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CORPORATE PARTICIPANTS

Ali Tehrani *Zymeworks Inc. - Co-Founder, CEO, President and Director*

CONFERENCE CALL PARTICIPANTS

Gena Wang *Barclays Bank PLC, Research Division - Research Analyst*

PRESENTATION

Gena Wang *- Barclays Bank PLC, Research Division - Research Analyst*

Okay. Thank you, everyone, for coming to Barclays health -- Global Healthcare Conference. My name is Gena Wang. I'm a SMID Cap biotech analyst.

It's my great pleasure to introduce our next speaker, Ali Tehrani, Chief Executive Officer and President of Zymeworks.

Ali Tehrani *- Zymeworks Inc. - Co-Founder, CEO, President and Director*

Thank you, Gena. Thank you to the Barclays team and -- for inviting us and for this opportunity to introduce Zymeworks to you. In the next 10 minutes or so, my intention is to try to give you a broad overview of our company, and then we'll go into our discussion with Gena.

Basically, Zymeworks is a clinical-stage company that is located in Vancouver, British Columbia, Canada and also in Seattle. Our company is anchored in 2 aspects: one being a number of proprietary and disruptive platforms that enable the development of multifunctional biologics; and the second component is a deep pipeline of therapeutics, both at the preclinical stage and also at the clinical stage. Taking that together, this slide is meant to provide an overview of how our business operates.

Starting at the very bottom -- sorry, I have to go one back. There we go. Starting at the very bottom. What you see are 6 active collaborations with major pharmaceutical companies that revolve around our technology platforms. These all revolve around the need of these pharmaceutical companies to build bispecific antibodies, multifunctional biologics.

The center point of all of these deals is our Azymetric platform that enables the development of bispecific antibodies, which I will elaborate on in just a second. Some of the key points about this is that none of these deals include target exclusivity. These are purely licensing deals where any of these companies just want to access our Azymetric platform or any of the other platforms to build bispecifics.

The most recent deal that we signed is with J&J. This deal was announced in November of 2017. It came with $50 million of upfront payment, and it's a deal that could be worth up to $1.45 billion. Alongside J&J, our other partners include Eli Lilly, Merck, Celgene, GSK, Daiichi Sankyo. And I should note that both Eli Lilly and Celgene are also investors in Zymeworks.

Moving slightly higher. Those same platforms that have been licensed to the pharma partners are being internally utilized by our R&D team to build the preclinical pipeline. Our intention is to further talk about the specifics of this preclinical pipeline in the second half of this year in an R&D Day. Some of the broad areas that we're looking at in our preclinical pipeline include bispecific antibody-drug conjugates, bispecifics that are utilized for T cell engagement and redirection and bispecifics in the area of checkpoint modulation.

And then, at the very top, what you see is information regarding our clinical asset, ZW25; and our other lead asset, ZW33. ZW25 is in an adaptive Phase I. We have previously shared data at San Antonio Breast Cancer Conference in December of 2017. I will give you a snapshot of that here today.

To get a little bit of a cultural look at our platforms, we have a number of platforms for the development of fit-for-purpose biologics. The flagship platform is the Azymetric platform. This platform enables the development of bispecific antibodies in different formats, in different geometries, and it's been the center stage of our deals that are outlined below for you.

Our second platform is Zymelink. Zymelink consists of a number of proprietary linker and payloads that enable the development of antibody-drug conjugates. And the third platform is called EFECT. EFECT enables effector function modulation through a different component of the CH2 domain of an antibody. And finally, we have a platform called AlbuCORE, which enables the development of multifunctional biologics as an alternative to antibodies.

There we go. So often, one of the questions when it comes to the development of bispecifics is: Well, why your platform? What are the distinguishing features? What this slide is supposed to provide to you is the answer to that question. Basically, in the world of bispecifics, we don't believe that one size fits all. In other words, there will not be a singular bispecific geometry or modality that is going to cover all the different biologies in target.

What it comes down to is how you bind to a target as opposed to just binding to 2 targets. And in the Azymetric platform, you can benefit from the most comprehensive set of geometries, be it a fully heterodynamic antibody or an antibody that is benefiting from common light chains or hybrids or some variations there such that you can focus on the development of your bispecific and the biology as opposed to being restricted by singular format.

So the Azymetric provides the most comprehensive set of formats to enable the best fit-for-purpose biologics. Alongside that, the Azymetric very well combines with our ADC capabilities, our linkers and payload through Zymelink, and it gives us the most amount of flexibility to focus on that fit-for-purpose outcome as opposed to being restricted by modalities. In totality, we have a very large and complete innovation engine, from target discovery all the way to the output and lead optimization, which gives us the ability to build a deep preclinical pipeline and a clinical pipeline, again, focusing on that fit-for-purpose and knowing that we rely on a fully integrated development -- drug development engine as opposed to just pieces of it.

