Ypsomed – Autoinjector Platform Deep Dive & Demand Outlook

14 October 2024

Key Insights

- C60% of chronic condition pipeline – ex-oncology – uses autoinjectors and c40% uses prefilled syringes. 90% GLP-1 pipeline uses autoinjectors. Specialist doesn't see GLP-1 market moving towards variable-dose pens, despite titration advantages. In APAC and pharmerging regions, vials will be preferred format for GLP-1s. As biologics become more viscous, demand will shift to larger-format syringes and on-body injectors
- Ypsomed and SHL are leading autoinjector players and the only suppliers with large-scale capacity. Key differentiator is that Ypsomed's customer service is superior, with SHL alienating customers. No functional difference between YpsoMate and Molly
- Despite large-scale syringe fill-finish capacity expansion, specialist isn't concerned about bottlenecks in devices' final assembly, given the CAPEX level here and lower regulatory requirements. Given the demand level from biologics, biosimilars, GLP-1s and other potential blockbuster indications, specialist would be surprised if autoinjector assembly capacity is underutilised. Ypsomed can reasonably drive high-to-optimal utilisation of new capacity
- Specialist doesn't see any pullback in pharma outsourcing. Outsourcing's advantages – ie, lower total cost of ownership, development risk and improved time-to-market – hold true, more so for GLP-1s. Only Novo, Lilly and Sanofi have in-house IP platforms due to insulin heritage. However, expect c30%-plus future price pressure for autoinjectors as competition increases, but not more, given price per unit isn't as important as aforementioned advantages. Ypsomed could capture 15-30% royalties, depending on volumes, from other contract manufacturing organisations manufacturing YpsoMate platform for GLP-1 customers. GLP-1 autoinjectors could cost USD 1.5 per device

Specialist Paul Upham (PU), Head, Smart Devices at Genentech Inc (F Hoffmann-La Roche AG)

Moderator Sebastian Skeet (SS), Third Bridge Sector Analyst

Agenda

- Current market capacity and demand outlook for injectable drug delivery formats, including pens, autoinjectors, patch injector systems and smart devices across GLP-1 (glucagon-like peptide-1) and non-GLP-1 end markets
- Ypsomed’s (VTX: YPSN) competitive positioning vs incumbents, including Gerresheimer (ETR: GXI), SHL Medical, Owen Mumford, West Pharmaceutical Services and Jabil (NYSE: JBL)
- YpsoMate deep dive – benchmarking vs competing devices on customer KPC (key purchase criteria), demand outlook in light of significant capacity ramp and expectations for average price and margin per unit

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Q: How do pharmas think about in-sourcing CDMO-owned IP, or off-the-shelf platforms, vs using in-house pharma-owned IP? If we look at Novo Nordisk, we discussed how it uses SHL's Molly for semaglutide, and we know it's using Ypsomed's autoinjector for CagriSema [cagrilintide/semaglutide]. However, Novo Nordisk did buy Biocorp in October 2023, so it now owns medical device capabilities in-house. We also know it has the FlexTouch pen IP in-house, which it's using for semaglutide pens in Europe. Eli Lilly owns the IP for its pens and autoinjectors as well. In a world where we have more and more GLP-1s on market and these therapies, as you alluded to, are competing on the device as well as the clinical data, do you see players such as Novo Nordisk, Eli Lilly and other biotechs looking to develop their own in-house IPs to differentiate?	**18**
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Ypsomed – Autoinjector Platform Deep Dive & Demand Outlook

Transcription begins at 00:00:07 of the recorded material

SS: Welcome to Third Bridge Forum's Interview entitled Ypsomed – Autoinjector Platform Deep Dive & Demand Outlook. My name is Seb Skeet and I'm delighted to have with us today Mr Paul Upham, Head of Smart Devices at Genentech.

Paul, before we start today's Interview, please state I agree or I disagree to the following statement: You understand the definition of material non-public information and agree not to disclose any such information, or any other information which is confidential, during this Interview.

PU: I agree.

SS: Paul, could you please start with a brief introduction of your background relevant to today's Interview?

PU: I'm currently Global Head of Smart and Digital Devices, both for Genentech and Roche Pharma, which Genentech is part of, and have been in this role about eight-and-a-half years, work in our technical R&D organisation with device teams developing pre-filled syringes, autoinjectors, on-body injectors, primarily focused on sub-Q delivery and then a few other routes of administration. Prior to this role, I was Global Head of Marketing for Becton Dickinson in their self-injection business and managed a portfolio of pre-filled syringes, safety devices, autoinjectors, on-body injectors and was in that role for about four years. Then, relevant to this conversation, I also spent 10 years in Becton Dickinson's diabetes care division, which was focused on blood glucose monitoring and insulin and GLP-1 delivery.

[00:02:03]

Q: Could you walk us through the value proposition of an autoinjector vs a pre-filled syringe or a pen for an injectable drug?

