Question & Answer regarding the development Status of STN2000100 (DE-128) and Timely Disclosure on April 12th

Q1-1:
The first question is about the feedback from the FDA. I am very aware that you cannot disclose the details, but is there anything more you are able to say? Was it something related to the data, or about the manufacturing or other aspects? If there is anything more you can explain, I would appreciate it if you could disclose the details.

A1-1:
(Suzuki) Thank you very much. This is Suzuki from the Planning Division. Morishima of the Product Development Division will reply to your question.

(Morishima) Thank you.The FDA's comments on the evaluation of clinical trials, in particular, are somewhat at odds with our opinions. We at Santen Pharmaceutical would like to continue to consider this matter from the perspective of patient benefit and risk profile, taking into account the FDA's guidance. In particular, we would like to discuss the weight of the items to be evaluated and the balance of the risk-benefit profile, since it is basically a medical device. In addition, we have made comments to the FDA regarding the evaluation process and the specializations of those who will be evaluating the results, and we are waiting for their response.

Q1-2:
Thank you very much. The second is about forecast peak sales. There was the figure of JPY10 billion this time, but I think that peak sales forecast was around JPY20 billion when you acquired InnFocus, mainly from the US. The peak sales forecast of JPY10 billion of the US, as I understand it, were originally about JPY20 billion mainly in the US, so I suppose that it means that sales outside of the US would be a little smaller, like JPY5 billion. When you say JPY10 billion outside the US, is it correct to understand that this means that sales outside the US are expected to be higher than at the beginning of the fiscal year?

A1-2:
(Suzuki) Thank you. As Mr. Taniuchi explained earlier, in Europe, we have already sold more than 7,500 units, and the sales potential has also increased, so the market is much stronger in Europe than we thought it would be at the time of the acquisition. The market is much stronger in Europe than we originally thought. In response to this, we have reviewed the development potential in Japan and Asia, and as a result, we have set this figure.

(Taniuchi) To add a little more context, I was in charge of Europe when the acquisition was made, so I remember it very well. At the time of the acquisition, the potential of this glaucoma surgery device in Europe had yet to be determined, and to be honest, we had no idea what the insurance reimbursement would be like or whether the unit price would be the same as in the US. After that, other products came out, and the image of insurance reimbursement and unit price became apparent, and as a result, the forecast has been increasing upward. Also, at the time of acquisition, we naturally took a conservative view of the acquisition, so we did not know what the product profile would be. In fact, as we sold the product ourselves and talked directly with doctors, we realized that there is such potential, and also that the insurance reimbursement and unit price, as I mentioned earlier, are in the high end of our expected scenarios, so we have raised the price slightly for Europe. As a result of the control launch in Europe, we are working to expand it to other regions. We are working to expand it to China and other regions as well. I hope you can understand that the reason for that earlier statement is that the outlook is bullish, and that is the background.

Q2-1:
I have two questions. Firstly, regarding 128. I heard from the IR team that your company has chosen and is requesting a meeting with experts among the multiple options presented by the FDA as the way forward. If the FDA does not accept this option, what are the next steps or options?

A2-1:
(Suzuki) Mr. Morishima will take your question.

(Morishima) As for the current situation, we are focusing on negotiations with the FDA. However, there are several other approval processes, and we are currently working on those in parallel as a plan.

Q2-2:
Understood. I would like to know one more thing. Originally, I think it was just a matter of delayed inspections and delayed approvals, but I think the situation has changed a lot since the discussions with the FDA at the end of February. Could you tell us a little more about the gap between these two and the background?

A2-2:
(Suzuki) Mr. Morishima, please.

(Morishima) For the FDA, inspections have been delayed due to the impact of COVID, and there have been some delays in communication, but in the end, we received a letter from the FDA in February giving their comment.

Q3-1-1:
I'm sorry, this is a similar question.

The feedback in February was not a final conclusion on the PMA as it stands now, but rather a final conclusion on not approvable and non-approvable, is that right? I think the process is different between devices and pharmas, so I'm not totally familiar with it.

Am I right in saying that the letter you received in February said something along the lines of "we won't approve this right now, but we can negotiate conditions"? The feedback from February is still a bit hazy, so could you tell us about that first?

A3-1-1:
(Suzuki) Mr. Morishima, please.

(Morishima) The letter said that they cannot give immediate approval, and that there are still issues to be resolved.

This is a different letter than the typical Complete Response Letter for pharmaceuticals. We have been instructed that there is room for negotiation, and if we intend to resume negotiations by a certain date, we should send a letter.

