Company Name: Daiichi Sankyo Company, Limited (DNSKY)
Event: Cowen 39th Annual Health Care Conference
Date: March 11, 2019

<<Antoine Yver, Global Head of R&D Oncology>>

Okay, so good afternoon. So hopefully, I don't know what the format is exactly it is only to talk or talk in Q&A. I think I have 15, 20 slides to show. First is a disclaimer this is obviously I'm talking from an R&D standpoint. My name is Antoine Yver, I forgot to introduce, I'm the global head of R&D Oncology for Daiichi Sankyo. I joined actually four years ago after I came from Astrazeneca where I was Global Head of Development for seven or eight years before that. And I've been in the industry for quite a while.

Just quick about what I created, when I joined, trying to recognize the value of Daiichi I could realize that the company had the potential to actually deliver a portfolio of seven new drugs by 2025 or what I call seven, eight at the time was seven, eight years. Seven new drugs, seven distinct drugs and creating really a delivery machine meaning not being not only a company with a great research, but also a potential to deliver these drugs. And you see that we are progressing relatively nicely on this objective.

With obviously a scale up of the enterprise, and the reason for this is because the company was not used to work in the specialty care, high value, high science technology, advanced premium drugs and certainly not in oncology and there's a ways of work which had to be scaled both in terms of how we work and to be organized as a company. Can we close the door? And ramp up.

And then really the uniqueness of the company is qualitative science and that qualitative science comes from the fact that it's traditional, very exceptional company in Japan, which recruits the best possible scientist every year. And they are working for life. And actually we do the science which is world-class science in Japan and that's what led us to have this portfolio of assets.

The seven and eight [indiscernible] (0:02:10) U.S. you have at the bottom, each of the box represented the strength in the need, so we have identified already four, five of the drugs that will be drugged by 2025 and still have many, many more years to do that. So I'm really confident that we will deliver these drugs. And we obviously have two drugs which are currently under regulatory review, Quizartinib and Pexidartinib. We have a drug which is attracting a lot of attention. The first of the ADC DS-8201 and we have many, many more than that. Some pretty consonants that we will do there.

This is a highlight of our portfolio. These are just the major pipelines. We are not presenting the whole pipeline. You also see that it's not organized by Phase 2, Phase 2, or Phase 3 assets, it's organized more by franchise. The ADC franchise on the top and I will spend the rest on the ADC franchise. We also have a very healthy hematology, hem franchise with AML and with breakthrough. You can see also that two of these drugs that could be franchised actually have drugs which are under review, Quizartinib [indiscernible] (0:03:10). Quizartinib is the first-in-

class CSF1 inhibitor for TGCT, which is both of those drugs are breakthrough-designated and have all the regulatory designation that you would want.

So it's a very healthy pipeline in and by itself. Then I will just discuss the ADC. I'm pleased to take question on others. From an ADC standpoint, we currently have seven assets under which are in clinical or preclinical stage. The first three are clinical stage. So first one is on the field of development and I'll comment about this. The next two is the number four and number five [indiscernible] (0:03:50) just entering the clinical research. So that's five assets in a clinical stage research. We have our current DXC technology which is are proprietary technology. We have obviously technology following this DXC technology, so we have our own NEXIUM compared to this which will come into clinic in 2020 or 2021, we have not disclosed what they are.

This is the DS-8201, the lead asset in this ADC franchise which us a program as we've described in the [indiscernible] (0:04:23). It's organized around three different tumor types, breast cancer, gastric cancer and then the combination of colorectal and non-small cell, as well as some combination initially with CPI-combination and HER2 CPI-combination, as well as the IO combos that you naturally would want to do because our [indiscernible] (0:04:39) kills very well tumor cells and also enhances the antigen presentation of EPC so it makes a lot of sense to try to turn the non-triple-negative breast cancer into tumors which are immunogenic and can be addressed by immuno checkpoint – immuno checkpoint inhibitors.

We are progressing very nicely on in the [indiscernible] (0:05:02) in the advanced breast cancer, 75% of all breast cancers. Obviously death rate is a substantial issue and secondhand killer in Japan and Southeast Asia and then it's going also to colorectal non-small cell, so pretty healthy coverage advantages. Obviously what you would want to do aspirationally is to move into the earlier phase for each of these tumor types. And you see on the right hand side data or targets, which obviously will be jaded on our ability to particular combine our drug with the standard of care is a drug that you would want.