To give you a snapshot of our lead clinical asset, ZW25, this asset combines the best of Herceptin, trastuzumab, with the best of PERJETA, pertuzumab, and combines it into one antibody. We already know that trastuzumab and pertuzumab combined provide benefits to patients, but unfortunately, these patients tend to regress, these patients tend to become resistant/refractory. And our objective here was to see if we can combine trastuzumab and pertuzumab into a bispecific and provide additional value to these patients. Essentially, the thesis is that 1 plus 1 equals 5 as opposed to 2.

So far, the data in our adaptive Phase I has been going really well. And as of San Antonio Breast Cancer Conference in December of 2017, we were able to show -- if this waterfall comes up -- that in a total of 22 patients, 19 of which were response-evaluable, we had 6 partial responses with a number of stable disease. So if you're unfamiliar with these graphs, every time the bar goes down, that means that the tumor for a respective patient is shrinking.

So as you see here, we have 6 partial responses. 5 of them are for breast cancer, 1 is for graft -- gastric cancer. We have 2 confirmed partial responses for breast cancer and 1 confirmed partial response for gastric cancer. We're very encouraged by this data. So the antitumor activity has been very encouraging. And similarly, the tolerability has been great. Throughout multiple different doses and schedules, we've seen, in the typical format, no more than grade 1 or grade 2 diarrhea. So tolerability has been excellent, and antitumor activity has been very promising.

The most notable piece here is the fact that these patients on our study come with being heavily pretreated in the past; on average, a median of 6 prior lines of treatment. So in the fourth column here, you see that the breast cancer patients were previously treated with a combination of Herceptin, PERJETA, Kadcyla and, in some cases, lapatinib. They became resistant/refractory and then came on to our study as true last line, and we're able to see the signal that I showed you on a previous slide where, again, there were 6 partial responses across the entire breast and gastric patients.

This slide here is meant to provide an overview of the patients that were gastric cancer. Again, you see that everyone had received trastuzumab, which is the standard of care in the case of gastric -- or HER2-expressing gastric cancer.

In terms of where the study is headed, we are completing right now our dose expansion, and our objective is to initiate cohort -- or combination study cohorts where we get to look at ZW25 in combination with other agents. So we're very excited about the single-agent activity of ZW25, and now we want to start to study the benefits of ZW25 in combination with other agents such as chemo agents and other targeted agents. And our

objective is to ultimately place ZW25 either as monotherapy or in combination in the higher lines of treatment when it comes to HER2-expressing cancers.

So in totality and coming to a close here, we believe we have a diverse business comprised of our deals with pharma, which are progressing really well. We have a preclinical pipeline that provides us with a lot of optionality, and we have a clinical asset that is generating very promising data and, of course, validating the other components of our business. And to wrap it up, we believe 2018 is going to be a breakout year where we would be presenting additional data for ZW25. We plan on additional INDs in 2018, and we may be signing additional strategic deals similar to our J&J deal and the other deals that we have done to continue growing our business.

Thank you very much for your attention.

QUESTIONS AND ANSWERS

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Thank you, Ali. So maybe we will start with the technology. Can you share with investors or with us the unique aspects of your technology? And what are the key features that your collaborators value the most?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Great. Fantastic. I was in a recent talk where a number of pharma executives were talking about the world of bispecifics and the fact that they're looking for multifunctionality in bispecifics. In the world of large molecules, having a multifunctional large molecule to truly address the different components of a pathway of a disease is critical to success, and our technology enables that fit-for-purpose multifunctionality. We have, as you saw, a number of platforms that combine really well together such that you can address all the different nuances of a disease and, ultimately, put that best first-in-class or that best best-in-class biologic on the table. And we do all of that without sacrificing safety or without sacrificing manufacturability. So the assets that are developed by our team for us and also by our partners for themselves hold the potential of being able to address many different components of a disease as opposed to a singular component and also be able to survive all the challenge of clinical trials in terms of safety, manufacturability, tolerability. So it truly comes as a complete package.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. Should we expect to see more licensing deals this year? And can you help us understand how you construct the collaboration deals to maximize the value?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Great. So yes, the simple answer is expecting more deals this year is very realistic. Our business is grown on doing these deals. We have 6 active deals, the latest one with -- being with J&J. The data that is generated for ZW25 is generating a lot of interest by others in our platforms, and doing more deals is totally realistic. In terms of the components of these deals, one thing we're very proud of is that we have not done any target-exclusive deals or any indication-exclusive deals. These deals leave our hands open to continue to develop assets for ourselves and be able to grow our own preclinical and clinical pipeline, and they come with significant upfront payment that come with preclinical payments, payments for clinical success, commercial-related payments and, of course, royalties.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

So do you have a sense like when will one of your partners' compounds enter the clinic?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