Q3-1-2:
: In the future, of course, it will be difficult to disclose the information because there are other parties, but including previous question just now, it seems there are many possibilities for negotiations, and as a result of the negotiations, your company will receive some type of 'homework.' For example, collecting more data, global data. Repeating clinical trials. I'm sure there are a lot of things to consider, and I'm sure the time frame will vary depending on those factors.

When the next round of negotiations with the FDA will take place, and when the results of those negotiations and the homework assignments are decided, could be in the second half of the year, or next year, or the year after that. Is this the right sort of understanding?

A3-1-2:

(Morishima) That's pretty much it. We have received the letter and returned our response to them, and we have also proposed a process for negotiations, so we will see how they respond to it. After that, we'll move on to negotiations with the FDA. I will report back as soon as I know more about this.

Q3-2:
Understood.

The second question is a brief one. Is there any contractual change in the relationship with Glaukos due to the delay in the approval, or is there any contractual obligation to pay anything to Glaukos?

A3-2:
(Suzuki) I'll take this question.

We are keeping Glaukos abreast of our dialog with the FDA, and continuing discussions. Based on the discussions with the FDA, we are confirming what we will do in the future in the form of collaboration, but at this point, there are no changes, for example, contractual changes, that would require disclosure.

(Taniuchi) I'd like to add a few words about Glaukos.

Naturally, we are working closely with Glaukos on this matter, and they have a lot of experience in working with the FDA on this type of PMA application. I am also working with the president of Glaukos on this matter.

Q4-1:
My first question is that I would like to know a little more about the thinking that led to this impairment. I think the decision to write down almost all of the US assets was based on reasonable, albeit conservative, assumptions, but it still seems to me that from an outside perspective, this may have made development much more difficult.

I don't think we can factor in excessive risk, so I would like to know the background to this situation, or the points raised by the FDA, as you explained earlier.

A4-1:
(Suzuki) I will take this question.

As Mr. Taniuchi explained at the beginning of this presentation, we do not believe that the possibility of approval has been eliminated. We are only assuming a delay.

However, there are multiple scenarios for the delay, including the scenario of additional study as mentioned earlier, and the timeline is quite uncertain. The amount was to be disclosed after confirming with the auditors, incorporating the risk maximally and evaluating the amount of the impairment from the conservative viewpoint.

Therefore, the assumption is that discussions with the FDA will continue and the possibility of commercialization in the US will be pursued. On the other hand, we have made the most conservative calculations possible for this delay.

Q4-2:
Understood. Thank you.

The second question is about the impact on the medium- to long-term vision issued on March 10. In your medium- to long-term vision, you mentioned that you would develop new business areas such

as devices in addition to the core businesses, so I wonder if this incident will have any impact on your medium- to long-term growth potential as you indicated earlier. I also wonder if your company's strengths can really be applied to an area such as medical devices. What are your current thoughts on this?

A4-2:
(Suzuki) Thank you.

First of all, regarding the device itself, it remains very important in terms of strengthening our glaucoma portfolio. We believe that having a device will naturally and clearly allow doctors to choose Santen, and as a result, we will have the advantage of cross-selling with our existing prescription medication business.

Therefore, we would like to continue to aim for approval in the US as well, and in addition to our already established presence in glaucoma outside the US, we would like to aim for a total solution in the form of business expansion with 128.

On the other hand, as for the growth potential in the mid-term plan, as you may remember, 128 is not included in the growth potential of new business areas*, but is included in the core business area. (*Correction after the meeting by Santen: DE-128 is included in the growth potential of new business)

So, naturally, the US portion will be delayed due to this impairment. On the other hand, as I mentioned earlier, we would like to keep the downside to a minimum, including through contributions from Europe and other regions.

In addition, I would like to add that the delay in the disclosure of the medium-term plan after March 10 was due to the need to refine the plan in light of the current business performance and the speed of recovery in China, as well as the 128 issue. That's all.

(Taniuchi) I would like to add a few words.

This is somewhat related to your first question, but in addition to our own research, we have been actively partnering with others to create innovation and seeds for growth, especially in the past three to four years.

When we take a bird's eye view of the next 10 years, from the 2020s to the 2030s, we need to prepare the seeds for growth and the areas that can become growth drivers.

In the case of DE-128, there is a lot of debate about whether or not the US outlook will become a little uncertain. As I mentioned earlier, we took an impairment loss to lighten our balance sheet, and we will continue to carefully monitor the overall rate of return.

I think it is important to follow this principle of making sure that the investments we make are profitable and reviewing those that are not.

As Mr. Suzuki mentioned, there will naturally be some downside effects toward 2030, such as a slight drop in the top line due to this, and the impact of the US business, but I do not believe that there will be any level of change in the axis of our strategy.

In the US, as I mentioned earlier, we have already acquired Eyevance, so we will use that to create a presence in the US by working diligently. The amount of the top line may change slightly, but I think that is it.

