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PRESENTATION

Junichi Onuma - *Daiichi Sankyo Company, Limited - VP of Corporate Communications Department*

Now we would like to start Daiichi Sankyo's R&D Day 2020. I am Junichi Onuma from the Corporate Communications Department. I'm delighted to serve as emcee today. Thank you for your time. Today, our President and CEO, Sunao Manabe; and our Global Head of Oncology R&D, Antoine Yver, will make presentations. After the presentations, we will have time to take your questions. Please note that the Q&A session will be recorded. Thank you for your understanding.

Now I'd like to hand it over to Manabe-san.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

Hello, I'm Sunao Manabe, the CEO of Daiichi Sankyo. Thank you very much for joining Daiichi Sankyo's R&D Day 2020 during the busy end of the year season. This is the second time for me to host our R&D Day as CEO. I make much more important presentations in the course over the year, but I always enjoy to present here. I will present our progress over the last year and then Antoine, our Global Head of Oncology R&D, will take you through where we are relative to oncology R&D as well as future plans.

I am satisfied with the development of our 3 ADCs since R&D Day 2019. First, ENHERTU. We have successfully launched ENHERTU in the U.S. and in Japan with the breast cancer indication. The product has been submitted for approval in Europe, and we think the review is on track. The second indication, gastric cancer, has launched in Japan. And in the U.S., FDA accepted our supplemental BLA, even though the data are all from [AGM] population. Lung and colorectal studies as well as early line therapy for breast cancer are all progressing well. Our partnership with AstraZeneca has entered the second year and the relationship between the 2 companies is excellent. I am absolutely confident that AstraZeneca is our best partner.

Next is our second ADC, DS-1062. A competitor was launched, but we continue to be confident that our DXd ADC is the best-in-class. I'm also confident that we selected the best partner for DS-1062 as well. Antoine will present some of our recent discussion with AstraZeneca. With regard to the third ADC, U3-1402, the lung data presented at ESMO gained our confidence for the product, and we will start our Phase II study. We could

be registrational, depending on the results. Our breast data presented at the San Antonio Breast Cancer Symposium, which will be discussed later, are important as they help us understand the biology of HER3. In addition, a Phase II study of colorectal has started.

The steady progress of the 3 ADCs gained our confidence for achieving Daiichi Sankyo's 2025 Vision. We have gained good progress for the Alpha Project 2. Clinical trials for the following DXd ADCs, DS-7300 and DS-6157, are on track. We are starting to see some early efficacy and safety critical information, which will be provided by Antoine later. Our top line results for DS-5141, the exon 45 skipping drug using our proprietary nucleic acid technology, EMA, should be obtained at the end of this month. Depending on the results, we believe that EMA can be our next platform technology after the DXd ADC.

DS-1055 was included in our second quarter financial results presentation in October. We are hoping that DS-1055 will become a novel immuno-oncology drug in the future. This is not on the slide, but on December 3, our CAR-T therapy, Axi-Cel, passed the subcommittee of Japan's Ministry of Health, Labour and Welfare. We are now preparing for the launch of our first cell therapy product.

In maximizing shareholder value, shareholder return is always a high priority. During the current fiscal year, we have increased dividends and are currently carrying out share buyback. In addition, we have decided on consolidation of treasury shares in next April. Another high priority is optimal investment in -- for future growth. With the current pipeline, we will be aggressive around R&D and capital investment. We will aggressively strive to maximize future profitability as well as shareholder value and sustainable growth.

Presenting enhanced capital investment globally is not easy. So I will show 3 photos instead for you to confirm the good progress. Commercial manufacturing for the following ADCs also need to be considered now. And we are increasing manufacturing capacity through capital investment and utilizing CMOs. While our current priority is to invest the pipeline for future growth, there is another important area when the world is suffering from pandemic. We want to contribute through COVID-19 countermeasures, vaccines and therapeutic agents.

Today, I will briefly introduce DS-5670, our messenger RNA COVID-19 vaccine. With Daiichi Sankyo's original cationic lipid, our objective is efficient encapsulation of messenger RNA into nanoparticles and efficient delivery to cells. We think that lipid is applicable to pandemic and other vaccines. Encouraging data is being obtained from nonclinical pharmacology studies and clinical studies currently planned to start in March 2021. We are currently putting together a new 5-year business plan that starts from fiscal year 2021. Core part of the plan will be our strategy to enhance the pipeline and the product portfolio. Firstly, the 3 ADCs for sustainable growth. We are planning to present the plan in March or April of next year, so please look forward to that presentation.

This is all from me for today and will pass the baton to Antoine. Antoine, you're up.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you, Manabe-san. Good evening from Basking Ridge, New Jersey, our North American headquarters. My name is Antoine Yver, and I'm the Global Head of Oncology R&D for Daiichi Sankyo. I'm really energized today to be in front of you, on behalf of Daiichi Sankyo, for the 5th R&D Day I have the honor to provide at Daiichi Sankyo. Four years after launching cancer enterprise as an internal platform for leadership in oncology, we're proud to now stand up on the global scene on our own feet as a global oncology leader now recognized for the quality of our own science and for delivering the science the patients deserve.

Next slide. Today, we'll review briefly our scientific and competitive environment before spending most of the time in reviewing data and plans for our clinical-stage DXd ADCs, before moving on towards our transformation towards a biologics and multi-modality company.

Next slide. First, our environment. Next slide, how did we collectively get here to our current world in oncology? So 2000 was a decade where excellent drugs like Gleevec, Iressa and Avastin unleashed the power of targeting and suppressing cancer pathways. The 2010s saw the wonders of immune checkpoint inhibition and the power of redirected T-cell therapy. Despite its excessive exuberance, considering the amount of money invested, so 2010 remains a glorious decade for I-O. As we predicted few years back from this podium, so 2020s are now recognized as a new era, where high-tech pharmacology propels a century-old idea where today's magnificent technology of ADC would change the treatment paradigm away from typical chemotherapy, where you poison both the person and the tumor, wait for the recovery of the person, hit again until you can't

do anymore. On the contrary, ADCs as a true chemotherapy-free approach offers continuous hits on the tumor, 24/7, enabling durability of direct lethal hit on the tumor itself.

Next slide. So what is important regarding the ADCs from Daiichi Sankyo? The uniqueness of our DXd ADC technology platform is the duration of effect. This is not a surprise as the technology was specifically designed for that purpose. It is an integrated multi-modality, high-tech molecular construct with a unique mode of action, a high-potency payload, 10x more potent than SN38, and a hyper-stable linker, an exquisite delivery to the tumor and a unique bystander antitumor effect by design, associated with a world-class protein engineering and manufacturing processes. At Daiichi Sankyo, we are now discovering major new avenues of science in acquiring mastery in a new critical pathophysiology regarding the receptor dynamic and its pharmacomodulation. Overall, duration of response is a direct and the most critical benefit of a Daiichi Sankyo proprietary DXd ADC design, and this is what can establish true chemotherapy-free regimens as new paradigm and mainstay of cancer treatment.