So this is aspirational for the majority of it, but this is where we can and we should go certainly tried to go. This is something you should, or you probably have seen, this is the waterfall plot that we have published at ASCO last year. I mean they speak for themselves. What's interesting, if you do not look at the blue label, you cannot really say which tumor type it is. So the drug works relatively consistently in terms of frequency response across HER2 breast cancer positive, which is at top left, HER2 low breast cancer, which is the top right. This is the oral cancer, you have colorectal non-small cell, you have biliary tract, salivary gland, which are included here and then the gastric cancer.

So a drug which is pretty consistently working if you are able – if you're expressing the HER2, the tumor expected HER2 [indiscernible] (0:06:34) HER2 your delve with the payload and the payload actually delivers a pretty substantial tumor control antitumor shrinkage. When you look at the spider plots in the HER2 low breast cancer, you'll see in the prior slide I showed [indiscernible] (0:06:51). But I did not mention, and maybe I can go back and not mention for these patients what I described in December at R&D days, that we have a duration of response in these patients, which in excess of 20 months.

So it's more than one year and a half duration of response in Phase 1 study, which is when we submitted this to a major oncology journal for publication, they ask us if we had a typo, because they just did not believe the 20 plus months. Literally speaking, it should be published immediately now. So what's interesting here is obviously you have a very healthy response rates [indiscernible] (0:07:44) and nothing works as HER2 targeting these tumor types. And that represent 50% of all tumors.

Important also is to know what the safety profile of the drug is. We have something which is mostly the most important [indiscernible] (0:08:02) are the mild suppression, which is absurd, which is [indiscernible] (0:08:12) which is mostly great and recover we do the adjustment and then obviously the ILD [indiscernible] (0:08:20). But the patient also complained a little bit of decreased appetite and fatigue a little bit of – I mean it's a slow – it's a low grade chemotherapy kind of feeling, which is not completely unexpected given the mechanism of action of the drug.

ILD is obviously a recognized risk for this drug, which we established at large. Just a little bit about ILD. In China where I've spent so many years at AP and AstraZeneca, we have more than 380 mitigation which are known to induce ILD. And ILD continues to be across these different drug-inducing ILD, mostly unpredictable and mostly idiosyncratic, meaning that you don't – you don't why it happens, just exiting no way.

It's recognized mostly because of the sign and symptoms of fever, the cough, or the shortness of breath. And it's diagnosed not precisely, but it's diagnosed by excluding any other potential sclerosis. As the treatment of ILD regardless of a drug which has induced ILD, the treatment of ILD is high dose steroids and obviously the withdrawing of the causal agent. And to give you an example, TAGRISSO, which is a drug I put on the market already. So U.S. label shows a 3.9% ILD in a 1,000 plus cases, we've 0.5% or 0.4% being fatal. And again a lot of drug and cancer drug and TAGRISSO are causing ILD. But it is a serious risk which has to be recognized and has to be monitored for.

What do we have? This is our safety. Now I'll show in two sides, or three slides on ILD. Here you have 665 subjects. This is what we published back in December of last year at San Antonio at all doses, and in the top row in red you have the investigator-reported, which was [indiscernible] (0:10:24), up almost 10% we have half of that in grade 1, grade 1 is just image. It's just you look at images and you see a gray CAT scan. If you have no sign and symptoms, obviously [indiscernible] (0:10:36) that resulting from the ILD or attributed to ILD. So five guests were initially reported in a context of an ILD.

Of these 66, 30 were cases 38 were adjudicated for an independent adjudication committee, that's what you do once you have these kinds of things. So we are in the process of doing that. Of this 38 cases, 30 of them were adjudicated ILD one of the five cases we're actually was not attributed to the drug, mostly because it was present at baseline actually.

But what's also – what we've learned also is that this is not an early onset. The median duration of treatment was in excess of three months in these patients and the time to onset was 150 days. So 149 days, so it says five months, it takes a bit of time too, this is why it has not been recognized early. And actually we had number of cases where patients kept – were complaining

that the doctors were attributing the sign and symptoms to the underlying disease and not to be lung disease caused by the drug. And actually we kept treating – which is very basic because that's what you observe, exactly, in these cases.

So in February, March of last year we implemented program wide, which we didn't want to do, which is to raise awareness of patients who verifying during [indiscernible] (0:12:02) so that we would report sign and symptoms of placebo ILD, we may not sit on this since it's my cancer, I'm wearing improve because I want to continue on the drug. We also trained the sites for monitoring and evaluation and treatment of the suspected ILD cases. It's all too early to measure the effect of this, mostly because this has been implemented between February and March, mostly March until it has been R&D approved. So we are six, nine months into it. Now we have to date we have more than 900 patients treated with DS-8201. My sense is that we will continue to see, give or take almost some time the same kind of picture, same kind of frequency.

