the art of boring™

EP 234 | Consumer Biotech: The Value Chain Beneath the GLP-1 Boom



[00:00] [Rob Campbell] [RC] Coming up on The Art of Boring: with all eyes on AI, what are some of the other areas seeing transformational changes in demand? Equity analyst Josh Samuel joins me from Singapore to dig into peptides, the drug class behind the blockbuster obesity treatments that you've all heard of, and the often unglamorous suppliers in the manufacturing chain underneath them. Along the way, a LEGO analogy, some similarities with semiconductors, and a fair degree of chemistry—the chemistry of peptides, that is, not the chemistry between me and Josh. My conversation with Josh, up next.

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[00:50] [RC] Welcome back to the podcast.

[00:53] [Joshua Samuel] [JS] Rob, good to see you again, and good morning.

[00:56] [RC] Thanks for staying up late in the day for you out in Singapore. I was looking back. I think it's been about two years since we last spoke about GLP-1s on The Art of Boring. I know you've been spending time in the space. Can you give us a sense of why you're spending time there and what's been happening?

[01:12] [JS] To make a long story short, the growth of GLP-1s has been exceptional. There's basically been no drug class like this. GLP-1s, since Ozempic was launched, have ramped to 44 million users within five years.

For context, compare that versus, say, the top three blockbuster drugs in small molecule—small molecule is the class of drugs similar to Panadol and the tablets that you take—and large molecule, which has been biologics, or the more popular drug over the past maybe 20 years. GLP-1 has basically ramped in a way that is beyond the blockbusters of any of these other drug classes. That's what got some of the interest.

But then the other part of it was understanding that you could say it's a different kind of molecule in itself, with its own value chain. With that comes a lot of opportunity in digging down the value chain, because effectively you'll see a new asset class being created within the pharmaceutical land.

If you put the numbers aside, I think at a high level what's interesting for me, and I heard this at a conference a few weeks ago in Europe: you can think of GLP-1s, or peptides—I'm going to use them interchangeably—as being what they call consumer biotech. Previously, drugs, you're taking them for illness or something like that.

GLP-1s came about to treat diabetic patients. But I think what's happened is that it's become a bit more than that. It's become mass market, and hence the name consumer biotech. That's the reason why there hasn't been



anything like this in the pharmaceutical land. It is pharmaceuticals, but it's going beyond that to something that's available to the masses.

[02:49] [RC] You mentioned a couple of terms that I'm wondering if you can better explain for listeners and for me: small molecules, biologics, and this new class of peptides. What's different about small molecules?

[03:00] [JS] You can think of them as drug products that are synthesized from chemicals. Effectively, small molecules are what's been around for over 100 years. I will use the example of Panadol once again, because at least in Asia, it's very popular. You take it when you have a fever. It's synthesized from chemicals, and you could trace this back to petrochemicals, effectively.

In scientific terms, it's stuff that weighs less than 1,000 daltons. That's how you put a molecular weight on these products. And then there are large molecules, which have been, the area of focus in the investing world over the past maybe 20 years. They're also called biologics, and these are much larger molecules, which weigh over 10,000 daltons. To create a small molecule, you use chemical synthesis. But to create a large molecule, you typically use a fermentation process.

I'm not a doctor or PhD scientist, just a business school guy. But in my simple layman's terms, one is done with chemical synthesis, one is done with fermentation, and they are really different classes of size. One is much bigger than the other.

And peptides sit in between. Up to the point of GLP-1, peptides were a ridiculously small market. If you, as a pharmaceutical innovator, placed an order for, let's call it 100 kg of peptide API—API is active pharmaceutical ingredient, or in simple terms, think of it as the drug substance, the stuff that makes your drugs—you order 100 kg of it, let's call it maybe five to seven years ago.

The CDMOs, which is contract development and manufacturing organization, or you could think of them as the Foxconn or the contract manufacturers that supply the pharmaceutical guys, those guys would be popping champagne. That would be considered a super large order, probably putting you in the top 10 globally for the year, done for the year. But that's because it was a niche asset class.

What's really interesting is that with GLP-1 and this whole class of drugs that has grown, people are now ordering in the tonnes. There's been a huge step change going on in the industry.

[05:01] [RC] You've seen a massive jump in demand for these peptides, GLP-1s being one of them. Of course, the major use case is targeting weight loss. Isn't this behind us, though? Eli Lilly's stock price has been on a tear for several years. Why are you looking at this now?