All of the deals are progressing really well. And the information that is being shared with us makes us very excited and we're in a position -- and very enthusiastic about the fact that our partners should be -- one or more of our partners should be entering the clinic more -- sooner rather than later. I can't obviously share the information, but we're very enthusiastic that it could be as early as this year.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Great. So maybe we move to ZW25. So in the second part of your adaptive Phase I trial, what patient groups are you including in each cohort? And how's enrollment going? Is there any difference in each cohort?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Great. So let me start with the second part first. Enrollment is going really well. As we announced before, we are enrolling in 4 different cohorts: HER2-high breast cancer, HER2-high gastric cancer, HER2-intermediate breast cancer and a basket cohort. And enrollment, as I said, is going really well. As you may have noticed, we just recently announced that we have expanded our trial into Canada. That's because the enthusiasm and the excitement by clinicians as they've been made aware of our data has been great, and we've been encouraged to go to many different sites as clinicians are excited to enroll patients into our trial. So we're excited to be able to fill these cohorts and to ultimately bring the data to the market when the data is mature and ready.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. When will we hear more about the data from the expansion cohort? And are you planning to present some data at ASCO?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Well, as I mentioned, enrollment is going really well. So we do have patients in our expansion cohorts as part of the trial. And our objective is to be present at every major conference. So we just need to make sure that -- we want to make sure that we bring a mature set of data forward so it is not to be unexpected for us to be present at every conference and to be able to provide some sort of an update on how things are going.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

So what would be your expectation in each cohort in terms of response rate and duration of response in order to be clinically meaningful and/or competitive?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

So if you look at last-line treatment in breast cancer, for example, a response rate greater than 20% to 30% is considered very exciting and promising by clinicians, and a disease control rate of greater than 50% is considered very exciting by clinicians. So far, as reported in our poster at San Antonio Breast Cancer Conference, our disease control rate was greater than 64%. So we're in good shape. We feel like the asset is providing very promising signals, is very tolerable and is generating clinician excitement. In gastric cancer, if you look at the GATSBY trial, for example, the progression-free survival was less than 3 months. And pembrolizumab, Keytruda, got an approval with less than 13% response rate. So the need is really high in gastric cancer. The PFS for first line is not that strong. And our asset, ZW25, has had very promising early data in both breast and gastric cancer. So we hope to have our asset do better than 20% to 30% response rate, better than 50% disease control rate in breast cancer. And in gastric cancer, essentially, the bar is lower because the need is much higher.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

So what's your thoughts on duration of response?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Duration is absolutely critical, and we want to see a duration of response somewhere greater than 4 months, ideally, in 6 months.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

So maybe one question, like how -- like realistically, how is ZW25 better than, say, using 2 antibodies separately?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Great. So as per the slide that I just showed, our breast cancer patients were previously treated by trastuzumab or a combination of trastuzumab and pertuzumab and they still became resistant, refractory, relapsed. And then they're treated with ZW25 and they see a signal again. What this says is that providing the 2 drugs in one and having them simultaneously bind to HER2 provides a signal better than the combo because in the combo situation, you essentially have one drug at a time interacting with HER2. Ultimately, ZW25 benefits from -- or provides benefit to the patient in internalizing the HER2 receptors and having them ultimately be destroyed. It also provides a cluster on the surface of the antibody -- on the surface of the tumor cell, essentially starting to choke it. And that clustering is important to the internalization. That clustering is important to effector cell recruitment, which could result in antibody-dependent cell cytotoxicity or other forms of killing. So ZW25 is a 1 plus 1 equals 5. It brings you many different and combines many different modes of action to best kill the tumor cells more than the combination where one drug at a time is interacting with the receptor.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. And then regarding your registration strategy, what would you like to see from the expansion cohort? And how would that inform you for the next step?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Right now, we're very much focused in collecting the data that enables a registrational pathway. As I mentioned, pembrolizumab, Keytruda, was able to get an approval with, I believe, less than 40 patients and a response rate that was less than 13%. So good data in areas that are highly unmet and there's a lot of need kind of do the trick themselves. So right now, our focus is to enroll patients, to collect data and let the data pave the path. Enrollment is going really well. The signal seems to be very strong. The tolerability is great. The safety is great. So we feel like we're right where we need to be on route to ultimately bringing this asset to the broader market.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. So we have time maybe for one last question. So when will we learn more about your internal program, pipelines?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Great question. Simple answer is in the second half of this year. We intend to hold an R&D Day, where we will be talking about some of our non-HER2 preclinical programs that could contain bispecifics, bispecific antibody-drug conjugates and other forms of bispecifics that are non-HER2. We're very excited to be able to share that with the world in the second half of this year.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. Maybe what are your criteria to selecting pipeline program?

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Unmet need and the ability to best address that unmet need in a sustainable, durable fashion. We're looking for first-in-class, fit-for-purpose biologics, and sometimes, we're looking for best-in-class fit-for-purpose biologics. But our objective ultimately comes down to sending patients back home to their loved ones disease-free. It is an awesome feeling to know that you've accomplished that. So we're always looking for solving the problem as opposed to providing certain answers about the problem.

Gena Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. Thank you very much. And we will have a breakout session across the [hall].

Ali Tehrani - *Zymeworks Inc. - Co-Founder, CEO, President and Director*

Thank you very much.