Next slide. Nevertheless, the competition in ADC is now real. But we are already tackling what is next. We respect our competitors, in particular, Trodelvy, which is a great drug with a bright future. We also see the likes of Merck, Pfizer, et cetera. But the ADC concept alone is old news. Daiichi Sankyo is already blazing new trails, aiming at chemotherapy-free regimen and further exploiting the unique biology of ADCs.

Next slide. We're making major headways in the pharmacological manipulation of the ADC receptor biology in selecting the right patients and tumors, in predicting outcomes and designing and arranging for the right patients.

Next slide. The immediate value of our top 3 ADC is very clear, breast and lung cancer. And this is our utmost focus, like summarized as an exquisite focus on handling, delivering on their obligation. For breast and DS-8201. In HER2 metastatic and early breast cancer, we have a suite of Phase III trial with the most respected global academic trial partners. In HER2 low, the DESTINY-Breast04 study is fully enrolled and is tracking to read out in fiscal year 2021.

For lung, with DS-1062, we are implementing a swift development post-I-O chemo. We have a definitely a Phase III just announced as well as I-O combination aiming at first-line lung cancer. More on that later. For lung also, U3-1402, our HER3 ADC, pursues a fast-to-market development in EGFRm, non-small cell lung cancer as well as a combination with osimertinib based on fascinating science of pharmacomodulation. As we shape the possibilities of our ADCs, we are resolutely focused on our duty, our obligation, deliver the science patients deserve.

Next slide. Let's move to our clinical-stage DXd ADCs. Next slide. And first, the 8201, also known as trastuzumab deruxtecan or T-DXd in short. Next slide. In brief, by representing major advances and value for patients, we will cover 5 different aspects. For gastric cancer, the Japan approval in September and the USFDA acceptance of a priority review submission with a PDUFA date of February 28, 2021. For breast cancer, we will spend time on the big story. And the big story is not even the positive opinion received this past Friday from the EU CHMP, which makes ENHERTU the first new molecular entity in more than 2 decades to be approved or recommended for approval in breast cancer on the basis of Phase II single-arm noncontrolled data. This is one of the fastest reviews by CHMP, faster than TAGRISSO, in particular, which speaks to the unique profile of this drug and the strength of the Daiichi Sankyo and AstraZeneca collaboration. No.

The big story is the publication at San Antonio Breast Cancer Symposium in the past few days of the unprecedented duration of response for ENHERTU monotherapy in 6 or 7 lines of treatment, a duration which mimics the duration of response reported in first-line HER2 metastatic breast cancer with a triplet of THP or Taxotere, Herceptin and Perjeta. We will also cover lung cancer, the I-O combo, an important new unpublished data on file for ILD.

Next slide. First, gastric cancer. Here is a brief reminder of the design of DESTINY-Gastric01, which randomized subject to either T-DXd 6.4 milligram per kilogram or the choice of irinotecan or paclitaxel.

Next slide. Here are the efficacy results, delivering the first evidence for ENHERTU of a clinically relevant and statistically significant survival benefit with a 4-month improvement in median, a hazard ratio of 0.59 and a compelling difference in response rates with many cases of all target lesion achieving 100% reduction.

Next slide. Here is the summary of the safety finding, including ILD, with an overall incidence of ILD at 9.6% and no Grade 5 death event.

Next slide. Looking ahead, in HER2 advanced gastric cancer, we're announcing DESTINY-Gastric04, a large randomized Phase III study in second line, testing DS-8201 monotherapy versus active control. The study start is imminent as are the details to be published on clinicaltrial.gov.

Next slide. Now on to breast. As said before, the European Union CHMP has just adopted a positive opinion, recommending approval for ENHERTU on the basis of an initial submission made as recently as this last May 2020, making this an extremely fast review. The indication, as shown on this slide, as well as the approved SmPC does perfect justice to the data presented as well as the patients' need. We're looking forward to soon receiving the European Commission approval.

Now, next slide. On to the duration of response. This is a schematic of the study DESTINY-Breast01, the basis for first approval in all 3 regions, U.S., Japan and now EU. It is a somewhat complex design. Highlighted in green is the main cohort of 184 subjects for evaluating efficacy at the dose of 5.4 milligram per kilogram.

Next slide. Here is a critical slide, not only for ENHERTU in patients worldwide with HER2 breast cancer, but also for the Daiichi Sankyo DXd technology, as these finding show the very special and unique nature of our technology, delivering unique durability of response, durability of effect. Let me explain. On the left-hand side is the monotherapy duration of tumor response. You see that duration of response is at 20.8 months and the slope of the curve, which indicates a stable residual risk over time so far.

On the bottom right, you see a table which gives updated response result. At 20.5 months of median follow-up, the confirmed overall response rate by independent central review is now at 61.4%, a slight increase compared to the U.S. and Japan labels, with also an increase in a number of complete responses. And in green is a key reference point. This is a golden THP regimen, a true global standard of care in first-line HER2 metastatic breast cancer. This is from the CLEOPATRA study with the triplet of THP with the duration of response observed there was 20.2 months. At 20.8 months in 6 or 7 lines and by monotherapy, our results are unprecedented in breast cancer and a testimony to the unique nature of ENHERTU.

Next slide. Here is an important slide as well. Now for ILD by independent adjudication committee. With updated follow-up, the ILD risk clearly appears to flatten after approximately 12 months of exposure.

Next slide. So why does durability of response matter? It justifies an accelerated ambitious HER2-positive metastatic in early breast cancer plan. Let me discuss 2 critical design features of this plan. First, what to do with respect to first-line treatment? The clear unmet need in first-line treatment is to increase overall progression-free survival and further prolong the duration of response to treatment. Consequently, for ENHERTU, we have an aggressive and bold plan aiming at first-line metastatic breast cancer. More detail soon. The prevention of brain metastasis is not the critical need at that stage. Brain mets failure after current first-line THP treatment is infrequent. It is terrible but affects only 13.7% of patients.

Second, the potential of ENHERTU to be superior to T-DM1 leads to 2 questions. First, after T-DM1 in second line, brain met failure is uncommon. Only 2% in patients who did not have brain mets at treatment start and only, if I may say so, 20% -- 22% if brain mets were present at start of treatment. The clear medical need in second-line treatment is to improve the frequency of overall response and more importantly, durability of overall response and of tumor control overall. Obviously, the direct treatment of brain met is warranted when brain mets represents the cause of failure.