As for glaucoma, our glaucoma business is also in areas where our drugs are strong, such as Japan and other global markets outside the US, where Santen's glaucoma products are very strong. If we

combine DE-128 from InnFocus with existing glaucoma drugs and future pipelines, we will have more information than the competition.

Therefore, we are looking closely at the direct impact of the plan, and of course there will be a financial impact, but I think that the direction of this mid-term plan and the direction for 2030 will be to sit tight.

Q5-1-1:
I think it is very difficult for us to assess the approval process of DE-128 in the US at this point.

On the other hand, in EMEA there are already 7,500 units with 300 doctors trained, and the sales have been disclosed at JPY5 billion, so even though it is a controlled launch, I think it has reached a certain scale.

From Europe, there is some form of clinical trial, but not clinical trial, because it is already on the market. I wonder if such data, like post-marketing surveys, have been compiled. Also, do you have any intention of disclosing this information, even if it is just for reference? This is my first question.

A5-1-1:
(Suzuki) Thank you. Mr. Morishima will take this question.

(Morishima) At this point, I believe that our application strategy will continue to be based on data from the United States. We also have had two-year data, which we plan to disclose, and we will present the two-year efficacy and safety data at the Canadian Ophthalmological Society conference in June.

In particular, we have already disclosed this data of INN-005 in the US, but we would also like to provide the US FDA with data on the simplicity of the surgical operation and the frequency of postoperative interventions by European doctors, and emphasize the benefits. We are reviewing this.

Q5-1-2:
So is it the case that you have not yet collected any comprehensive data in Europe, from after the launch to now?

A5-1-2:
(Morishima) We have been conducting post-marketing surveillance, and the data is accumulating, but we have to re-evaluate whether it is at a level that can be used for FDA applications.

Q5-1-3:
I guess the most important thing is whether you have the data or not, regardless of using the data for the application to FDA. I think this data would be very valuable in evaluating the product, so if you have such data, would you be able to disclose it?

A5-1-3:
(Taniuchi) Thank you.

As Mr. Morishima mentioned, although these data are not large-scale studies like clinical trials, we are accumulating real-world evidence on a daily basis, such as clinical results and results of usage at each facility. This is being presented at conferences, but I would like to think of a setting where I can explain it. Thank you.

Q5-2:
Understood. Thank you.

As Mr. Taniuchi has answered my question just now, there is something else I'd like to add briefly. Lately, there have been some inconsistencies, such as the postponement of the announcement of

the mid-term plan, and I feel that as a pharmaceutical company, smooth disclosure will help to move things forward.

Is your answer just now, as you mentioned earlier, a reconfirmation of the plan to increase shareholder value set out in the medium-term plan to be launched in May? Under the current circumstances, I think it would be difficult to come up with a plan to return profits to shareholders.

A5-2:
(Taniuchi) First of all, there is the issue of the impairment in this case, but as I mentioned earlier, there are many aspects of our current business performance that are performing well.

In particular, we have seen a solid increase in our market share. In these times, all companies are going through a lot of trial and error, but we are adapting to these new circumstances, conducting sales promotion activities and increasing sales. Or, for example, increasing our market share. This is the kind of strength and resilience that we will need for the next mid-term plan. I think this part is a major strength for us.

We are getting a good response to the measures we have taken, such as the LOE countermeasure and the solid sales turnaround in each region and in China, as I showed you on March 10.

With this, we would like to firmly establish a sustainable trend of increased sales and profits, and of course, we would like to strengthen shareholder returns in a slightly different way than in the past.

This is all I have to say today, but I would like to make a thorough announcement about this in the mid-term plan.

Q6-1:
On page 11 of today's slides, you have introduced what you hope to achieve in the next mid-term plan. I think that the strengthening of the foundation at the bottom of this slide is a concept that you have presented for the first time. I am now looking again at the materials from the long-term vision briefing in July last year and the strategy briefing in March, and the above three are basically the same as what you said at those meetings. I understand that strengthening the foundation is something new this time.

What issues do you see in this foundation section, including this recent 128 issue? What are your plans to improve and strengthen this area over the next five years? I think it would help our understanding if you could introduce specific points that you have identified with the 128 issue.

A6-1:
(Suzuki) Thank you very much. First, regarding 128.

The main points here are ‘medical device’ and ‘US market.’ I think there was an impression that we had sufficient capabilities in these areas, but there are points for further development here. I believe that we need to make further improvements, especially in the area of regulatory affairs relating to development.

As is the case with the next medium-term plan, the position of the United States is very important, and if we want to promote growth with a strong presence in the United States, we have no choice but to bring in challenging development themes. In this case, we recognize that the developmental regulatory affairs and development capabilities are extremely important, so we would like to make changes in these areas, which will lead to strengthening of our R&D organizational capabilities, a part of that ’foundation.’