PU: I think the simplest way to address the value prop is to say autoinjectors' value comes when you have home administration or patient self-administration of a subcutaneously delivered medication, occasionally intramuscular for things like EpiPens, for example, but the dominant is subcutaneous route of administration. It's really that setting outside of the clinic and hospital that has driven the value of autoinjectors in particular. Prior to autoinjectors being available, people were using pre-filled syringes. They were even doing drawing up medication from a vial with a disposable plastic syringe and doing self-injection. This was very common with insulin early on, but it's that setting outside of the clinic and hospital. Maybe a way to illustrate that is to say there are products that are presented in pre-filled syringes that are used by patients who self-inject, but, predominantly, those are used by healthcare professionals who are administering a subcutaneous injection in a hospital or clinic setting. Given the indications for use, given the particular therapy, given the potential safety or side effects, it might be primarily indicated for use by a healthcare professional in those settings. As soon as you have the ability

to allow a patient to self-administer their medication, they can now use either a pre-filled syringe or an autoinjector, and the autoinjector advantage comes in being simpler to use. It comes, typically, with the needle being hidden, which is important for some patients who might be hesitant to self-administer a drug if they see the needle going into their skin. That's a mixed audience, but I think the convenience and ease of use that is associated with autoinjectors, both in hiding the needle but also in automatically inserting the needle into the skin and then administering the dose, not requiring a patient, for example, to push on a plunger rod with their thumb while holding the needle in their skin, all of those things stack up in the value proposition for autoinjectors.

SS: It sounds as if shifting the treatment setting out of the hospital or in-office setting and into the home is really key here, and presumably, that's a narrative that the pharmaceutical customers like because it perhaps expands the TAM or lowers the barriers to use. Is that fair to say?

PU: Yes, I think that's where it starts. You do see products on the market for home or self-administration, but they're only available in pre-filled syringes.

[00:06:04]

Q: What proportion of pre-filled syringe formulations are available for at-home administration vs requiring an HCP [healthcare professional] administration?

PU: I would say roughly, on today's market for the products that can be subcutaneously administered in a pre-filled syringe, it's probably north of 60% are available for home self-administration. The exclusive use in hospitals and clinics maybe is in that 30-40% range, something like that.

SS: So, autoinjector devices increase the proportion of patients able to dose at home, but this doesn't necessarily translate into a step change.

PU: Right. The pre-filled syringe, which is a component of every autoinjector unless it's a cartridge base, and I know we'll probably chat about that, but the pre-filled syringe in and of itself has value in both settings. For a healthcare professional, it means no longer having to draw up a dose from a vial using a disposable syringe. It means more efficient operations in the clinic or hospital with those pre-filled syringes, and so the advantage for pharma companies and for patients ultimately is in that increased access if you can get it approved for home or self-administration. Then you have a choice, "Do I only provide this pre-filled syringe for home and self-administration, do I provide both pre-filled syringe and an autoinjector, or do I switch the home and self-administration market entirely to autoinjector (talking over each other 08.14)?" That's the logical path that often follows.

[00:08:23]

Q: Are there any clinical advantages? I've read certain studies that found that autoinjectors provide higher peak volumes of the injectate, indicating greater dispersion, for example. Does that translate into any meaningful clinical edge here, or does that not really move the needle?

PU: My opinion is that doesn't really move the needle. It isn't a consideration, especially in distinguishing between a pre-filled syringe and an autoinjector.

SS: It's really about lowering the barriers to access and reducing the inertia from physicians and patients

alike due to increased convenience.

PU: Yes, and with the autoinjector increasing convenience and ease of use, which is likely going to be associated with increased adoption.

[00:09:17]

Q: As you alluded to, autoinjectors are typically syringe-based, but I understand there are a couple of cartridge-based autoinjectors as well. Could you walk me through the pros and cons of using the different formats?

PU: I think, clearly, the dominant format is a pre-filled syringe and an autoinjector and agree that we've seen a couple examples using a cartridge-based system. I think, and we'll probably talk about this as well, the advantages with cartridges are that a typical standard cartridge holds up to about 3ml of medicine and a typical pre-filled syringe is either 1ml or 2.25ml, and so that means autoinjectors are typically 1ml or 2.25ml. If your dose, which is established independently prior to choosing a device, for example, is 2.5ml or 2.6ml or 2.7ml, you might be considering something like a cartridge-based system in order to get all of the dose in a single injection by emptying a 3ml cartridge. That would be one pro for the cartridges. The con for cartridges is that it's an entirely different fill-finish operation, and so the way that you put the drug into that primary container, if it's a cartridge it's one way, if it's a pre-filled syringe it's another way, is very different. Cartridges have a stopper at both ends, typically it might require a separate needle attachment or some sort of integrated needle that is different than a pre-filled syringe for an autoinjector that's using a cartridge.

That fill-finish operation for many pharma companies can be a con because maybe they've built most of their industrialisation or even their contracting with CDMOs on a fill-finish operation for syringes, and now, if you have one product or two products out of, I don't know, 10, 20, 30, that are going to be in a cartridge, you have to design new equipment, you have to allocate new floor space for that, depending on the volumes. That, to me, is the biggest con with the cartridge-based systems, is if, as a pharma company or a CMO, you don't have significant experience or capacity with cartridge fill-finish operations, that's a big step change in investment. Now, on the other hand, if most of your business is cartridge-based, so take, for example, the insulin manufacturers who frequently were using cartridges in variable-dose pens, they're going to have significant fill-finish operations associated with cartridges, and maybe they've got a nice mix of the industrialisation capability and capacity for pre-filled syringe and cartridge. It's not going to be as much of a step change for them.