Our DESTINY-Breast03 study in second-line metastatic breast cancer, head-to-head versus T-DM1 will answer the question. It is scheduled to read out in second quarter fiscal 2021 with an exact timing yet to be determined. I will describe more on this later. Second, in early breast cancer, we are proud to have launched, with the NSABP and all other highly reputable academic groups, a large post-neoadjuvant trial in high-risk early HER2-positive breast cancer.

Next slide. Here are the 2 pillars for our approach to establish the role of DS-8201 in first-line metastatic breast cancer. First, DESTINY-Breast09, which is a randomized, active control Phase III study of DS-8201 monotherapy versus DS-8201 in combination versus standard of care of THP. We have completed our deep and detailed interaction with the FDA and other agencies and are ready to roll. Second, DESTINY-Breast07 as well as the BEGONIA study at AstraZeneca are combination studies which will inform at least another Phase III in the first-line setting versus THP.

Next slide. Here are some more details about DESTINY-Breast05, our post-neoadjuvant study versus T-DM1. This is run with the U.S. NSABP as well as the German GBG group and the AGO-B group, SOLTI and many others, including in Asia. This study is conducted in subject with residual invasive disease in breast or axillary lymph nodes following new adjuvant therapy for high-risk HER2 early breast cancer with total of 1,600 patients approximately and IDFS as a primary endpoint.

Next slide. What about HER2 low, in other words, HER2-negative breast cancer, either HR+ or triple neg breast cancer? In late-line post-chemotherapy, our entry point is DESTINY-Breast04. The rationale for that study is in J101 study, where we observed a confirmed overall response rate of 37%, a median duration of response of 10.4 months in the HER2 low metastatic breast cancer cohort. DESTINY-Breast04 has fully enrolled approximately 540 subjects and tests DS-8201 versus the physician choice of eribulin, gemcitabine, paclitaxel or nab-pac, with PFS by blinded independent central review as the primary endpoint. An event-driven analysis is projected in the second quarter of fiscal 2021.

In first-line chemotherapy, we're running DESTINY-Breast06, 850 subjects. DS-8201 versus physician choice of capecitabine, paclitaxel or nab-pac, with PFS by BICR as primary endpoint. Finally, in earlier metastatic breast cancer line, bold innovative plan will be announced. Of note, in HR+ and early breast cancer, the adjuvant segment is not our area of focus. And between José Baselga, my counterpart and my long-time friend at AZ, and myself, we know very well, drug development and breast cancer. We will make no more comments.

Next slide. Moving on to lung cancer. A quick review of critical data presented at ASCO last June in HER2 mutant non-small cell lung cancer. An impressive response rate, duration of response, [PFM] that formed the basis for USFDA breakthrough designation. We expect the final analysis of the HER2 mutation expanded cohorts to take place in the first half of 2021, with analysis criteria meeting the FDA's expectation.

Next slide. So what do we do to design and maximize the benefit of durability? In HER2 mutant, on the left-hand side, beyond the DESTINY-Lung01 expansion, which I've just described, we are conducting DESTINY-Lung02, comparing 2 doses of 8201 after detailed FDA consultations. And we'll start DESTINY-LungXX, a placebo first-line Phase III study, in the planning stage for now and aiming at first half of fiscal 2021.

In HER2 expressing, the current generation of IHC monoclonal antibody cross-reacts with -- in lung cancer with non-HER2 protein, some non-HER2 epitopes, some of which have now been identified. The next-generation IHC is under development for lung cancer. Meanwhile, we wait for the fully enrolled DESTINY-Lung01 IHC-expressing cohort to mature.

Next slide. Now colorectal. A quick review of critical data presented at ASCO in June in HER2 expressing, meaning IHC 3+ colorectal cancer. A 45.3% overall response rate with a median duration of response not reached at the time of this analysis. We are conducting a nonregistrational study, DESTINY-CRC02, testing 5.4 and 6.4 milligram per kilogram and also sorting out the role of RAS mutation, if any.

Next slide. We have covered a lot of ground so far, and the next 3 slides are graphical integrated schematic representation of the clinical development plan year for breast cancer. Note that some of these are purely directional. Next slide. And here, for gastric and lung cancer. And next slide, for CRC as well as other cases I've not described in much detail.

Next slide. Here, you see the DS-8201 critical short-term Phase III study data forecast. First, DESTINY-Breast02 in HER2-positive metastatic breast cancer third line versus standard of care. The event-driven final analysis is projected for the second quarter of fiscal 2021. We still, at this time, a pretty wide 95% confidence interval on the date projection of approximately 5 months.

Second, the critical DESTINY-Breast03 in HER2-positive second-line metastatic breast cancer, the head-to-head comparison versus T-DM1 with an event-driven planned interim analysis projected for second quarter fiscal 2021 and the same uncertainty of approximately 5 months on the actual data cut-off date. And finally, the DESTINY-Breast04 in HER2 low metastatic breast cancer versus standard of care with an event-driven final analysis projected for second quarter fiscal 2021 and a smaller uncertainty of approximately 4 months.

Next slide. Now moving to the nivolumab combination just presented at San Antonio Breast Cancer a few days ago. Here is the study design.

Next slide. In here, the efficacy highlights, not that we could expect to predict the success and efficacy of the I-O combo. There are just no good surrogate markers for the benefit of adding I-O to a standard of care in a non-I-O-sensitive tumor.

Next slide. And here are the spider plots. The quick -- the key question of this study was to establish that both drugs can be safely and durably administered at therapeutic doses.

Next slide. Here is the safety. On the left, the ILD, in percent, first, the total of any grade and then, from left to right, by increasing grades. We clearly do not see any compelling risk increase. We're obviously planning to move with I-O combination with DS-8201 and also borrow these data for the other DXd program to perform accelerated safety assessment. This represents a nice transition to another important subject, presenting now data not published before.

Next slide. Here, you see the preliminary cumulative ILD data from all Phase III monotherapy study now ongoing. It uses the same format, percent, first total and then increasing grade from left to right. Since these study are controlled, we assume that all ILD cases, regardless of randomization arm and adjudicated by the adjudication committee, are, in fact, related to the DS-8201 treatment. We've then estimated the number of subjects treated with DS-8201 in this study at approximately 979. The graph shows a very reassuring picture, our ILD safe-use campaign seems to be effective. It combines clear selection out of patients with risk factor, awareness and rapid investigation of any possible case as well as good treatment of any case.

Next slide. Here, you see the post-market cumulative pharmacovigilance reported data, left in the U.S., right in Japan. More than 1,000 patient years exposure in the U.S., 2 fatal cases and an added 160 patient years in Japan and no death reported.

