. Metformin tablets to start with, and then you move on to insulin, pens, etc. I don't have a crystal ball, but I would say orals may have a place as a gateway drug, but I don't see it cannibalizing the effectiveness of the injectables.

Shane Sullivan: How do we think about the eventual emergence of generic GLP-1s as well? Historically, have generic injectables tended to stick with the systems used in their branded predecessors?

Ashraf Zaman: I think this is slightly different and I'll tell you why. We have different generations of GLP-1s, although they're all GLP-1, what makes a Mounjaro very different? It's not just a GLP-1, it also works on GGG. It's a GLP-1 on steroids, if you like. What it does and why it's more effective than semaglutide and the others is because not only does it do all the things that GLP-1 does, but it has a way of affecting what's called your GGG; it affects your hunger thing. You're not thinking about food, it's the best way to describe it.

A lot of people who are obese, the reason they're obese is they're just thinking about food all the time. Their next meal, what am I going to do? What am I going to eat? Food plays a huge part of their thought process, and this drug is amazing. It actually not only acts as a GLP-1, but also acts on your hunger, let's say, thought process, you're just not thinking about food. When you have generic or for example, Trulicity, it's just going to be a GLP-1, it won't have this extra GGG. So it won't be as good. It will be, let's say a first-generation generic, or maybe it can be used for diabetes. Still, that's fine, but it won't replace those fast-acting Mounjaro.

Then you have what might be the third-generation of GLP-1. If you look at the pipeline of Novo Nordisk, CagriSema is actually a mixture of two different liquids that, by the way, require a very specific bypass, dual chamber syringe available for only one arrangement at the moment. Then you've got maybe a third

generation, which we don't know yet. The clinical trials are still being done. We don't know how effective that will be, how safe that will be. But the way I see this panning out is that with each reiteration, you're actually getting a better drug, a better molecule.

I don't think the generics will have as much of an impact on the GLP-1 obesity weight loss market as other ones have done traditionally in the injectable space.

Shane Sullivan: Even still, is there a possibility that generic Trulicity, for example, could ditch the pen or autoinjector and say, "Let's just do syringes." or do you think that's unlikely?

Ashraf Zaman: They could do, and it could save cost. But then imagine the patient is using Trulicity and then it works. They've been using it, they go to the pharmacy, and they say, "From now on, you're going to get this naked syringe." I think the patient will say, "Hang on a minute, my diabetes has been under control with this other drug. I don't want to go to this naked syringe." I'm a pharmacist myself, so I've seen push backs from many customers that are stabilized. It's not an easy thing to control your diabetes. You've got it stabilized, you don't want to start something changing.

I think it would be very difficult to create a value proposition for a generic player to go into a naked syringe. They could come up with a different autoinjector, which is easier to use or etc. But coming up with a naked syringe I think would be challenging to get the market adoption.

Shane Sullivan: Fair enough. Well, Ashraf, we are just about out of time. I'm not seeing any questions from the audience either. Anything we may have glossed over that you would to highlight before we close out for today?

Ashraf Zaman: No, I think it's been great. I hope it's been useful to some people and I appreciate the time.

Shane Sullivan: Absolutely. Thanks once again for participating. Very helpful discussion, I think. For those in the audience listening in, if you're interested in scheduling a follow-up call, please get in touch with your Guidepoint representative. Otherwise, I hope everyone has a great rest of the week.

Ashraf, thanks so much again. It's been a pleasure.

Ashraf Zaman: Thank you. Take care. Bye.