[00:13:26]

Q: Given that a pre-filled syringe is either 1ml or 2.25ml, does that imply that the choice of formulation and primary packaging container is part of the drug design and development process from the very beginning?

PU: I would say it's certainly early in the drug development and design process, and so, in my experience, those conversations with the formulation teams working on the drug development, where it's typically in phase 2 where you're establishing dose and you're doing those dose-ranging, dose-finding types of clinical studies, once you've established that dose you're starting to have a conversation about including your marketing team and your device team to say, "Who is the market for this? Do we want this to be self-administered? Is it safe? Does it have a good safety profile, good side effect profile where we think it could be self-administered outside of a clinic or hospital?" If that is the case, now you

have this dialogue with the formulation team and you say, "Here are our options. We can be in a pre-filled syringe at one or two-and-a-quarter, we can be in an autoinjector at one or two-and-a-quarter, we can be in a cartridge at 3ml, and here are the costs associated with each of those, and timelines for development." Now you start to work with your commercial and your formulation team to say, "What is the sweet spot for this?" What happens often with dose for especially biologic medicines is they can concentrate the liquid formulation in order to reduce the total liquid volume that has to be injected. The trade-off there is that viscosity tends to go up, and all pre-filled syringes, autoinjectors and pens, have a limit on how viscose a drug can be delivered in. The trade-off conversations that you have to have quite early are about dose size, viscosity, dose frequency, because your formulation team could come back and say, "The only way a person can get a single dose of this drug at a deliverable viscosity, we can get it down to 5ml." We have to have a conversation as a cross-functional team to say, "Does that mean we're going to ask somebody to do two subcutaneous injections at two-and-a-half with a cartridge? Is it possible to make this a weekly delivery? Is it possible maybe to consider going to an on-body injector monthly?" All those conversations need to start happening as the formulation and clinical teams are figuring out exactly what that dose size is and what the delivered volume and viscosity are going to be in. That's a long answer, but that is the conversation that happens early.

[00:17:20]

Q: Essentially, once you have the dose, you can then concentrate the formulation to the point that it can fit into the pre-established 1ml or 2.25ml pre-filled syringe and, thus, autoinjector formats. To that extent, more often than not, you can use an autoinjector because of the ability to concentrate your liquid formulation. However, as we move away from your standard mAbs [monoclonal antibodies] and towards ADCs [antibody-drug conjugates], bispecifics and other such therapies, the viscosity increases, which introduces challenges in concentrating the formulations. Are we going to get to a point where you can't fit these biologics into the currently available 1ml or 2.25ml formats?

PU: Yes, that's already happened, and I can tell you, especially having talked to peers in pharma companies that maybe have less well-developed device and formulation teams, sometimes the device teams get very absurd requests to say, "You told us you could deliver up to 2.25ml, we got this drug concentrated down to 2.25ml, but now the viscosity makes it like peanut butter or hummus." Imagine trying to push that through a tiny syringe, and you're now going to be running into physical challenges where your devices and syringes are breaking as you try and apply enough force to deliver that molecule through these small needles, and you're risking damaging the molecule itself. To the first part of your question, a formulation team could concentrate down to an appropriate volume, but if the viscosity goes too high, it will be impossible to deliver it. What we're seeing in the market is, because of that volume-viscosity trade-off and the desire to not have gigantic needles that are so painful that a patient wouldn't want to use them, we're finding the demand for these on-body injectors.

SS: What about cartridge-based autoinjectors?

PU: I think it's a small difference to go from 2.25ml to 3ml, and so that's a really narrow window of improvement.

SS: Are we not seeing larger-format syringes and autoinjector devices? Ypsomed, for example, has a 5.5ml YpsoMate. Do you not see the market moving towards higher-volume autoinjectors, as opposed to towards on-body injectors?

PU: I think we will see the adoption of the higher-volume autoinjectors, and that'll fill an important niche for therapies that are dosed between 2.25ml or 3ml and, say, 5ml or 6ml (inaudible 21.03), and so

that's useful and valuable because it avoids having to do multiple injections for a single dose. What we're also seeing simultaneously in the market is even larger volumes, so there's a pretty decent market for medicines that have to be delivered above 5ml per dose. They're typically either monthly or twice-a-year types of therapies, and that's driving the interest in the on-body injectors as well.

[00:21:43]

Q: Let's dig into the different demand drivers for autoinjectors. Starting with biologics – whether mAbs, ADCs, bispecifics, etc – there seems to be a well-understood structural shift away from vial-based therapies to pre-filled syringe autoinjectors and perhaps, to a lesser degree, pens. Could you put any numbers to the magnitude and pace of that shift towards standalone pre-filled syringes and autoinjectors?