Next slide. So where do we stand? We focus on a massive opportunity for DS-8201 to address many unmet medical needs and increase our competitive edge by acceleration, large-scale and global program, bold plan aiming at first-line HER2 metastatic breast cancer, as early HER2 breast cancer and a critical role for HER2 low breast cancer. We also pursue a broad tumor expansion, and we will build on the I-O DXd combo.

Next slide. Moving on to DS-1062, our TROP2 DXd ADC, datopotamab deruxtecan or Dato-DXd in short. Next slide. Here are key characteristics for DS-1062. It is engineered to be best-in-class TROP2 ADC. It carries all the characteristics of our DXd ADC technology, so critical to deliver its most important feature, durability response and overall tumor control. All 7 technology features listed on the right-hand side equally contribute to the profile.

Next slide. Here is the first-in-human study design in subject with advanced or metastatic non-small cell lung cancer relapse from or refractory to standard of care and for the very vast majority, I-O and platinum-based chemotherapy. The dose escalation is completed and as the enrollment of a dose expansion for a total of 180 subjects across 3 doses in dose expansion. The triple-negative breast cancer cohort recently added is also nearly complete.

Next slide. A quick glimpse at data. Here, spider plots across the 3 doses with still immature data at the September 2020 cutoff, and the pattern clearly matching that observed with the DXd platform, i.e., excellent durability.

Next slide. On the ILD side, here are the graphs. Top left of the total incidents, regardless of the doses and tumor type, and the next 3 for the doses of 4-, bottom left, and 6- and 8-milligram per kilogram on the right. What do we do with this? We are running.

Next slide. TROPION-Lung01 is a pivotal Phase III study in post-I-O and chemotherapy in non-small cell lung cancer. Patients with non-small cell lung cancer without actionable mutation and 1 to 2 prior line of platinum-based and immune checkpoint inhibitor treatment are eligible regardless of TROP2 expression by current test. All subjects will provide a fresh biopsy to support our prospective plan to retrospectively test. A total of 590 subjects will be randomized 1:1 to DS-62 at the dose we have selected of 6-milligram per kilogram, or docetaxel 75-milligram per meter square, with a primary endpoint of PFS by BICR and overall survival.

We are really excited by the level of evidence we have observed to support this critical study. We also have a massive in-house as well as an externally partnered research effort on the biology of TROP2 as a receptor for ADC therapy, and we are very confident to bring substantial discovery to this field. These very new understandings will inform the study as well as our development plan and the DXd franchise at large. This is where Daiichi Sankyo also leads and blazes a new trail, made possible by the advent of this highly innovative, high-tech pharmacology.

Next slide. What else are we doing with our partner AstraZeneca? We are bold. We're looking at non-small cell lung cancer first-line, non-small cell lung cancer activating mutation, breast cancer and beyond. In non-small cell lung cancer, first-line is a clear and immediate objective. To that effect, enabling immuno-oncology Phase I combination plan is underway, TROPION-Lung02 with pembrolizumab in collaboration with Merck and TROPION-Lung04 with AstraZeneca durvalumab. Finally, for lung, TROPION-Lung05 is for DS-1062 monotherapy in non-small cell lung cancer with activating mutation.

For breast cancer and beyond, the triple-negative breast cancer Phase I cohort has nearly completed enrollment, as I said before, and is maturing. For breast cancer at large, we are planning a very substantial plan. And other tumor cohorts are also planned. We appreciate you may be looking for more details. We are short here on purpose. The Daiichi Sankyo and AstraZeneca have a clear game plan: We have a bold, large clinical development plan, which we will characterize in due time. Our strategy is to win with utmost focus in lung and breast cancer. This is a very reason why we choose to collaborate with AstraZeneca.

Next slide. Moving on to U3-1402 or patritumab deruxtecan or, in short, HER3-DXd. Next slide. Here are the highlights of our non-small cell lung cancer EGFR and Phase I study as presented at ESMO this year. The subjects are resistant to or refractory to EGFR TKIs as well as platinum-based chemotherapy. If they had a T790M mutation, they also must have failed osimertinib before being considered for this study. Both the waterfall plot and the spider plot appear familiar for our DXd technology.

Next slide. And here is the highlight of safety. Very consistent with previously seen profile. Combined together, these results form the basis of our recent extensive consultations with FDA and the design our pivotal study.

Next slide. Here is a design HERTHENA-Lung01, a pivotal Phase II study in advanced EGFR-mutated non-small cell lung cancer to start in January 2021. EGFRm lung cancer is a tumor type where we have now observed stable and free expression and U3-1402 offers a unique, simple opportunity post-TKI and chemo. This is also important as we have now observed compelling opportunity for pharmacomodulation of the receptor and receptor ADC interaction in combination with osimertinib.

Next slide. Here is a new study also to start in January 2029 (sic) [January 2021]. Testing in Phase 1, the combination of 1402 with osimertinib. While this is a combination trial with an AstraZeneca drug done in partnership, please remember, we do not have a co-development collaboration with AstraZeneca for 1402.

Next slide. Now moving to breast cancer. Here's a snapshot of updated data breast Phase I cohort just presented at San Antonio Breast Cancer Symposium across HER3 high, HER3 low and 2 doses of 4.8- and 6.4-milligram per kilogram. These look fine on the surface.

Next slide. The spider plots seem to raise question on durability with some heterogeneity on how tumor growth control is observed over time.

Next slide. Here is a safety summary. Again, very consistent with prior reports in the low frequency and severity of ILD. The real questions are suggested on the next few slides.

Next slide. First, even before treatment with U3-1402, in breast cancer, we observed, on the left panel, a reduction of IHC level of HER3 expression. More importantly, on the right panel, we see a very substantial and frequent decrease of HER3 membrane positivity level between pretreatment level and at cycle 2, day 3 or cycle 3, day 3, meaning approximately day 24 or 45 post-first dose. We are actually beginning to decipher quite well the HER3 receptor biology implicated here and will present more data at the forthcoming scientific conferences. Very seemingly, a strong element of tumor type and specificity, which is not surprising.

Next slide. Here, we see that HER3 expression in breast cancer by membrane IHC positivity on the top 2 graphs or by mRNA expression, the bottom 2 graphs. This expression does not correlate with best tumor response as assessed by blinded independent central review. Much work to do if we want to find the right selection test in breast cancer. This is now a key part, with TROP2, of our massive precision medicine and translational science effort at many globally leading places such as the Memorial Sloan Kettering Cancer Center, the Dana Farber Cancer Institute, Gustave Roussy Cancer Campus, Sarah Cannon as well as the National Cancer Center in Japan, and of course, our great internal labs.