So what did we have with – so what did we learn out of this experience? We look at all risk factors, but also which you want to do. Even when everybody says you cannot explain you still wanted to find risk factor because one well-known risk factor in a ILD for cancers Japan and we found that the Japan origin was clearly a risk factor, you see [indiscernible] (0:13:09) you also have the dose which was associated, higher dose being associated with a higher risk of ILD. And to a certain extent the number of [indiscernible] (0:13:27) HER2 studies. We have to still look at a lot of other factors including exposure, exposure of the total ADC exposure of the payroll exposure. And we actually found that it's not the payroll, which is – it's the total ADC which is more predictive and the payload itself, the free payload. So it's not a systemic toxicities more and HER2 directed toxicity to the extent that we can say.

What is the experience in breast cancer HER2 expressing at the recommended dose? All of his patients, 269 which we did at 5.4 mg/k, which is the dose that we would seek for first approval. In these 269 patients you have 5.6% ILD frequency reported by [indiscernible] (0:14:19), one with five of this 57 where were assigned as drug related. I expect the true number at the end to be between this and what we saw before, so between 5% and 10% frequency overall.

The majority continue to be in the grade 1 meaning that [indiscernible] (0:14:40) are proactively seeing stopping the drug. They actually allow patients to stop the drug and resume the drug if a great one, goes away. And I also expect that we will stand between 0.4 and 1% for a great five in ILD. So we understand well, we've looked at all of our potential area of interest, including cardiac toxicity, because the HER2 targeting, we didn't see anything actually. So I think we are well characterized the safety of the drug.

Now I'm moving to the second ADC, which is U3-1402 which is an HER3 agent. So it's the exact same technology, the DXd technology, but using our proprietary pertuzumab, which is a nerve free agent which had been studied as a HER3 monoclonal didn't work in cancer. But we know the safety of that drug. When we combine the two of the HER3 versus – and the DXd the ADC technology, we have done breast cancer dose escalation. And then dose extension study which is the [indiscernible] (0:15:57). We found, I think, there's another slide with some results here.

<<Unidentified Company Representative>>

I hope so.

<<Antoine Yver, Global Head of R&D Oncology>>

If not, we feel the earlier duration in dose escalation was essentially almost the same response rates. So waterfall plots, but you observed with HER2, which was relatively reassuring because it just proved that we have another vector a free, you actually can deliver the payload in the same manner, what is relatively same manner and be able to observe response rate and also proves that the technology was profitable.

We are also – we started actually almost a year ago now at Dana-Farber with Betty Jane. Phase 1 in lung cancer, in EGFR mutant lung cancer because all – more than 80% of the lung cancer EGFR mutants express HER3. So you don't have to select the patient for the HER3 expression. And we will report this Phase 1 at ASCO this year, this lung cancer. And the lung cancer is actually a fast-to-market opportunity for this drug because you know, you're essentially post TGI, post – and these patients are now begin to show response rate, good durability, good safety, you can go fast and that's our fast to market.

The durability of the response, this is again in Phase 1, in Phase 1 you have two doses on this graph and you see a good durability, you also see that [indiscernible] (0:17:30) so realty is HER3 is not overlapping with HER2, but completely it's a different expression and it represents almost 50% of breast cancer half or through the expression, 80% plus lung cancer EGFR HER3 expression, we also know that prostate cancer expression as well as colorectal in great function. So it's an interesting drug, interesting target probably not going to go as fast as DS-8201, because we biology of HER2 as a receptor is much, much well characterized. So we still have to understand what's going on in terms of expressing and predicting response.

But we definitely have a drug because you have good durability, this is one year, you have good durability of the drug in Phase 1, you have good response, good durability so far, good safety. So we have a drug which is just probably over the lung cancer stroke, probably going to take a little bit longer than DS-8201.

Yes, this is a quick overview of safety, the therapy over 33% based on one subject it grew because of the [indiscernible] (0:18:46) pretty well tolerated. So with a couple of respiratory event of special interest but only two potential grade 2 pneumonitis which actually recovered both after drug withdrawal. So we're very – I mean for an early, early view of the drug we're showing you.

The last thing, I think, I will present is the third ADC, which is a TROP-2 ADC, this is a very – it's quite different from the TROP-2 that has been making the news recently. We went into lung cancer because triple negative was occupied by two. So there's no point, I mean I just wanted to prove that we had the different drug before going as the triple neg breast cancer. So obviously IMMU-132 doesn't work in lung cancer so much and the expense was limited, I think the response rate was something like 14% to 15% so the idea was to go in lung cancer which

expresses HER2 – I am sorry TROP-2 very frequently. So we are just not selecting on TROP-2, but we verify those TROP-2. You can see that we are now at Cohort 7 we didn't see anything, we have not reached the maximum tolerated dose.