PU: It's a good question. I think you have a couple of factors playing in there. One is the competitive environment helps shape some of this. Say you're pharma company X and you're introducing this new product, but it's not first-in-class, maybe it's best-in-class, I don't know that it would matter, but for sure it's not first-in-class, you're going to look at the competitive environment and say, "What's being offered on the market today? Is it predominantly pre-filled syringes? Is it predominantly autoinjectors? Is it mixed?" Especially if it's mixed, you have to understand why it's mixed, because you might, as a new entrant with that medicine, need to offer both a pre-filled syringe and an autoinjector. I'll give you an example of why it might be mixed. If it's a therapy that has been treated by patient self-administration for many years, there's a significant population of patients who will have only been using pre-filled syringes throughout their therapy. Say, for the last 10 years, there's been a self-administered therapy for disease X, you're likely to find a significant population of patients who've had the disease for a while and are very comfortable using pre-filled syringes to self-administer, but with every disease, you have the patients who've been diagnosed for a significant amount of time and you have the newly diagnosed patients. It might be that for the newly diagnosed patients, because autoinjectors are available and on the market, even in other disease areas, there's an awareness that there's this alternative method and you might see more of your newly diagnosed patients being prescribed and choosing the version that's presented in an autoinjector. As a pharma company, you have to look at the current market situation and not only know what that split might be between PFS and autoinjector but understand the reasons why, because you're going to develop, say, a 10-year forecast, and if you're expecting more newly diagnosed patients from the time your product launches, you're probably going to want to plan for a larger percentage of autoinjectors vs pre-filled syringes.

[00:25:18]

Q: As we'll come back to later, Ypsomed has essentially tripled its autoinjector capacity. What is the range of levers the company can pull to drive the utilisation of that capacity? The GLP-1 [glucagon-like peptide-1] is obviously the major driver, but if we look at the innovative and biosimilar biologic pipeline, could you guide our thinking on the proportion of that pipeline that's using autoinjector devices vs pre-filled syringes vs vials, and how that's changing?

PU: I'll give you my best guess, which is most pharma companies, if they're developing medicines for chronic diseases, so that's really where this opportunity for self-administration starts, is when you're addressing a chronic illness as opposed to something like breast cancer, for example, where there's a shorter time frame often associated with treatment and it's typically drugs that maybe don't have as good a safety profile. Both those factors play into saying that's not the market for pre-filled syringes, subcutaneous injection, etc. With chronically managed illnesses, that's where you're going to see the use

of a device for self-administration or home administration. I think as you look at the broader pharma market or any pharma company that's developing medicines for these chronic illnesses, if they're developing new medicines they're probably looking at maybe the competitive environment and saying, "If I'm developing, for example, a GLP-1, that market is dominated by autoinjectors and pens. It's rare to see somebody administering a GLP-1 with a pre-filled syringe." A lot of that decision-making early on was associated with patients who were new to injection as a concept, and so an autoinjector became the preferred format in that early market research because of the hidden needle, because of the ease of pressing it against your skin and the needle automatically being inserted and the drug delivered.

That made it much more appealing to patients, and so if, for example, you're looking at GLP-1s, you're looking at the competitive environment, and you're going to say, "I might only launch in an autoinjector if I'm developing a new GLP-1," but you might look at another therapeutic area, maybe rheumatoid arthritis or maybe ulcerative colitis and Crohn's, and you'll look at the market and what you'll see in the market is, "20% of these patients are using pre-filled syringes, 80% are using autoinjectors. What choice am I going to make, and do I think, if I only offered an autoinjector, I'd be missing some percent of the population, or am I going to steer towards newly diagnosed patients?" All those factors go in, and I would say, across pharma, we're seeing an increase in the use of devices across their portfolios because we're seeing an increase in addressing chronic illnesses that can have self-administration or home administration of the medicines, and we're seeing a shift away from pre-filled syringes towards autoinjectors because of the experience and feedback from patients about how convenient and easy it is to administer with them.

SS: It's not as if, to your knowledge, there are any data points out there that suggest – and these are made up numbers – 30% of the biologics market in these chronic indications, so ex-oncology, are using autoinjectors and the remaining 70%, prefilled syringes.

PU: I would say in a given therapy, it's probably, at best, a 60/40 mix, 60% autoinjector, 40% pre-filled syringe, and then individual therapies like GLP-1s are maybe 90%-plus autoinjector.

[00:30:32]

Q: GLP-1 – looking at Novo's semaglutide as an example – is offered in pen format in Europe and autoinjector format in the US. What do you think is the reason for the differences across regions?

PU: That is a good question. I don't know the exact answer why, but I can tell you my guess would be that it has something to do with these fill-finish operations and available manufacturing capacity and that the pen format is going to use a cartridge, the autoinjector format is typically going to use the pre-filled syringe. If you have a global launch like that, and you have experience, so that's one of the unique characteristics for some of the insulin manufacturers who have now gotten into GLP-1s, is that they have cartridge fill-finish experience, capability and capacity, as well as, maybe for some of their other medicines, pre-filled syringe fill-finish capability and capacity.

[00:31:56]

Q: As the fill-finish bottlenecks ease, do you think we'll move towards an autoinjector-only world, whereby the European and US devices are autoinjector, or do you think the opposite is true and we could move towards pens?