Next slide. Finally, ILD for U3-1402, clearly not an issue at this development stage.

Next slide. Moving on to our next-to-come DXd ADC. Next slide. This table summarizes key features and status for our next-in-line ADC. DS-7300 is our B7-H3 and is now in its 15 months since starting the first-in-human study. We have completed enrollment in dose level 7 at 12-milligram per kilogram and assessment up to dose level 6 with, so far, not a single DLT observed. Even in an unselected patient population, we have observed multiple separate RECIST-confirmed responses.

DS-6157 is progressing nicely. DS-6000 is a new, not yet disclosed until now ADC, targeting cadherin 6 with a drug antibody ratio of 8 of the DXd technology. It aims at ovarian and renal cell carcinoma. We're planning to hopefully initiate the first-in-human study in the next quarter. Finally, DS-3939 is our TA-MUC1 ADC. Still a good year-plus away from going in the clinic.

Next slide. Here are some of our key non-ADC so-called Alpha asset and their status. We recently announced initiation of a first-in-human study of DS-1055, our anti-GARP+ or anti-activated T-cell Reg asset. DS-3201 is our dual EZH1/2 inhibitor. It is in pivotal phase in Japan under SAKIGAKE designation for ATL and in global pivotal phase -- in Phase II in relapsed and refractory PTCL. We are actively exploring the clinical relevance of a dual inhibition in other hematological malignancy.

Axi-Cel or Kite C19, which we licensed for Japan from Kite, pre-Gilead-Kite acquisition, is expecting approval in Japan this very month. Pexidartinib is progressing nicely in Japan and Southeast Asia. And for quizartinib, despite our setbacks in U.S. and Europe for the relapsed/refractory indication, we continue to believe that the placebo-controlled QuANTUM-First Phase III study in first-line AML is a critical and important study and will be the first of its kind to report final analysis in second half of fiscal 2021.

Next slide. Overall, I hope we've been able to give you a tangible measure and feel of the continued transformation of Daiichi Sankyo towards being a biologics and multi-modality global company.

Next slide. As briefly alluded to by Manabe-san earlier, we are serious and delivering extremely well on our ADC clinical and commercial supply strategy. We are delivering on the needs and on our promises. We are meeting commercial and development obligation with a massive scale-up and acceleration. We're also powering through some residual pinch point so that DS-1062 supply will not slow down the Daiichi Sankyo-AstraZeneca acceleration.

Next slide. As previously explained, we truly believe in our uniqueness in being serial innovator. We investigate deeply the biology and pharmacology of ADC at the receptor and cellular biology level, as previously said. Our next ADC construct continue to track for fiscal 2022.

Next slide. Here is our top line news flow for the next 6 months and also key catalysts. This completes the primary presentation, and we will now take questions.

Junichi Onuma - *Daiichi Sankyo Company, Limited - VP of Corporate Communications Department*

Today, in addition to Sunao Manabe and Antoine Yver, our Head of R&D Division, Wataru Takasaki, will be on hand to answer your questions. We will answer your questions through the conference call. So if you have questions, please join the call. The conference call details, including telephone number, will be sent to you by e-mail upon registration through the entry form, which we sent in advance. Participants who do not ask questions may continue to watch the Q&A session through live broadcasting.

Operator

[Interpreted] The Q&A session will start at 7:55 p.m. Thank you for your patience. We have a consecutive interpreter in the Q&A session. Thank you for understanding.

QUESTIONS AND ANSWERS

Operator

[Interpreted] Thank you for waiting. Now let's begin Q&A session. (Operator Instructions)

Hidemaru Yamaguchi - *Citigroup Inc., Research Division - Research Analyst*

[Interpreted] Yamaguchi from Citigroup. And I'd like to ask a question one by one in Japanese. My first question is about DS-8201, and Antoine-san mentioned that you have a more aggressive plan for early metastatic breast cancer, you're considering. So is -- are you referring to something different from the current idea in this respect? If you have any particular idea, please share.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] Manabe-san speaking. For this question, Antoine, please answer this question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

This is Antoine Yver. So thank you. We have more plans than what is presented. We are presenting one study now. And this study will be followed by other study, at least 1 or 2 study informed by the BEGONIA study in particular. So we are planning to have more than one study to define a new standard of care for first-line metastatic breast cancer, HER2-positive. I hope I'm answering the question. We will disclose later the detail.

Hidemaru Yamaguchi - *Citigroup Inc., Research Division - Research Analyst*

[Interpreted] I have another question. I have another question. Regarding DS-8201 in lung cancer. It has been granted a breakthrough designation, and you're now accumulating final data of the patient. And once you collect the data in the United States, it sounded that it's possible to file immediately after the collection of the data in the United States. Is my understanding correct? That's my second question.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] Manabe-san speaking. Antoine, please answer this question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Yes. Thank you for the question and clarification. Yes, the plan is to submit as soon as we have accumulated the necessary data from DESTINY-Lung01 expansion, primarily. This will be a submission in the U.S. The European plan are still under discussion. So the U.S. will be primarily based on the DESTINY-Lung01 and will be later supported by the DESTINY-Lung02.

Hidemaru Yamaguchi - *Citigroup Inc., Research Division - Research Analyst*

[Interpreted] This is my last question regarding DS-7300. This could be the fourth ADC and its data may become available soon. So I'd like to ask Manabe-san whether this could also be a target or the subject of the alliance?

Unidentified Participant

[Interpreted] And regarding this matter, Manabe would like to respond. Manabe would like to respond.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] This is often-asked question, also about the third ADC, 1402. But regarding this DS-7300, for the time being, we'd like to do the development in-house for this compound. And for the fourth product, we still do not have the data yet. So we do not have any specific or concrete plan for the alliance for the time being. Thank you very much.

Operator

(foreign language)

Shinichiro Muraoka - *Morgan Stanley, Research Division - Research Analyst*

[Interpreted] Muraoka from Morgan Stanley is speaking. I also like to ask the question one by one. First of all, I'd like to ask you about the DS-1062 in triple-negative breast cancer. And I heard that enrollment is almost complete. And can we expect the ORR data at ASCO meeting next year? And also, if the ORR is going to exceed 33% in triple-negative breast cancer, meaning it's going to exceed Trodelvy, can I understand that you can file immediately based on this level of data, if you have such data?

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] Manabe-san speaking. I'd like to ask Antoine to respond to this question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you. So the enrollment is almost complete. We will not publish at ASCO, but at San Antonio, most likely. ASCO will be too early because the data cutoff is in 1.5 months from now. So there's not enough time. We are not speculating about the results and not speak anything about the potential submission in triple-negative breast cancer. Our fast-to-market is currently -- our effort are in lung cancers.