[05:17] [JS] The first layer that benefited from this was the innovators. Eli Lilly and Novo Nordisk stock prices have been great for a variety of factors, execution-related, etc. But then I think what's interesting now is that some of these drugs are going off patent. That's really interesting to us because, from the innovator side, your pricing is as good as it gets. But when these drugs go off patent, we're talking about a further increase in the total addressable market. Recently, Sandoz, which is a Swiss generic manufacturer, at their capital markets day were estimating that this could increase the size of the market by another two to seven times over the next, I think, five



to 10 years. I think from a volume perspective, we're still in early days. And that's just one part of it. The second part is the introduction of oral peptides.

So far, most of these drugs, or let's call it 90%-plus of these drugs, are being delivered through subcutaneous injections. What's being pushed now into the market is oral pills. The market is expanding to two delivery mechanisms.

When you combine these factors, I think it's quite an interesting setup, where you have generics entering the market and you have oral pills, which are also coming in.

What excites me is the value chain that sits underneath the innovators. We can talk about the CDMOs. We can talk about the consumables that are used to manufacture peptides. But with volume growth, there are going to be a lot of beneficiaries, and we're at the inflection point where some of these companies are starting to become big enough in the entire investable universe.

[06:48] [RC] Can you talk a little bit more on the oral side? It's my understanding—you mentioned APIs before—these drugs delivered orally required a step function more in terms of APIs.

[07:03] [JS] A peptide comprises amino acids. Tirzepatide, which is the popular one by Eli Lilly, is a 39-chain amino acid. Amino acid is something like protein, so your body tries to ingest it as a pill.

That's why most of these drugs are being delivered subcutaneously. They call it bioavailability. The bioavailability if you're using an injection is over 90%. If you were to take it as a pill, your body is going to try to eat it. So the bioavailability, if you don't do any funky chemistry work, is probably down to less than 1%. In theory, you go from something that's 95% efficiency to less than 1%.

In theory, you would need 95 times more drug substance, or API, going from an injection to an oral pill. Of course, companies like Novo Nordisk have been innovating here. More realistically, with a bunch of other technology, they're able to get it down to something like a two to four times increase in the amount of API. That's if you're Novo Nordisk. If you're not Novo Nordisk, you're probably talking about somewhere in the range of eight to 10 times, based on our conversations with some of the contract manufacturers. Nevertheless, we're still thinking about a step change in the amount of drug substance required.

Why this is important is because it's the same: whether it is an injection or an oral pill, the API is the same product that you have to buy from a contract manufacturer.

[08:28] [RC] There's been this explosion in demand that may benefit the innovators. However, they're coming off patent, and whether it's two to four times or more than that, the explosion is going to benefit those who are further down the value chain. Can you take a moment to explain how peptides are actually made? I think that will give us some insight into where those bottlenecks might be.

[08:47] [JS] The way you manufacture a peptide is very different from biologics, and it's quite different from small molecules. Remember, I said tirzepatide, which is Eli Lilly's flagship product at the moment, is a 39-chain peptide, meaning there are 39 different kinds of amino acids that are linked together. Think of it as a LEGO block.



You first have the base plate, which is a resin. For simplicity's sake, there are two ways of doing it. There's fermentation, which Novo Nordisk uses, but I'm talking about Eli Lilly here, and they've chosen to use chemical synthesis. So you have a base plate, which is the resin, and you assemble the LEGO block piece by piece, and when I say piece by piece, it's 39 different pieces.

You put in the first amino acid, you flush it out with solvents, you put in the second one, and so you assemble the block. Now, there's been innovation here, and what Eli Lilly does is they do it in fragments. So maybe there are concurrently three or four different fragments that have been built, and then they combine the fragments together.

But long story short, it's still LEGO. There's a bit of a TSMC story here. We've invested in semiconductors, and one thing we've learned is that when you have a multiple-step process, the yield starts to become very important. We are talking about 39 different steps. Having a 99% yield in each step, it starts to compound the errors over time, so end-yields will actually be much lower.

And so the process manufacturing know-how becomes very important, which is why we've invested in some CDMOs, because process engineering is key, execution is key, and these guys are able to figure out the yield side of things very well.

Starting with the resin, you build the LEGO blocks. Once you're done with it, you then have to purify it, because we need the exact 39-chain peptide to be the stuff that goes into your bloodstream. You can't have the 38-chain or the 37-chain peptide or the 40-chain peptide.

The final process is called purification, where you use a different kind of resin. This is called silica gel. It's very interesting because you need the precise type of silica gel to ensure that the silica gel is more or less the perfect fit for that kind of peptide. The peptide sticks to the silica gel, whereas every other impurity gets washed off. That's the manufacturing process behind peptide production.

[10:56] [RC] Through that chain, Josh, where are the biggest bottlenecks? From my seat, I have no idea what seems easy, what seems hard. What are the key parts in that chain?

