Citi's 2025 Biopharma Back to School Conference Fireside Chat Transcript

John Whittaker

Analyst, Citi

Okay. Nice to see everyone here in the room today. I'm John Whittaker with the Citi Investment Banking Team. Excited to have a discussion with Ascentage here this afternoon. And Veet, obviously, you're new to the seat, congratulations, and I think it would be helpful – certainly introduce yourself and I think it would be helpful to provide a bit of a background on Ascentage, the company overall and obviously you just had your first half update a couple weeks ago and highlighted some key progress and milestones to be attentive to on the horizon. So, maybe take a couple minutes to talk about the company and some of your key updates from August.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Yeah. Sure. Thank you, John. Thank you for having me. Happy to do that.

Yes. I joined Ascentage as CFO couple months ago, beginning of July. Been a couple months, but it feels like it's been a couple of years' worth of activity. So, maybe I can start by talking about the innovative pipeline that we have. As it relates to the company now, we have two differentiated novel oncology products now being sold in China. So, our first asset, Olverembatinib, is a third generation BCR-ABL TKI. So, this is a very important area where the company got – initially it got what's known as conditional approval in China about in 2021. This is very much like accelerated approval in the US. And eventually the company got full approval and importantly for both patients with or without mutations. And in fact, the label was quite favorable, in that it's applied for patients who are resistant to first or second generation TKIs and/or intolerant. The and/or intolerant part is important because these patients, as a result of these TKIs that are first generation, second generation, can have issues, like diarrhea, etc, and they go on to another TKI.

And so, in our case, this is kind of considered near second line, one could even say considered as a 1.5 line. So, very pleased with Olverembatinib's progress. It eventually then got on to the NRDL which is, as you know, the mechanism in China for reimbursement, which is very important because initially patients have to pay like RMB 10,000, RMB 15,000 a month, which is difficult for these families. So, to get on NRDL opens up about 70% of the population for market access. So, that's very important for Olverembatinib. And you can see that what's also very

interesting about this asset, which provided a lot of tailwinds for the company last year and was one of the reasons why the company generated momentum for the dual listing in the Nasdaq.

Initially this company became public on the Hong Kong Exchange in 2019 during the wave of China essentially supporting innovation in general. And in 2018, as you know, I won't take you through all the details, I'm sure you know it very well, but we kind of exploited this exchange opportunity, allowing non-revenue life science companies to go public. So, 2019 was when we did that.

In the span of essentially five years, we eventually became a dual listed company. Stock has generated good momentum, including entering in Takeda option agreement in June, 2024. I believe we're fortunately the top performing Nasdaq IPO in the last several years and that's among 30 plus biopharma companies that have gone public. And that's because of Olverembatinib and the deep pipeline in the clinic in China being developed during that time.

So, the last six months actually have been particularly exciting. We got the second drug approved, Lisaftoclax, which is a selective Bcl-2 inhibitor. This is very important because, prior to Lisaftoclax, venetoclax has been the mainstay, the only approved Bcl-2 inhibitor, and that was approved nine years ago by AbbVie, right. This is a very good time for the company with Lisaftoclax where there is pretty broad indication set in terms of what Lisaftoclax can target as it relates to NHL subtypes. The approval was in CLL, SLL. And, also we were fortunate on the label in that case as well where it's directed towards patients who have taken at least one systemic therapy, including BTK inhibitors.

So, not refractory. It's not an R/R population. So, I'll bring back the same kind of consideration. It's like 1.5 lines or even 1.1 lines. So, very pleased with having that profile of approval. And of course, with Lisaftoclax, this is one that we plan on exploiting on our own. We made some heavy investments as it relates to commercialization, being aggressive, because we need to take advantage of these first-mover advantage tailwinds and exploit that. So, we actually doubled our sales force in three months leading into approval.

And then we have a number, as I mentioned, of active programs ongoing in the pipeline. I think one thing is exciting is our triple kinase inhibitor, the FAK, ALK, ROS inhibitor, that actually opens up a foray into solid tumors along with two others, our MDM-p53 inhibitor and the Bcl-2/ Bcl-xL inhibitor going after NSCLC, ACC, neuroendocrine tumors, ovarian and others.

And then we also have an EED inhibitor as well. So, we're going after an epigenetic target, which targets both – key areas of anemia and lymphoma. We have patient data in sickle cell, but we're – I think for the near term, exploiting the oncology side. And that's not to mention what's beyond that, which is our protein degrader capability. So, we're very excited about that, going to be talking more about that in the months ahead. So, please stay tuned.

John Whittaker

Analyst, Citi

Well, congrats on all the progress and the breadth of the progress as well. I think we all appreciate just how deep the pipeline is and how productive the R&D engine has been at Ascentage. Obviously, getting the approval this summer for Lisaftoclax was a big milestone for the company. And to your point on the label being broader, not limited to relapsed/refractory patients and that opportunity– you used earlier in terms of line of therapy. How should we be thinking about kind of the go forward milestones for the product? Obviously, we will now be looking at sales at each of your updates, semi-annual, if not more frequently. So, I think the commercial launch and the uptake will be important. As you said, you've made a significant investment to really turbocharge the launch, but there's also some active studies that continue to create opportunities to expand the label. Is that right?