PU: It's a good question. I think the other factor that may have come up with semaglutide is by putting it in a pen, in some configurations there's an opportunity to use a pen's function for dose-dialling to handle your titration. What I mean by that is, for a lot of these especially GLP-1s, the patient's first doses, maybe over the first five or six months, are lower than the dose they're going to be on for the rest of the time they're taking the therapy. You want to titrate up to the therapeutic dose in order to reduce the incidence of side effects and the severity of the side effects of starting with the highest dose on day one. The way you do that with an autoinjector is you have two SKUs. You have a small-dose autoinjector and a larger-dose autoinjector, and maybe the patient gets prescribed the small dose for the first six months and the large dose going forward after that. There's potentially an opportunity with a variable-dose pen, even if the variable dose is just dose one, dose two, to have that exist in the same SKU.

SS: I suppose, given the magnitude of the syringe fill-finish capacity that is being built out both at captive and CDMO [contract development and manufacturing organisation] sites, it's likely that the direction of travel, at least for the foreseeable future, will be syringe-based autoinjectors. Is that fair to say?

PU: I think so, but my only caution against making that broad generalisation would be, and I don't have this feedback, but I would want patient feedback about whether there's an advantage to using the variable-dose pen. I think the pre-filled syringe with an autoinjector is even easier for patients than a pen format, because, with a pen, you have to attach a pen needle and detach the pen needle.

SS: You can't use a syringe with a pen, it's only a cartridge. Is that correct?

PU: Right, and so I think your broad general statement is probably true. If all fill-finish questions were resolved, I think, at the end of the day, the pre-filled syringe with an autoinjector ends up being easier for everyone.

[00:35:16]

Q: Speaking of autoinjectors, I believe Novo Nordisk uses SHL Medical's Molly platform for Wegovy. Is that correct?

PU: I'd only be guessing, so I can't say for...

[00:35:36]

Q: Is there anything that makes a good autoinjector device for patients with obesity? Are there any specific requirements here?

PU: There are a lot of human factors, considerations that go into designing these devices, and some of them are very patient population-specific. I think specifically to obesity, my opinion is there isn't anything that stands out as unique in an obesity population that would require an autoinjector to have a certain set of features or capabilities that they don't all have. Today, the biggest difference in autoinjectors is whether it's a two-step or a three-step autoinjector, and that mostly has to do with the patient's confidence in performing the injection. Otherwise, the basic functions are nearly identical.

[00:36:54]

Q: We know that, for example, Eli Lilly has moved to vial formats, presumably as a near-term stopgap in light of shortages for tirzepatide. I've heard that Novo Nordisk may be exploring vial-based formulations as well. We know the the semaglutide patent is expiring in China in 2026 and there could be generics in other markets around that time as well. If we think about the demand outlook for autoinjectors vs vials, what are your expectations in western markets and some of the pharmerging markets?

PU: I think in the western markets, like you said, the vial format is a stopgap because we haven't achieved fill-finish nirvana where all of those capacity issues are resolved. I think the opportunity with vials is in lower-economic-resource markets, because the cost of goods ultimately can be lower by delivering vials to those markets. It's a much simpler fill-finish operation, it's a well-understood primary container. I would expect in western markets, I would be surprised if we see much vial and disposable syringe use, but in economically underserved markets, I think that will be probably the dominant option.

[00:38:47]

Q: How exactly does the assembly process work for the packaging of a sterile-filled, prefilled syringe or cartridge into an autoinjector or pen, respectively? Is that performed by the fill-finish CMO [contract manufacturing organisation]? Is that usually done by a separate third party such as captive pharma facilities, or players such as Ypsomed or West Pharma?

PU: Yes, it's a mix depending on the pharma company's internal capabilities. I would say basically you have the manufacturer of the pre-fillable glass syringe or plastic syringe, so the pre-fillable syringe, companies like Becton Dickinson and Stevanato and Schott and Gerresheimer, and a pharma company is procuring X volumes of those pre-fillable syringes and having them shipped to a filling site. That filling site could be an outsourced CMO or it could be the pharma company themselves, depending on their capability and experience. The pre-filled syringe gets filled and stoppered at that site, so when it's filled and stoppered, and say it's in a nested tub, then some CMOs have the ability to start the assembly of the pre-filled syringe into the autoinjector components. They likely wouldn't finish the assembly, but they may be able to, for example, insert the pre-filled syringe into the front end of the autoinjector and then ship those components to the place where there's the final assembly and packaging operation. That's another example where maybe that's the pharma company, maybe the pharma company chooses to own final assembly and packaging operations, maybe it's another CMO, and so you've got pre-fillable syringes getting filled and stoppered, and that's one company, next company might be doing final assembly and packaging or just final assembly, and then third place is doing packaging and sending it out to distribution. Again, depending on the maturity of the pharma company, all of that could happen within their four walls or maybe it's really one CMO and the pharma company. I would say, on average, it's probably one CMO and the pharma company, where the pharma company does the final assembly and packaging and sending it out to their distribution centres.

SS: The fact remains that the final assembly requires specialist equipment that is distinct from the filling lines.

PU: Absolutely.