This is the drug, which is the same ADC technology except that instead of using an eight drug-antibody ratio as we had probably prior to we were using four just like T-DM1. T-DM1 has four payloads per monoclonal, DS-8201 has eight payloads per monoclonal, RFE has eight payloads per monoclonal, here we have four. The reason we choose four here is because of a preclinical toxin [indiscernible] (0:20:32) because TROP-2 is naturally expressed on number of normal cells. So we found a better safety window. So we have eight milligram for GAR of four which is essentially equivalent to 4 milligram for DS-8201.

We are observing what we are expecting to observe. We will present the data at ASCO, I think this year itself. After we do this, if we – we will go into dose expansion in lung cancer, we believe that we have a drug or actually because of the contact, we may expand with indication which probably will be triple negative breast cancer. So far we had not disclosed but obviously the complex warrant to disclose, the second indication we have not disclosed but we are probably accelerating the triple negative before waiting for the full dose expansion in lung cancer.

I think this is the one before last slide I have, it's our upcoming milestone from the ADC franchise, what we have said for the DS-8201 is that our fast-to-market and first market entry would be in breast cancer. Our base plan is to submit in 2020. We said that we would – for two years from now, I've said that we were contemplating trying to submit in fiscal 2019 meaning during this current calendar year starting from April. And we said that we would make the decision around this time between March and April of this year. So we have not made the decision, yet but we continue to have the options to make the decision but have not made the opposite decision. We currently are tracking and continue to track to be able to submit during fiscal 2019.

At ASCO we will disclose U3-1402 and DS-1062, the HER3 in the Trop-2 data in non-small cell lung cancer. For AML, we have that drug which is, as I said, currently under review with the FDA PDUFA dates at end of May, May 25. We have an accelerated assessment in Europe. We filed in Japan as well. So we filed all three submission in 23 calendar days I think, which I've done before at AZ but that was first for Daiichi Sankyo. And then two months later we submitted to FDA Pexidartinib, which was also a first for Daiichi Sankyo to submit a second dose access for a new drug. And that drug now has a PDFUA date of August 1 in the U.S. So we have two drugs under review globally or in the U.S. And we're looking at the second market for Pexidartinib when the third drug at the top, which we could be filing this year as well.

If we file DS-8201 this year we will achieve what only what Genentech has achieved, which is to file for three new drugs in less than 12 months. And one was Roche and two were Genentech, so I'm okay with that. I looked in the past 25 years no one – no other company has filed an oncology for free best of first-in-class drug. Few companies which filed three drugs in the same year I did at ASO we did IMPALA, Pexidartinib, Tagrisso, esaxerenone for 12 months, esaxerenone was a U.S. mandatory which was easy.

Three new drugs it’s quite to see– it's quiet. So you think of a company that three years ago when I left AstraZeneca people were asking me you're going to Daiichi what? Nobody knew. Daiichi Sankyo is an oncology company, I think, we can be proud of that, but we do in from a portfolio standpoint, but also what I'm most proud of is that the company we recognize the company to be a science and technology company.

So, we are more than just a portfolio company. We are a company where our research is actually producing phenomenal discovery. And we did not disclose and discuss our next generation of ADC, but our researchers are now working on what's coming next. It's going to be in clinic in 2021. So two years from now which we already know what it is, I mean pre-producing that. And we have not disclosed any of that to make Daiichi that it's going to be substantially with the next one and then one after next.

The next one is really interesting, I mean I describe that as if you should take ADC as a monoclonal linker and the payload for the three components, our next technology is four components that’s four different things. And it's not masking, it's not an easy thing, it’s not about masking. And it's really – and one after it’s really disruptive.

So I'm very proud because this company now is confident to be a global player, is capable of being a global player, begins to deliver and is no shy of being a traditional Japanese company meaning trying to not to mimic Western company be led as a Western company, but actually to be led by Japan but not from Japan, but from the U.S. And to be true to what it is, which is humble, which is modest Daiichi is on science. So I think I'll stop here, I have four minutes left. Questions?

Q&A

<A – Antoine Yver>: Sure.

<Q>: [Question Inaudible]

<A – Antoine Yver>: Yes.

