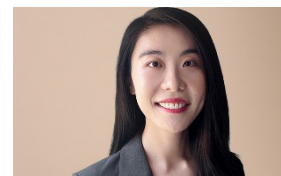


The Skinny on GLP-1 Investing



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ALEX BERNSTEIN: Hello, I'm Alex Bernstein and you're listening to The Alger Podcast: Investing in Growth and Change. In 2023, GLP-1 made overnight headlines as one of the most innovative, crossover weight loss drugs to hit the healthcare industry in years. But some investors may be surprised to learn that GLP-1 has been under observation in this manner for quite a long time. Here to take a deep dive with me on the subject of GLP-1 are Alger Senior Healthcare Analyst, Keye Chow and Associate Analyst Yinglu Zhang. Keye, Yinglu, thanks so much for joining me this afternoon.

KEYE CHOW: Oh, thank you. Great to be here.

YINGLU ZHANG: Thank you. Thanks for having us.

ALEX: Before we get into the subject of GLP-1, we've just come off a bit of a difficult year for healthcare stocks in general. Can you give an overview of where we are, investment-wise, in the healthcare industry?

KEYE: Well, Alex, I think 2023 has been a tough year relative to the rest of the market for healthcare. There's a number of reasons for that. We're in an election year, and typically it's just kind of conventional wisdom that people get nervous about healthcare and reduce their healthcare exposure going into an election year. An election year is when politicians, when they run for office, talk about all the bad things they're going to do to the healthcare players, particularly in pharma.

So, there's that. And then there has been regulatory uncertainty in terms of new regulations that have been passed that have negatively impacted different players in the healthcare industry. For example, Medicare Advantage got a rate cut that will last three years. And there was a lot of healthcare spending in 2020, 2021, and we're still kind of digesting and coming off of that overhang of excess, abnormal

spending that was related to investing in discovering therapies for treating COVID. So, all those factors have come in to make this a tough year for the healthcare stock market.

ALEX: Yet you remain pretty excited for the coming year?

KEYE: It's an exciting year, particularly in the area of life science innovation. Alger, as a growth and innovation-oriented investment firm, we're very oriented towards innovation, not only in terms of science and technology but also in commercialization and how patients are treated, and so we focus on that. We continue to see innovation in medical technologies in terms of where previously acute surgeries are taking place. We're seeing an ongoing shift to outpatient settings. We're seeing an ongoing shift in having treatments and technologies that enable patients to not have to stay in the hospital. We're seeing more technologies that allow patients to stay at home more and be well taken care of at home. So, I think when we talk about innovation, people always think, oh, a great new robot or, oh, a new discovery in gene or cell therapy, and those are all true, but there are really simple innovations as well.

ALEX: Well, I know everyone wants to hear about your thoughts on GLP-1, how we got here and where we're going. Yinglu, were you surprised to see GLP-1 suddenly take center stage this past year?

YINGLU: Well, I'm surprised but also not surprised because the GLP-1 drug has actually been around for more than two decades. So, it started as one class for the diabetes patients. The first GLP-1 drug, Exenatide developed by Lilly, was approved in 2004 for glycemic control in type 2 diabetes patients, and after that, multiple pharmas including Lilly, Eli Lilly and Novo started improving on the class for better efficacy in glycemic control, and it was discovered that actually, these drugs deliver meaningful weight

loss benefits in diabetes patients.

So, that's when pharma started testing these drugs in obesity patients who need to lose weight but don't have diabetes, and it turns out that GLP-1 drugs work very well in these patients, and patients could lose up to 20 percent of their body weight.

KEYE: So, I think a lot of the excitement has been the media, the investors and just the consumers, the general public getting really excited that, hey, this obesity, which we all in some way know is negative for health ... we don't know the causality a lot of the times, but we know it's very linked to different health conditions. Obesity impacts people's identity. It impacts their self-image. So people are really excited about the opportunity that, hey, there might be some wonder drug that's going to help everybody lose weight, be healthier and feel better about themselves.

Then, I think, in some of the early trials around obesity, people are showing that they can lose up to 20 percent of their weight, and as long as they stay on their drug, it stays off. So that's all really promising. And if we just do the math on the United States having 40 percent of its population who are technically obese and over ten percent who are severely obese, that there's all this excitement that, wow, we could apply these therapies, these GLP-1s to tens of millions of people. So, I think that's where all the root excitement comes from.

ALEX: Yinglu, you mentioned a moment ago that GLP-1 has actually been around for two decades which I think might surprise a lot of people. Can you talk a bit about how it started and even what it actually is because I'm not sure how many people really know.

YINGLU: So as I mentioned, it started as a diabetes drug, and GLP-1 works through multiple organs in our body. So for glycemic control in diabetes, it pushes the pancreas to produce more insulin, and it also acts on the brain to suppress your appetite and also on the stomach to slow your gastric emptying. So patients will feel less hungry and reduce their food intake and, therefore, lose weight.