[00:42:15]

Q: We understand that the major bottleneck for the GLP-1s up to now has predominantly been fill-finish. Relative to the sterile fill-finish capacity that has been built out for syringes, how much capacity for the final assembly of these primary packaging formats into their respective devices has been built out alongside that? I spoke with a specialist in a previous Forum Interview [see Fill-Finish CDMOs – Capacity Utilisation, Inventory Dynamics & Demand Outlook – 20 Sept 2024], and my understanding is that we're already at 100% utilisation of the 1.2-billion-1.4-billion-syringe fill-finish capacity in western CMOs [contract manufacturing organisations]. We're also going to see an increase over the coming years of another 1.2 billion in 2025 and another billion in 2026. Relative to that capacity build-out, how much capacity do you think is being built out for the autoinjector final assembly?

PU: It's a good question. I certainly don't have a number, but what I can say from talking to my peers in pharma, my impression is that they're less worried about the final assembly capacity. I think there are more options for that. It requires less controlled environment the way fill-finish requires, because you're no longer handling the molecule, the medicine. I think you see more opportunity for pharma to build out that final assembly capacity, but my impression, just from talking to folks in the market, is they're less worried about that capacity than they were about the fill-finish.

SS: You don't see a scenario whereby the bottleneck just moves downstream from fill-finish to the final assembly of the device?

PU: I don't think so. I'd be surprised if that happened.

[00:44:30]

Q: Outside of GLP-1s, how much concern is there around the availability of autoinjector devices more broadly? Are non-GLP-1 pipeline programmes increasingly opting for prefilled syringes due to potential supply risks?

PU: It really depends on the unit volume. GLP-1s just are such a gigantic market that the unit volumes are so high. I think even for some of our medicines that are in autoinjectors in other therapeutic areas, the unit volumes are a rounding error compared to GLP-1s, and so not as big of a concern.

SS: Are you seeing your pharma peers increasingly opt for prefilled syringe devices, as opposed to autoinjectors, simply because of concerns around the availability of fill-finish or final assembly or, indeed, the availability of the devices themselves in the first place?

PU: I haven't seen them opting for PFS due to that. We already talked about the Lilly, Novo examples of vials because of the fill-finish, but I haven't heard that anyone is looking at a PFS vs an autoinjector due to some sort of capacity constraint.

SS: To confirm, outside of Novo Nordisk and Eli Lilly, we aren't seeing ex-GLP-1 pharma pipelines look at vials when previously they were looking at prefilled syringes or autoinjectors.

PU: I think if they are looking at vials, the question is are they looking at different markets than the western markets, and is that what's driving that choice?

SS: It goes back to what we discussed earlier around Western regions vs pharmerging.

PU: Yes.

[00:46:32]

Q: Let's discuss Ypsomed. As you've alluded to, there are several players with off-the-shelf autoinjector IP. There's SHL, Nemera, Owen Mumford, West Pharma, Gerresheimer, Jabil and Ypsomed, to name but a few. Could you walk me through Ypsomed's competitive positioning relative to the aforementioned players, or any others I didn't mention, and what makes any player stand out?

PU: I think, in my opinion, the two stand-outs in the market today are Ypsomed and SHL, and a lot of that has to do with their significant experience with autoinjector design and development, and the number of customers and products that they have on the market. I would first segment those two contrasted with everyone else in your list, for a couple of reasons. Everyone else in the list, like Nemera, Owen Mumford, West, Jabil, individually some of those companies have a design but next to zero experience actually commercially launching, while others in that list have some experience commercially launching an autoinjector. That level and duration of experience really matters, especially to a pharma company that's looking at global launches. A lot of that experience comes down to knowing how to work with a pharma company. The conversation we had earlier about the device team and the commercial team and the formulation and the clinical team having this cross-functional conversation about how to optimise for this, a very similar conversation has to happen about an autoinjector, making sure that a particular pre-filled syringe format, the needle dimensions... even though we're talking about 1ml capacity and 2.25ml capacity, it doesn't mean that every medicine is delivered at either 1ml volume or 2.25ml volume.

You fill to different levels depending on the dose, so even just understanding, "How well can this autoinjector manufacturer understand the autoinjector device configuration that's required if we're putting 0.5ml in a plastic pre-filled syringe with a 27-gauge needle vs our other medicine that's going to be at 1ml in a glass pre-filled syringe with a 29-gauge needle? Does that autoinjector manufacturer know how to accommodate all the available pre-filled syringes? Do they know which dimensions are subject to the greatest tolerances or not, etc?" I think what we see with Ypsomed and SHL is that experience and capability. Then if I were to distinguish between Ypsomed and SHL, to me, it comes down to classic customer relationship management. Of course things like unit price, volume and cost of goods and ability to work with your supply chain matter, but I would say especially contrasting those and comparing those two, if a pharma company is looking at SHL vs Ypsomed, they're going to be looking at that customer relationship management and how well they can work and integrate with the device and the pharma team, etc. It becomes more of those classic B2B factors that have nothing to do with the autoinjector that end up being most important.

[00:51:13]

Q: Based on what you've heard from colleagues, is there a difference between Ypsomed and SHL in the more traditional B2B service-level metrics?

PU: I think at least what I've observed is that Ypsomed seems to do a better job having a strong, positive, customer-oriented service operation, and so their willingness to collaborate, their willingness to engage early, I guess, from what I've observed, I've been impressed with how they've managed those relationships.

[00:52:13]

Q: Specialists in previous Forum Interviews have outlined how SHL has frustrated, for want of a better word, some of its customers and has somewhat of a bad attitude. Are you aware of the company alienating its customer base?