As Mr. Taniuchi explained earlier, our core business of prescription pharmaceuticals for ophthalmology is growing steadily, and we have the development capabilities in Europe, Japan, and China, so we will ensure the growth of this business.

In particular, overseas, as well as in Asia, unmet needs in ophthalmology, such as infectious disease, blindness, and anterior segment eye disease, are still large, and we believe that there is tremendous room for expansion of existing assets in this area. We will continue to work hard on this area during the next five years.

On the other hand, as you mentioned, there are places where the business environment is changing, such as China, so we would like to manage our business by setting KPIs that include, for example, the coverage rate in private hospitals, and recruitment.

In these areas, but in others too, Santen has been developing its business in regions with growth potential. In future, I believe that we need a global strategy execution system. The term "strengthening of the foundation" is used to describe the need to reinforce the system, including global development, manufacturing, and integrated marketing.

Q6-2:
Thank you very much. At a meeting a while ago, it was mentioned that investment comes before developing this type of global system. I seem to recall that Mr. Taniuchi used the expression "overhead."

So, I remember that he showed us how to think that when sales increase, inefficient areas will become more efficient and the profit margin will increase. If you strengthen the foundation of your business, can you tell us what you think about the improvement of the profit margin by increasing the top line?

A6-2:
(Suzuki) I'll answer this question.

For example, in the document, I have used the term TSR, but whether it is ROIC or TSR, I recognize that it is extremely important to increase profit margins and profits, as you have just mentioned, over the next five years.

Therefore, we will review and reclassify investment projects as necessary, and in strengthening our business, we will first incorporate improvements in the top and bottom lines, and then reflect the strengthening of the foundation as I mentioned earlier.

(Taniuchi) I would like to add a few words.

Regarding the first point. What I think is that during the 2010-20 VISION 2020, we set a goal to have a global presence from Santen in Japan. As I look back, especially in the first three years, I think I didn't really know where to start.

We were working in China at the time, but even if we wanted to go global, we didn't have anything yet, and we didn't know how to get in. We struggled for about three years, but in the middle of that, products started to be released and we grew from the middle of the year due to the acquisition of MSD.

In addition to these factors, the world has been changing more rapidly over the past 10 years, and there has been a great deal of change in technology. You can't verify the potential of a product until you have it, and I think learning doesn't occur until you actually develop and sell the product.

So, in that sense, it is true that this time has been a little painful, but it is a learning experience. However, I still believe that the most important responsibility of management is how to connect the lessons learned from this kind of experience to the next.

As for 128 itself, which you asked about, we bought it from a company that had already completed about half of the clinical trials when we acquired it, so naturally there was some learning in the pharmaceutical and clinical areas. I think we have returned to our starting point to ensure our capabilities and to strengthen our human resources and leadership, while at the same time taking on the challenge of new technology.

As for development, we have already changed the organization of the development system, including leadership, and are working to strengthen it. The results of these efforts have been seen in the various clinical development programs that are currently underway, which are running very smoothly.

In addition, in the new fields of cell therapy and digital technology, we will reinforce our human resources and learn from the successes and failures of other companies. I hope you will understand that the phrase "strengthening the foundation" expresses our intention to do just that.

Q7-1:
I would like to make one point as well, if I may.

This is about DE-117, unrelated to today's main topic. In one of the clinical trials, it failed to meet its primary endpoint. However, I think it was mentioned last time that there were discussions with the FDA, and about an application being filed from a risk-benefit standpoint.

This is a completely different product from DE-128, and I think the events will be different, but in terms of risk-benefit, 128 is currently under discussion and the discussion is being postponed, so I am concerned that the same thing may happen with DE-117. Is it correct to say that that DE-117 can be placed on the market as before, and that the consultation is proceeding well without any problems?

A7-1:
(Suzuki) I will address part of this question.

First of all, the risk-benefit that you mentioned, that was in relation to 128.

There is a wide range of issues regarding regulatory requirements unique to medical devices, and we are currently working on these issues.

As for 117, Morishima will answer about that.

(Morishima) Thanks.

As I have explained before, the two pivotal trials met their primary endpoints. The only thing is that in the situation where the pivotal trial in the US did not meet the endpoint, several exchanges with the FDA confirmed that we had enough level for an application. Compared to medical devices, we are more familiar with pharmaceuticals, so there have not been any problems in communication.

However, we will continue to communicate closely with the FDA in order to file and get approval. So far, the review process is progressing, and we expect to have an opportunity to report on the results in the first half of this fiscal year*. That is all. (*Correction after the meeting by Santen: Scheduled in second half of this fiscal year)