[11:06] [JS] I'm going to focus on the parts that we think are most investable. The final step, which is purification, is one that you can't really escape. If you're doing fermentation, which is what Novo Nordisk is doing, or if you're doing chemical synthesis, you still have to purify your product at the end of the day.

We actually found out there is one company that has about 70% market share globally for this step. It was a quite discovery for us because it's a specialty chemicals business. It doesn't screen up as a healthcare company.

When we came across it, on the typical screening, you would say it's only 15% or something like that of its sales, which is the healthcare. But this business is so profitable that it is generating almost 40% of its profits at the moment. Those are the areas of the value chain that we like, where there are companies with a moat that dominate a mission-critical pinch point in the value chain.



Why is it mission critical? Because remember, yields are very important. I'm probably exaggerating it if I say it's the same as TSMC. It is much simpler than that. But you want to make sure you get the highest yield from every step.

This purification is used in multiple steps. When you're doing the fragments, you need to purify that too. But you also need to purify to make sure you get the right drug substance. It's the same media that is used for these purification steps, be it in the front end or back end.

If you choose a suboptimal type of silica gel, you get a lower yield. That will affect your cost; it will affect the whole ROI of your manufacturing setup.

[12:29] [RC] There's one other thing specific to healthcare, I believe, that may be different than semiconductors. Can you talk about how drug approvals actually encapsulate the manufacturing process too?

[12:40] [JS] First, you have the preclinical work. Once you get an approval to test the drug, it goes to phase one, phase two, and phase three trials. These are multi-year processes.

Typically, once you're past phase two, whatever vendors you are using, be it on equipment or consumables like the silica gel, they're more or less locked in. If you were to change it, or try to change the manufacturing process, you would basically have to go and file for approval and redo the tests. It's expensive and time-consuming.

You don't want to do that because—this is more for the innovator side of things—time to market is of the essence. You want to be first to market. The longer time you take to go to market, you're going to have a shorter patent-protected period or exclusivity period.

Typically, once your consumable is locked in in phase three, it's very difficult to switch. It's not worth the administrative hassle: you're going to save a few hundred thousand dollars, but then you're going to have to pay maybe a million bucks somewhere else. It's not worth it in the grand scheme of things.

[13:37] [RC] Can I stick with your semiconductor analogy? A huge explosion in demand, with bottlenecks potentially on the manufacturing side of things, and with specific companies owning really key parts of that manufacturing process in extremely niche aspects, whether it's silica gels or others. What else is the same, or what else is different, about that comparison between those two sectors?

[14:02] [JS] Outside of the AI trade, which is very popular, there are still other parts of the market that are growing. What I want to say is that this is an area where there's actually still very decent growth. I was looking at one team report. They were talking about a 9x increase in API demand associated with peptides. Most people would guess that's semiconductors, but it's actually peptides. The growth potential is somewhat similar, as a high-growth market.

It's driven by multiple factors. I want to discuss the introduction of oral peptides, which is additive to the market. As far as due diligence, I actually went to go and see an endocrinologist, just for fun, and to understand why I should take peptides and stuff. He was explaining to me how the oral pills are actually meant for a different type of patient than the injectables.



The injectables are probably, you could say, for the more serious cases. They're meant for obesity, people who have heart conditions. And then on the fringes, oral pills can make more sense for people who have fewer pre-existing conditions or less serious weight-loss targets that they need to hit. That's what's happening in the market right now: injections are still growing, but oral is also growing at the same time. That's one interesting angle: you have multiple idiosyncratic growth options that are driving this sector. There's the oral pill, and there are the generics that are coming in. Those are quite big forces behind it. And then, not to mention, there's the innovation that's going on. The game is not over for Eli Lilly and Novo Nordisk.

What's going off patent is what we call single agonists. These drugs are trying to target a particular hormone receptor. When you say a GLP-1, it's targeting a GLP-1 receptor. That was the original stuff that we are talking about. But what Eli Lilly and Novo Nordisk are doing is that they're now having dual agonists and triple agonists. Tirzepatide targets two receptors, GLP-1 and GIP. Triple-receptor peptides are targeting three.

Why are people doing that? It's because it's more effective. You get better weight loss with fewer side effects, for example. We're talking about: can you lose weight without losing muscle mass? And we're talking about surgical-level weight loss here. It's the holy grail.

The growth we've seen so far has been driven by innovators, and that's what really excites me. The base case is that this thing is still going through innovation. And then you have the 2x to 7x potential increase from generics opening up the single agonist market. It's very interesting to have seen so many growth options.