PU: I've heard the exact same thing and observed the exact same thing.

SS: Do you think this is why Novo Nordisk may have switched from the Molly platform to the YpsoMate as it goes towards CagriSema [cagrilintide/semaglutide]?

PU: That's a very good question. I would say it could be one of multiple important factors.

[00:53:11]

Q: Do you think there's a fundamental technical difference between the SHL Molly and Ypsomed's YpsoMate that makes it better-placed for the GLP-1s or higher-viscosity biologics that are coming down the pipe?

PU: In my opinion, no.

SS: It really comes down to the reputation, the service level and the technical know-how it has in-house.

PU: Yes, and that also includes ability to deliver on time, the quality of what's received, the ability to integrate with the team. If company A or company B have a similar product, but company A can deliver it to you six months faster than company B, but maybe company A is not as great managing their relationship, that's going to be an interesting conversation inside the pharma company about, "Do we want the good relationship or do we want the drug faster to market because we make a lot more money every day we get it out sooner?"

[00:54:33]

Q: Has SHL had DIFOT [delivery in full, on time] issues?

PU: No, not that I'm aware of. I'm just giving that as an illustration of it's more than just the relationship that goes into some of these choices.

[00:54:52]

Q: You mentioned vertical integration or supply chain management. I know Ypsomed is integrated into Ypsotec, for example. Is that a differentiator as well, so Ypsomed being integrated into the milling of components and so on, or not really?

PU: I guess it would be demonstrated in what I was talking about before about this fundamental understanding of tolerances and the overall system design. In terms of having access to, I don't think it's an advantage, but if it means their development teams can move faster or answer questions better about key system design aspects, then it could be an advantage.

[00:55:52]

Q: As you've alluded to, it seems there have only really been two horses in the race until recently. In Ypsomed's FY24 earnings call, management said, "Our space is pretty limited. It's basically SHL and Ypsomed," and I think, by that comment, the company is referring to the available capacity and the pedigree these two players had in this particular space. However, it's clear that players such as Gerresheimer are investing significant resources here. The company has launched or is going to launch an autoinjector device that specialists in previous Forum Interviews have highlighted as being particularly exciting. How significant are the aforementioned reputation- or pedigree-related barriers to entry for a player such as Gerresheimer as it builds out its platform and manufacturing capacity?

PU: If we contrasted somebody like Gerresheimer with a completely new entrant, the advantage that Gerresheimer would have would be its long-standing role in drug delivery for pharma companies, and so maybe, in a way, they're forward-integrating into the value chain by getting into autoinjectors. Their advantage is going to be historical experience and recognition by the pharma industry as a player who understands some key aspects of drug delivery. That would be an advantage Gerresheimer would have over, for example, a completely new entrant who had some sort of novel autoinjector technology. To me, the key question for a company like Gerresheimer is going to be how are they going to try and differentiate themselves against the Ypsomeds and SHL. If, for example, they're going to say, "We just have additional capacity, and so our autoinjector design meets table stakes, but it isn't anything special, but we can give you additional capacity," that is a way they could try to compete, but I think if they want to truly compete against the SHL and Ypsomeds of the world, they have to bring all of these things to the table.

SS: Do you think a player such as Gerresheimer can, given its legacy in this space across other medical device formats, its positioning as one of the larger players for primary packaging solutions, the reputation it's built in that particular sub-sector, etc?

PU: I think, on the one hand, I would say they can if they do it right. I can draw a little bit on my experience at BD, which is a dominant player with pre-filled syringes but is not the dominant player for autoinjectors and pens. They have autoinjector and pen share, but that reputation and ability to show your success is a key factor, especially for the bigger pharma companies. It might require that you slowly build your portfolio, for example, as Gerresheimer, maybe they slowly build their portfolio of wins with autoinjectors, but it's not maybe necessarily going to be with the biggest pharma companies. When they show up and present to a device group at a pharma company, they need to be able to show the experience they have, and maybe they get that experience with smaller pharma to start.

[01:00:06]

Q: I understand autoinjectors – ie, the YpsoMate – are driving more than 50% of Ypsomed's delivery systems revenue, and upwards of 75% of new project acquisitions. The company has also disclosed plans to ramp its capacity to one billion devices per annum by 2030, which is a tripling of its current capacity. Yet, as we've discussed, it seems there's a long tail of players looking to enter the autoinjector game, Gerresheimer being but one. What do you think is the risk of this space becoming increasingly commoditised? How would such commoditisation pressures manifest themselves? Would that be on price? Will we see Ypsomed struggle to drive the utilisation of its new CAPEX projects?

PU: I think if the GLP-1 explosion continues or if we have one more therapeutic area that looks like GLP-1s, I would almost argue it should become somewhat commoditised. I think the competitive advantage for the pharma companies is going to be, if they're in these super high-volume autoinjector

therapeutic areas, in other things that they're offering around those. For the Ypsomed, Gerresheimers, SHLs of the world, the opportunity to extract more value from a non-commodity autoinjector is going to be in other therapeutic areas where maybe there are more specialised needs.