<Q>: [Question Inaudible]

<A – Antoine Yver>: I will give you a color. One of the filing I did 20 years ago it was in early breast cancer. In the early breast cancer, I joined breast cancer – given tricyclene radiation therapy you even use 2% of AML period. When I was at Astrazeneca we did Tagrisso not Tagrisso, Lynparza PARP inhibitor, PARP inhibitor induces MDS and AML 1% of the patient, you die from that, literally everybody will die. This is exactly in the range of which you have to recognize not to neglect, but this is a risk that within the risk of what you expect, that's number one.

Number two, you also that the risk factor if you have less advanced number of line, you actually have the risk factor of ILD seem to be less. I'm not saying it will be less, I'm just saying that based on the observation we had on 265, actually it was 400, we had lesser risk. So lesser risk,

lesser risk to invest in and an acceptable risk generally speaking, I'm very comfortable to bring this. And actually industries want to bring us – to bring the drug right now on first line adult, because I want to know how to combine. I hope it answers your question.

<Q>: Yes.

<Q>: [Question Inaudible]

<A – Antoine Yver>: So I believe our drug is an ADC, meaning it depends on the ability to come to, it works in tumor which expresses TROP2 and anything you see stable so that needs to be administered every week. So we predict that our responses will be attached to the TROP2 expression and can be given every three weeks.

At this point in time, if the drug continues to be as it is in lung cancer and we will go in breast cancer rapidly. In triple-neg you can go. I mean Immunomedics has proven that you can essentially have a fact to markets the Fast Track in triple negative on the basis of single arm data. So we'll do the same. I've done it multiple times. So I'm not shy in doing that. I didn't want to go there, if they were to be approved in January this year, coming few years later. So there's no point having, if you have a same drug coming three years later, I'm not interested in doing it. This is why I want it to be differentiated.

But now the triple-neg TROP-2, we are first-in-class in TROP-2, I believe it will have – they will take two to three years to recover from that. That's my instinct and I have good reason to believe that. So I think we have two, three years window to operate, plus we believe our technology is more stable. I mean we – it's a true ADC, which is more stable and a different system is profile, toxicity profile, very consonant. But I mean, all depends on the data. Any other questions?

<Q>: [Question Inaudible]

<A – Antoine Yver>: No. I mean, no detail of data, obviously we said now for probably six months or six plus months, is that it would be unrealistic not to look. If we can generate more value by from an R&D standpoint it means going bigger and faster and be able to take more risk or more money at risk. If you spend specifically $400 million, on your own on the drug and if you double then you can increase the fraction which we put at risk for high-risk, high-reward. So that from an R&D standpoint you just go faster and also, I think, I can use more muscle in term we will be able to deliver. Daiichi Sankyo is not yet where the big and critical players are in terms of multiple Phase 3.

Again, ADC the PARP inhibitor is the same time we were under review so essentially more or less where we are with DS-8201, we have 13 Phase 3 underway, now we have four Phase 3 underway. So I think we could do and we should do bigger from an R&D standpoint. From an commercialization standpoint we obviously have a territory plus readiness to launch. Now you can build, and we can, and we will build our sales force. But there's probably a benefit in rapid uptick and you have a compounding effect. So we are actively looking but it will depend on finding the right partner and also for truly generating more value.

We're not interested in monetizing the assets, we’re interested in creating more value and if we add more value then we obviously share the reward. But it's more about creating the value and monetizing now earlier. Anything else?

<Q>: [Question Inaudible]

<A – Antoine Yver>: So HER2 in breast cancer, too high in breast cancer is pretty standard. HER2 low is absolutely not standard, I can tell you discovered pretty interesting thing in the practice of testing a virtual, because the pathologies where they handled the sample, how we've fixed the tissue actually varies greatly within countries and across countries, and that affects the HER2 low. So standardizing, this is interesting feeds, but we've done it before. Again, I've done with gBRCA, I’ve done with T790M. I have done with – I mean there are ways to this, for the average we thought to also push out own testing.

For lung cancer we go obviously, it's more mutation than expressions if we go NGS. The other test we essentially that adjusted or adapted the existing test and then we are looking at next generation of test which will predict, because you're not and you have a cell expressing but also the HER2 original link, because we have a bystander effect. Our belief, is we work in HER2 low, it means that we are able to kill cells which are not expressing. So how do you predict the architecture of HER2 expression in a tumor, where not everything expresses HER2? What is the right mix? So we also are developing these tests, working together. So there's a lot of work in that, actually a lot of work.

Very good. I think we are out of time.

<Q>: Yes.

<<Antoine Yver, Global Head of R&D Oncology>>

Okay, good. Okay, thank you very much for your attention.