The final piece on growth, I would say, is Novo Nordisk. They are really betting heavily on oral peptides. In fact, at their capital markets day a few weeks ago, I think they mentioned they're going to 10x their oral peptide capacity. I did the math on that. The 10x in oral peptide capacity, if you assume a 2-4x step-up in API between oral and injectable, is equivalent to the entire market right now, coming from one company.

For anyone who's doing the silica gel or some of these other consumables, you can see how there are multiple ways to make money. You don't need all the stars to align. Just some of them aligning would already be enough to decently grow the market.

[17:21] [RC] High growth—does that come with high valuations too?

[17:25] [JS] We first started investing in this sector at the start of this year, and it wasn't on the consumable side. It was actually on the CDMO side. We were getting reasonable valuations; we were getting IRRs in the low double-digit range. I think that's partially thanks to the whole AI trade, because the AI trade has been taking a lot of attention and focus away from other sectors. Earlier, at the start of the year, when we first identified there could be opportunity here, people weren't already pricing in some of these growth options.

Unfortunately, on the CDMO side of things, what has happened is AI drug discovery has become the new buzzword. There's been some hype around that, which has meant valuations can be quite volatile. Then people start to ask, is this going to be an AI bottleneck? Oh no, not again.

But on the consumable side, I would say that some of the companies we've bought—silica gel, 70% market



share—were trading at 16 to 17 times earnings. The market is not dumb. There's risk: the rest of the business is caustic soda manufacturing, which is very sensitive to energy prices. You can imagine what's going on in the world right now with the Middle East and oil prices. That's not great for the business.

But I think this is the beauty of our philosophy: we're looking out three years, five years, and this peptide business is going to grow. There are multiple ways the market grows multiple times. A 20% to 30% growth rate sustained over a three- to five-year horizon isn't too extreme for some of these businesses.

And you consider: this business has 40% of its operating profit already from a silica gel that is used for peptide manufacturing. Three years from now, four years from now, this business is going to look more like a healthcare company than a specialty chemical business. Pharmaceutical consumable companies in the U.S. trade at 25 times EBITDA in developed markets, and this business is trading nowhere near there.

So this is one of those situations where you're paid to wait, and the market wasn't pricing it in. It's not treating the stock like a healthcare stock. It's treating it like a specialty chemical stock.

[19:30] [RC] We've spent most of this conversation focused on a very specific part of the healthcare arena: the value chain with peptide manufacturing. But you mentioned you were just at a healthcare conference. Josh, to close here, I wonder, can you step back a bit? What are some of the other bigger trends in the healthcare space that you think are worth paying attention to?

[19:56] [JS] The most cliché one is going to be AI drug discovery. But I would say that's actually not the thing that interests me the most. There are so many other trends beyond that. There are changes in regulation that will mean there are winners and losers in some cases.

The simple one is the implications of the changes in regulation for analytical software, because what's happening globally is that it's becoming easier to launch a biosimilar, which is the generic for a large molecule. Previously, you needed to do phase three trials, and that's been curtailed. But to replace that, there's more analytical work.

We already own one of the companies that is playing a mission-critical role, helping with the increased regulatory analytical work that comes along with the changes in regulation.

The other interesting insight was around how small molecule drug discovery is at an inflection point. Remember, we talked about small molecules being around for over 100 years, and typically it's a two- to three-step process.

One interesting learning was that close to 70% of small molecules that are under development at the moment are, you could say, moderate complexity or highly complex. We're talking about four to seven steps, a step change that is going on**.** That's going to be the icing on the cake.

There are implications for this, of course, and we are in the process of initiating on companies that actually benefit from this step change.

There are many insights coming out of the pharmaceutical space. It's always great to be on the ground. That's 75 meetings over seven working days at two different conferences: attending panels, talking to people at booths,



and asking questions. That's the beauty of AI: it's enabled me to spend more time on the ground.

And then you get these insights connecting the dots: going to the people and talking to them, and going back and connecting the dots and finding great insights for our clients and our portfolio.

[21:53] [RC] Hopefully one of the other benefits from AI with this extra time is more time for you to join us and share with listeners some of your insights. We'd love to have you back in the coming months to talk a bit more about some of those other themes.

[22:03] [JS] I'm looking forward to that, Rob.

[22:05] Likewise. Thanks, Josh. Have a great night.

[22:07] Thank you.

[22:09] Hi, everyone, Rob here again. To subscribe to The Art of Boring podcast, go to Mawer.com. That's M A W E R dot com forward slash podcast, or wherever you download your podcasts. If you enjoyed this episode, please leave a review on iTunes, which will help more people discover the Be Boring, Make Money philosophy. Thanks for listening.

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