[01:01:57]

Q: Given all of the competition from Gerresheimer and so on, how do you see Ypsomed's typical price per unit for the YpsoMate evolving? What is it today, and where do you see it trending?

PU: I think at the basic level, when these companies are dealing with our procurement functions, it's coming down to a comparison of these unit costs, and I would go back to the trade-off that I talked about earlier for us as pharma companies, which is if we can get to market sooner, we make a significant seven- and eight-digit millions more per year by getting to market sooner. Unit price is one in a Pugh Matrix of factors that we're considering, but timeline is maybe a higher priority in some therapeutic areas.

SS: Nevertheless, as all this capacity is built out across the range of competitors, do you see price per unit, on average, decreasing for the autoinjector?

PU: Yes, for sure, and I certainly hope for it as the customer.

SS: By how much, do you think?

PU: Good question. We already do volume-based pricing today, and so if we're saying, across all those different volumes, what percent would we expect it to drop as we get more and more of these on the market and new competitors enter, maybe a 30% drop over the next 10 years.

[01:03:53]

Q: Let's revisit what we were discussing vis-à-vis the demand for autoinjectors going forwards. In terms of the emerging biologics pipeline, the biosimilars, GLP-1s and perhaps some of the other evolving therapeutic areas – such as Alzheimer's, which is increasingly moving towards subcutaneous – do you think that, within that alone, there is enough demand to ensure that Ypsomed could drive high 80-90% utilisation of the one-billion-device manufacturing capacity that it plans to have online by 2030? Or, do you think, given the competition and the pace with which that biologics pipeline will transition away from more legacy formats, that there could be a world where it's reasonably operating at under-utilisation?

PU: My opinion is we are just seeing the beginning, and I'd be surprised if any time in the next 10 years we're seeing under-utilisation of autoinjector capacity. With all the competition, I'd be surprised.

[01:05:15]

Q: How do pharmas think about in-sourcing CDMO-owned IP, or off-the-shelf platforms, vs using in-house pharma-owned IP? If we look at Novo Nordisk, we discussed how it uses SHL's Molly for semaglutide, and we know it's using Ypsomed's autoinjector for CagriSema [cagrilintide/ semaglutide]. However, Novo Nordisk did buy Biocorp in October 2023, so it now owns medical device

capabilities in-house. We also know it has the FlexTouch pen IP in-house, which it's using for semaglutide pens in Europe. Eli Lilly owns the IP for its pens and autoinjectors as well. In a world where we have more and more GLP-1s on market and these therapies, as you alluded to, are competing on the device as well as the clinical data, do you see players such as Novo Nordisk, Eli Lilly and other biotechs looking to develop their own in-house IPs to differentiate?

PU: I think Novo, Lilly, and also I would add Sanofi to that mix, are special because of their history with insulin, and that's the only reason you can profile them the way you have profiled them. I'd say for, quote, unquote, the rest of us in pharma, unless it's a special therapeutic area with very specific needs, most of pharma is not looking to own that IP.

SS: The faster time to market, the lower TCO [total cost of ownership], the improved risk profile associated with using CDMO platforms as opposed to developing in-house IP, all of those advantages hold true in a GLP-1 world. Is that correct?

PU: I think so, especially in GLP-1.

[01:07:17]

Q: We know Novo Nordisk is using Ypsomed's autoinjector for CagriSema, and we know Ypsomed will be manufacturing 50% of the volumes. Other CMOs will be manufacturing the remaining 50%, for which Ypsomed would get a licence fee. For such a high volume contract, what kind of royalty structure could Ypsomed capture for outsourcing its autoinjector platform to another CMO to manufacture?

PU: In actual dollars or Swiss francs, is that?

SS: In percentage terms, so if Ypsomed is out-licensing the YpsoMate platform to Phillips Medisize, or West Pharma, then how much is Ypsomed capturing as a proportion of the unit cost that Phillips Medisize is selling into Novo Nordisk?

PU: Really good question. I don't have a great basis for giving you a good estimate, but even on the commercial side, I would say if they could get 30%, that would be maybe at the top end.

SS: 30% royalties, so if Phillips Medisize is selling the autoinjector at USD 1, Ypsomed will get USD 0.3 on that?

PU: Yes.

SS: Specialists in previous Forum Interviews said it was probably closer to 10-15%. To use you as a soundboard, do you maintain that 30% is most likely, or would you adjust that?

PU: I would say 30% at best. It depends on the duration of the contract, it depends on the volumes. I could give you a very broad range and say anywhere between 15% and 30%, depending on whether you want an optimistic or a pessimistic...

[01:09:33]

Q: Specialists in previous Forum Interviews assumed that Ypsomed or SHL would be selling the

autoinjectors used for Wegovy at around USD 1.5 per device. Do you agree with that? Do you think the calculus would be any different for CagriSema?

PU: No, I think that sounds about right.

SS: You think it wouldn't change much for CagriSema.

PU: No.

SS: We will conclude the Interview there. Clients, thank you, and thank you, Paul. Everyone, have a wonderful morning or afternoon.

PU: Thanks, take care.

SS: You too, sir. Bye-bye.

Transcription ends at 01:10:15 of the recorded material

If you'd like to speak to Paul Upham in a private call or meeting, please let your relationship manager know.