Shinichiro Muraoka - *Morgan Stanley, Research Division - Research Analyst*

[Interpreted] My next question is about U3-1402 in lung cancer. You have Lung01 study with U3-1402, and this study is going to start from now on. And regarding the results, are they going to become available in 2022 or rather 2023? Or is it possible to see a data in 2022 as well? What I want to say is that regarding 1062, lung cancer results will become available mainly in 2022. And almost, at the same timing, can we also expect the results from the U3-1402 lung cancer study, 01 study, as well?

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] Manabe-san speaking. Antoine, please answer this question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you. So the end of the lung study 01 for HER3 will depend if we complete enrollment at 210 subjects in each of arm #1 and arm #2. That will depend on external data on whether or not we carry both dosing regimen forward or drop one. So the end of enrollment and results are most likely to be in 2022 at the same time as lung for 1062. Remember that 1062 is in non-EGFR mutant and 1402 is in EGFR mutant, both in late line.

Shinichiro Muraoka - *Morgan Stanley, Research Division - Research Analyst*

[Interpreted] This is my last question. It's not about oncology, but your vaccine product, DS-5670 for COVID-19. You are going to initiate a Phase I study in March. And the Shionogi part of the top running group, compared to that, just 3 months behind. So you have to consider your supply at this moment. And Shionogi is saying that they can provide doses -- 30 million doses in the middle of next year. So what about the level of Daiichi Sankyo's capacity?

Unidentified Participant

[Interpreted] Manabe would like to respond to this question. Manabe would like to respond.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] In March next year, we are aiming to start the clinical activities. And we already are preparing for the CTM or investigational product. But with regards to commercial production and also the implementation of the studies, we still do not know what is going to be like Phase I, II and III studies. And we are increasing our capacities but I'd like to refrain from giving you an accurate answer to your question at the moment.

Shinichiro Muraoka - *Morgan Stanley, Research Division - Research Analyst*

[Interpreted] One additional question. Are you having an idea or considering possibility of the scale of dozens of millions of doses for your vaccine? That's the additional question.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] We are hoping that we can achieve that level. But number-wise, it could be difficult.

Operator

(foreign language)

Kazuaki Hashiguchi - *Daiwa Securities Co. Ltd., Research Division - Research Analyst*

[Interpreted] Hashiguchi from Daiwa Securities. I also would like to ask a few questions. First, I'd like to ask you about the data on the combination of ENHERTU and Opdivo. And the efficacy in the combination may not be so different compared to the monotherapy, but it's important to see -- consider the potential of the combination of ENHERTU and other DXd and I-O therapies. Do you have to consider what kind of data you can obtain? And what's your view on the synergy effect of these combinations? That's my question.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] Manabe-san speaking. Antoine, please answer this question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you. The Phase I data in the I-O combination had one purpose, which was to prove that both drugs could be given at therapeutic doses. And we were very pleased in patients with 5 prior lines of treatment to be able to give the normal doses. And at the time on -- of data analysis, 56%

of patients were on treatment. And at that time, the median duration of treatment exceeded 6 months. So we have a regimen which can be given at full dose and give good result and continues on treatment.

There is no measure of the potential for synergy, especially when I-O is as in breast tumor -- breast cancer, not an active therapy. The only proof of synergy will be by doing the randomized Phase III combination study versus standard of care to prove the added benefit of I-O, and this is our plan.

Kazuaki Hashiguchi - *Daiwa Securities Co. Ltd., Research Division - Research Analyst*

[Interpreted] My second question is about the safety of DS-1062. This time -- today, there was a presentation of the data on ILD only. But what about the adverse event and toxicity for the GI, the membrane toxicities. And in the 6-milligram per kilo, what kind of data do you have? Compared to the data presented at ASCO, what is your latest data on the toxicity other than ILD for a 6-milligram per kilo dose? And how this is going to change the sales potential, if any?

Unidentified Participant

[Interpreted] For the AEs and toxicities, other than ILD, Manabe-san would like to ask Antoine to respond.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you. So we have not updated the data for the other toxicity. We will present data in -- months from now at World Lung Cancer Conference (sic) [World Conference on Lung Cancer] in January. The only data I presented are a snapshot of the duration of response by -- not the duration, the spider plots and a snapshot of ILD. We have not observed any concern, new, in non -- in the non-ILD general safety profile. So we have not observed anything of relevance for the conduct of the clinical development of 1062. But we will update in details at World Lung Cancer.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] Manabe speaking. Because of those situations, there is no change to the sales potential for the time being.

Kazuaki Hashiguchi - *Daiwa Securities Co. Ltd., Research Division - Research Analyst*

[Interpreted] This is my last question. This is about DS-6000, and you're targeting cadherin 6. And I'd like to know the characteristics and the features of this target or the drug. A few years ago, there was a Phase I study for an ADC by another company, but I don't think their development is making progress since. I would like to ask you why you are targeting cadherin 6? And why do you think this ADC target can be promising? And why do you think the other company was not so successful in their development? And why do you think you can be successful by using DXd?

Unidentified Participant

[Interpreted] And Manabe-san would like Antoine to respond to this question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you. So we are confident in the target and we have the necessary preclinical. We have a drug-antibody ratio of 8 for this particular target, which indicates that, in our preclinical and toxicology studies, we believe that 8 is a correct drug-antibody ratio, just like 8201 or -- we also have belief in this target, which is highly expressed in renal cell carcinoma as well as in ovarian cancer and differentially expressed compared to normal.

I cannot speculate why the prior company failed. There are many reasons why an ADC fail and many of these reasons are not linked to the target. Most of the time it is a construct itself, which is insufficient, which doesn't have the full necessary technology to succeed. So I cannot speculate, but we are very confident, and we will give more details as we actually progress the asset in the clinic in the next 3 or 4 months.

Operator

(foreign language)

Fumiyoshi Sakai - *Crédit Suisse AG, Research Division - Research Analyst*

[Interpreted] Sakai from Credit Suisse speaking. I have 3 questions. First of all, I'd like to ask you a question about ILD risk management for DS-8201. There are cases -- you talked about the ILD cases for top 2 ADC as well in the presentation. But most of the time, these cases can be controlled and managed with steroids in principle, I think. And Antoine-san also said that it's possible to manage the risk based on the experiences you have accumulated. And can I understand that most of the cases can be controlled substantially with steroid treatment? That's my first question.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] Manabe speaking, I would like to ask Antoine to respond to this question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you. A very important question and a lot of efforts to educate, to monitor, to assess and to treat any potential risk of ILD in clinical development, but also in the market. And we also exclude patients with prior history, which of lung disease, which may make them at risk. So yes, the ILD can be managed. It cannot be eliminated. I think the Slide #43 in the presentation, where we present all Phase III monotherapy studies as of less than a month ago, is very reassuring. These are primary data.