But other than weight loss, we're also seeing benefits in comorbidities of obesity. So, we're seeing reduced risk of cardiovascular risk. We're seeing improvement in renal function and liver disease, and we're also seeing benefits in indications that are strongly associated with obesity such as sleep apnea.

ALEX: Do you think we ever get to a point where it's specifically being branded and marketed as a weight loss drug?

YINGLU: Yes. So, for Novo, Semaglutide, it was already approved for weight loss management for obesity patients. For Eli Lilly, their Tirzepatide was also recently approved in obesity patients, and they have just started selling them as a weight loss drug for obesity patients.

KEYE: Yes, and they actually have different names.

YINGLU: Yes. So, they have different brand names for different indications.

KEYE: It's the same drug, but they decided to call them different names.

ALEX: Interesting. Can you talk about some of the current perceived barriers these drugs may be facing as they further enter the market?

KEYE: Well, maybe Yinglu should start with the issue that everybody seems to not pay enough attention to, which is persistence.

YINGLU: Yes, sure, and that's related partly to the side effects as well which is mostly nausea and vomiting. An important factor that we think many potentially overlook but we take into consideration is persistence, meaning how long patients stay on the drug before they decide to stop. Now based on data from earlier generations of GLP-1s, we know that 50 percent of diabetes patients will stop after one year either due to side effects like I mentioned or because of inconvenience of administration because it's a weekly injection.

Now we're hearing from Lilly that their latest generation of GLP-1, Mounjaro, is seeing improved persistence over the earlier generations, but we still think it's inevitable to see some patients stop the drug after some time either because they can't tolerate the side effects anymore or they have reached their ideal weight. So, it's a factor that we still can't overlook and that will be important to think about when thinking about the market opportunity of GLP-1s.

KEYE: Another thing that people are aware of but perhaps don't pay enough attention to is the coverage, meaning like who's going to pay for all this. Today, I think the coverage for obesity use by payers is actually flat or actually contracting, and a lot of the use for obesity is actually out-of-pocket pay today.

Just recently because there's been such a surge of excitement and usage, a lot of self-insured employers have started cutting back on their coverage or trying to limit the coverage so that – these are expensive drugs – that people are not just trying it out and effectively kind of wasting money. This somewhat ties to the persistence issue as well. You don't want people incurring tens of thousands of dollars and kind of getting no enduring benefit out of it.

ALEX: Do you see the price eventually coming down?

KEYE: Yes, we absolutely do. We think the vendors probably expect the price to come down, and it's actually the key debate when it comes to the healthcare system wanting to and being able to give access for the obesity indication. I think it definitely will come down, and another important driver for prices coming down will be, I think, in 2026/2027 we should start getting oral versions.

YINGLU: Yes, we are seeing multiple companies developing oral GLP-1s, including Lilly and some other companies, and we think it will become an important segment of the market and taking market shares from injectables.

ALEX: You've mentioned a couple of companies. Who do you like in the space and why?

YINGLU: So, there are multiple companies we like in this space. Amgen is developing a long-acting GLP-1 drug that could enable monthly or even quarterly dosing which will be much more convenient for patients. We think patients will definitely prefer less frequency dosing than the weekly injection which is what they're getting right now.

ALEX: With so many players now getting into this space, has it been challenging to determine who the possible long-term leaders are?

YINGLU: I think there are many working on the space, but we tend to follow the science and pick out the ones we think have the best science, with the highest probability of success and who are in the lead. So, Scholar Rock is one we like that they are combining myostatin inhibitors with, potentially, GLP-1s for improved quality of weight loss, and Zealand Pharma is another name we like. They are not only targeting GLP-1s. They are looking at GLP-2s and also glucagon receptors, going to the de novo science for better quality of weight loss.

ALEX: Yinglu – what's the one message you think investors should take away from this conversation?

KEYE: Well, I think that a lot of exciting innovation, important innovation is still happening, and that's a lot of what our investment focus on is here at Alger and particularly in our life science strategies. But it really permeates the entire firm and is that we're looking for important innovations that will change the lives of patients, and we're looking to benefit our shareholders through those discoveries.

YINGLU: I was going to add that I agree with Keye that there's a lot of exciting innovation right now in the space that could not only improve patients' lives but drive significant growth for company value, and the sector has underperformed, but now sentiment could be turning. So, we think it's a great time to be looking at healthcare investing.

ALEX: Keye, Yinglu – thanks so much for joining me this afternoon.

KEYE: Thanks, Alex.

YINGLU: Thanks, Alex. Great talking with you.

ALEX: And thank you for listening. For more information of investing in health sciences and for more of our latest insights, please visit www.alger.com.

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The following positions represented the noted percentages of Alger's firm-wide assets as of October 31, 2023: Amgen, Inc., 0.69%; Eli Lilly & Co., 0.92%; Novo Nordisk, 0.03%; Scholar Rock Holding Group 0.00%; Zealand Pharmaceutical, 0.00%.

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