The denominator is an assumption, and we assume all cases were from the treatment. But this is very reassuring as we have very, very few cases overall, much fewer than what we had observed initially. And very few grade 3, 4 and 5 cases out of 1,000 -- nearly 1,000 patients. These studies are ongoing, but most of these studies will report in the next year. So most of the treatment are very advanced. And we have seen for 8201, that the risk after 12 months plateaus. So really, this picture is reassuring to us.

Fumiyoshi Sakai - *Crédit Suisse AG, Research Division - Research Analyst*

[Interpreted] Could you also talk about the effectiveness or the efficacy of steroid treatment for ILD as well?

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Yes. What this is -- one of the last observation we made was that investigators and doctors recognize ILD much, much better now, but they tend to under-treat, meaning treat with that high enough doses of steroid or for too short period of time. So the last efforts we have had in the marketplace and in clinical development was to educate doctors about the importance of steroid, and this is probably what is the reason why we're observing the number we're observing in market -- in the post-market data as well as the Phase III monotherapy study. There, it's very important and they need to be administered correctly. They do have an effect. That's what we seem to be seeing.

Fumiyoshi Sakai - *Crédit Suisse AG, Research Division - Research Analyst*

[Interpreted] I have another question. This time about TROP2 ADC DS-1062. And I understand that this is an all-comer study. And you are -- there is no particular impact of the TROP2 expression on the patient's response rate. This is how you are assuming in this study, it seems. So I'd like to confirm whether my understanding is correct, that you're assuming that there's going to be an impact of the TROP2 expression on the response rate.

And also, I might have missed. But this time, you talked about the spider plot. And I thought that 8-milligram per kilo dose, a high dose can be difficult to be used. You were saying before that you were exploring or try to find the dose among 4-, 6- and 8-milligram per kilo. But looking at the results, can I understand that you have a certain direction for the dose selection for the future? So these are my 2 questions on TROP2 ADC.

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] And Manabe-san speaking. Antoine, please answer this question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you. So we have -- I'll answer the second question. We have decided on the dose in launching the TROPION-Lung01 Phase III study, which is pivotal after IO and chemotherapy non-small cell lung cancer. We are testing DS-1062 at 6-milligram per kilogram versus docetaxel.

So we have chosen the dose of 6 in collaboration with AstraZeneca. On your question about TROP2 expression. With the current test, we are not observing a predictive value of TROP2 expression on response rate. We are very confident that we will find the correct measure to predict patients will most benefit from this particular therapy.

We are not describing this method or methods now, but we are very confident we will have a method to discriminate. And in TROPION-Lung01, all subjects will provide a biopsy so that we can prospectively plan to retrospectively test for the marker selection.

Fumiyoshi Sakai - *Crédit Suisse AG, Research Division - Research Analyst*

[Interpreted] This is my last question. And I'd like to ask this to Manabe-San. What's the update on the litigation pending on ADC with Seagen? To this question, Manabe, would you like to respond?

Sunao Manabe - *Daiichi Sankyo Company, Limited - President, Group CEO & Representative Director*

[Interpreted] Manabe would like to respond to that question. And Seagen is saying that based on their patent they have acquired recently, they are saying that we are infringing their patent. And Daiichi Sankyo believes that Seagen's newly acquired patent itself is invalid. So we don't think we are infringing their patent.

So we'd like to clarify our assertion in the rule of law or court through this ruling by the justice. And we filed a lawsuit against them in November with the Federal District Court in the State of Delaware, and that's the current update. And if there is any progress in this case, I'd like to report this to you. Thank you very much.

Akinori Ueda - *Goldman Sachs Group, Inc., Research Division - Equity Analyst*

[Interpreted] Ueda from, Goldman Sachs Securities. And first, about 8201, and I have an additional question about ILD with DS-8201. There was a chart on Page 44 in the presentation, and you talked about the incidence of ILD in Japan and the United States. But it seems that there is a big difference in the incidence of ILD between Japan and the United States. So are there any factors behind the big difference in the ILD incidence?

And also to identify patients at high risk of ILD, before, you were saying that you're also looking at their past history of treatment with multiple drugs -- particular drugs. But how are you identifying high-risk patients right now? So that's my first question.

Unidentified Participant

[Interpreted] And Manabe-san would like Antoine to respond.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

So number one, you are correct. The number of events reported in Japan relative to the number of events reported in the U.S. appears to be different. These are number of events reported through the pharmacovigilance system. It is likely to reflect 2 things.

One is that ILD awareness in Japan is much higher and thus, more likely to be reported. And more importantly, there's also a higher incidence of lower grade, so grade 1 or grade 1 and grade 2, in Japan, not only for 8201, but generally speaking, for drug inducing ILD. So really, the key numbers here are less the any grade and more of the deaths or fatal cases. And what was reassuring in these pictures that we only had 2 and 0 in the U.S. and in Japan.

With respect to the high-risk, what we've identified are risk of -- as risk factor are pulmonary -- history of pulmonary disease such as BPCO, obviously, hemopathy, ILD risk factors, abnormal lung function at the entry. The prior treatment has not been and is not an exclusion factor. So the prior anti-cancer treatment is not an exclusion factor, although we seem to observe that the longer the patients have had cancer treatment and the more likely that the patient has ILD, it's probably the cumulative total dose of cancer treatment, which makes it a risk factor, but we are still investigating that aspect.

Akinori Ueda - *Goldman Sachs Group, Inc., Research Division - Equity Analyst*

[Interpreted] My second question is about DS-1055. And I'd like to know your development strategy. Theoretically speaking, there can be an add-on effect by the IO therapies, and they're more doublet IO therapies, the IAPD-1, PD-L1 antibody to be combined in the doublet therapy that's increasing these days. So is there any possibility of combining DS-1055 on top of the other 2 IO antibodies to make triplet therapy? And what is going to be your development strategy? That's my second question.

Unidentified Participant

[Interpreted] And Manabe-san would like Antoine to respond.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

So thank you. We are excited to enter IO with an asset of Daiichi Sankyo Discovery. DS-1055 target is not a new target, but it had been before tested by others, and they failed. We believe our construct is more likely to succeed. The first-in-human study will have to establish, not only the safety, but also some biological evidence that we reduce the regulatory -- activity of regulatory T cells to reduce the number of the activity T-regs in the tumor. Then our development is to indeed combine with immunotherapy agent 102, but this will come once we have established a safe dose and a dose which is biologically active on the depletion of activity T-regs.

Akinori Ueda - *Goldman Sachs Group, Inc., Research Division - Equity Analyst*

[Interpreted] My last question is about DS-5670. And you are using your own unique liposome. And it's different from what Pfizer and Moderna are using. So you may have to take more time in your development and look at this more carefully perhaps. So for the antigen protein, are you using S protein? And are you also using the pulling metastasis to stabilize the structure like Pfizer or Moderna? So this is my last question.

Unidentified Participant

[Interpreted] And Manabe-san would like to ask Takasaki-san to respond.

Wataru Takasaki - *Daiichi Sankyo Company, Limited - Executive Officer and Head of R&D Division*

[Interpreted] Takasaki would like to respond. First of all, our unique cationic lipid, we think it has a very high efficiency in the delivery of messenger RNA. And also, the lipid composition ratio and also the ratio of messenger RNA, we have already established these ratios. And we are now discussing the way of mass production right now. Therefore, we have high expectations about its efficacy and the effectiveness. But with regards to the antigen, please allow us to refrain from disclosing.

Tatsuyuki Arai - *BofA Merrill Lynch, Research Division - Junior Analyst*

[Interpreted] Arai from BofA Securities. We are behind. So I would like to briefly ask 2 questions with regards to DS-1062. And what you are planning to develop this in first-line lung cancer settings? And what kind of milestones you need to achieve to enable your development of first-line lung cancer indication? And this is my first question.

And secondly, about the difference compared to the Trodelvy from Gilead. They also developed -- they developed the compound in lung cancer, developing this in lung cancer. And they also have data of about 20% response rate. And I understand that DS-1062 has a different structure compared to Trodelvy. But based on the current available data, how much expectation do you have about DS-1062, vis-a-vis Trodelvy?

Unidentified Participant

[Interpreted] Manabe-san would like to ask Antoine to respond.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

Thank you. So I would answer the second question first. Our belief is that the DXd technology is unique in allowing for durability of treatment. We've proven that multiple times, not only with 8201, but with our other clinical-stage assets, but the most important effect of this technology is how stable it is in the blood, how high potency with biosimilar it is in the tumor and how little systemic toxicity there is. And versus Trodelvy, for instance, where the drug is relatively unstable, must be administered day 1 and day 8, and creates a safety profile, which is closer to that of chemotherapy with GI toxicity, neutropenia, febrile neutropenia, death by neutropenic infection. We have, with 1062, a construct, which we believe is best-in-class and primarily with duration of response. I will let the translator and come back to the first question.

With respect to the second -- to the first question, the milestone to go first-line is simply to have a safe combination with an IO region. We have an active collaboration with Merck, and we have started the TROPION-Lung02 on an accelerated schedule because we've proven with levo and DS-8201 that the combination of DXD and immune checkpoint is safe, in particular, in liver and in lung toxicity. So we feel comfortable to have an accelerated testing of the DS-1062 and pembrolizumab combination in the TROPION-Lung02. And as soon as we have enough safety evidence, we will move in first line. We are actively discussing with Merck the detail of that extended collaboration for these particular study and indication.

Yo Mizuno - *Tokio Marine Asset Management Co., Ltd., Research Division - Analyst*

[Interpreted] Mizuno from Tokio Marine Asset Management speaking. And I'd like to briefly ask 2 questions. First, about DS-8201 on its pan-tumor study. And I think this study can be passed to approval regardless of the organs with HER2 positive -- positivity. So what kind of results would be necessary to use it as a path to approval? And that's my first question.

And my second question is about the muscular dystrophy. You are having the data on the first drug for this indication, EMD, and you are also developing follow-on compounds as well. And do you need the success of the first drug to proceed with the follow-on compound development, I'd like to confirm.

Unidentified Participant

[Interpreted] Manabe-san would want Antoine to answer the first question and want Takasaki-san to respond to the second question.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

The pan-tumor HER2 is an important study, which will give us initial evidence of activity across different tumor types with less frequency of HER2 expression or HER2 mutation. To have an indication regardless of the tumor requires that we select the patient on the biology, which is unique and similar across all of these different tumor types. So far, HER2 expression by IHC has not met this criteria. We have discovered that the typical IHC for HER2, in some cases, identifies antigen, which are not HER2 antigen. And we are creating the next generation of test.

So we may or may not be able, in the near future, to have a test which is valued across all tumors. We are actively looking with different major collaborators to define which test. Meanwhile, we are conducting the pan-tumor assessment and keeping the tumor blocks for future testing.

Wataru Takasaki - *Daiichi Sankyo Company, Limited - Executive Officer and Head of R&D Division*

[Interpreted] Takasaki would like to respond to the second question about 5141. Because of its action it seems to have on cardiomyocytes, so we are having high expectations on this project. And by the end of this month, we will have top line results.

And with regards to the so-called follow-on projects, they're using the same ENA technology, but the sites of shipping is different for these follow-on projects. And we are also beginning to observe nonclinical profiles as well. So regardless of the outcome of the status of the development of 5141, we'd like to continue promoting R&D for the follow-on projects as well.

Seiji Wakao - *JPMorgan Chase & Co, Research Division - VP*

[Interpreted] Wakao from JPMorgan speaking. I only have one question about 8201. And I'd like to ask you about the level of your expectations about the adjuvant with DS-8201, if you're able to comment. And you are demonstrating high efficacy and durability of effect. And also, the manageable ILD profile. And I'm sure that you are having higher expectations for the first-line settings. And can we apply these features also to the adjuvant as well? And compared to the terminal cancer patients, these patients in those settings still have some physical stamina. So do you think that you can have high expectations? Or if any, you still have to look carefully at the adjuvant? Any particular element, if any.

Unidentified Participant

[Interpreted] Manabe-san would like Antoine to respond.

Antoine Yver - *Daiichi Sankyo Company, Limited - Global Head of R&D Oncology*

So I'm glad you asked this question. DESTINY-Breast05, which is described on Slide 30, is really an exciting study for Daiichi Sankyo. This is a study which is starting just 1 year or less than 1 year after the first approval. All the major world group in breast cancer collaborated with us for the past 12 months to design and launch this study. And we are really excited because this is a head-to-head study versus T-DM1, where we absolutely believe DS-8201 to be substantially superior to T-DM1.

T-DM1 has proven a role in the adjuvant setting or post neoadjuvant, to be technically correct. And what this particular study, where we will compare with T-DM1 is on the 60% to 70% of patients, who do not do very well in the post neoadjuvant setting with T-DM1. And we're really very confident that 8201 will substantially improve the benefit for patients in this particular setting. So it's an extremely exciting study, and we have very high expectation on this study.

Operator

So it concludes the Daiichi Sankyo's R&D Day. Thank you for your participation today.

[Portions of this transcript that are marked [Interpreted] were spoken by an interpreter present on the live call.]