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Yeah, that's exactly right. So, very good question. Yeah. So I think we have lots of, I would say, commercial and mature catalysts ahead. So I'll kind of walk you through it.

John Whittaker

Analyst, Citi

Yeah.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Yeah. So, as it relates to sales, so let's take Olverembatinib, now it's on the NRDL for all approved indications, right. So, there's a price set for that. That's a stable price. So now I think we can give some good – the market can get some good visibility on the growth of Olverembatinib. We're very happy with the first half report where we disclosed that we had 93% period-over-period jump in sales and that's driven by a 47% increase in hospital penetration because, as you know, in China, you got to get to the hospitals first, so...

John Whittaker

Analyst, Citi

Right.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

...which is exactly what we're doing with Lisaftoclax. So Lisaftoclax, we are going to be similarly applying for the NRDL as well going into next year. So, eventually, we'll give the some guidance there on timing. That's the commercial areas. Also, as you know, we got this very strong validation from Takeda as it relates to the option on Olverembatinib. So, that's ongoing. We have a very good relationship with Takeda, as it relates to all the trials we're running globally, including in the US. And so, those are kind of some key commercial late- stage assets or catalysts.

And then, of course, as relates to Lisaftoclax, right, a major, call it some luck, call it also some foresight about preparing for a major market opportunity, which is HR-MDS, right. So, we got the VERONA news from AbbVie where the hazard ratio and overall survival was 0.904. And with GLORA, I think three things it's important there, GLORA-4 here in the U.S. is one trial that we essentially now have clarity about how to execute because of the VERONA news. That's a key thing because clearly it was a bit of an overhang for us actually. We were kind of waiting for that to come out. And it was kind of rumored at ASCO that VERONA would turn out the way it did. And then the confirmation came at EHA and I think that also is what contributed to our series of events that led to some good stock momentum and we appreciate working with you on taking advantage of that in the follow-on that we did in July. So, kudos to the Citi team there as one of our partners.

The second thing is, this is I think quite remarkable and perhaps even rare, dare I use this word, which is the protocol. The clinical protocol is identical between China, Europe, and the U.S. This is also something we're very excited about here. So, it's a pretty, I think, clear trial design going against AZA. We all know kind of the response rates with AZA, right, the ORRs kind of being around the 25% range, at least in r/r AML. And our data to-date show that we've well exceeded that. So, that's another important point.

And then, of course, HR-MDS, right. So, this is a disease category where there hasn't been a targeted therapy approved in 20 years. Now that we have a very exciting registration trial going on in HR-MDS and also validated kind of the differentiation we have as it relates to venetoclax, not – that's besides a differentiation as it relates to dosing, but the toxicity profile much more favorable on the Lisaftoclax and remember it got approved as a single agent. So, that's key here. And venetoclax also didn't make it similarly in multiple myeloma as well, not once, but twice. That's another opportunity. And to your question about catalysts, stay tuned there because I think we'll have more to say on the multiple myeloma side.

Now, of course, venetoclax is a good drug, right. It's a drug that's been very effective and potent. And another they're – I think they're going to continue to be a very important drug in AML, right. They're essentially a standard of care in AML. But we have very strong data that shows a potency and a good safety profile in patients that are refractory to venetoclax in AML. So I think we're going to get some good opportunity there and just going to continue to show the validation.

And then, of course, there's CLL, right, where we have two other studies, we have GLORA and GLORA-2. And I think this is very important to spend like a minute on because I think we get the question a lot about how do we differentiate ourselves against our competitors. And it's no secret, BeOne is a name that comes up a lot, and how do you – what is your strategy there given what all the good work that BeOne is doing? Well, with GLORA, GLORA-2 and now with the single agent Lisaftoclax proven ability to get approved, we're giving essentially patients a potential choice here in terms of managing their CLL, right. We have Lisaftoclax alone and then we have patients that already have a history with the BTK and want to work in Lisaftoclax and that's GLORA and also patients who want to have or are having fresh start therapy with the BTK inhibitor. In this case, we're pairing with Acala by AstraZeneca. So, I think this gives us – these are all multi-billion dollar markets and gives us good opportunities – we're pretty much hitting every important blood cancer except for DLBCL. So I think that's something established that will provide lots of catalysts going forward.

John Whittaker

Analyst, Citi

Well, I would look forward to the update on MM and I think bringing that more into focus your commentary on HR-MDS being a very underserved market and a large market opportunity. Is there a defined timeline for any updates on that HR-MDS specifically?

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Yeah. No, like at this point, we just launched a trial that you bring up a very important point. I think this is going to be an important catalyst for the company in the next few years, the progress there. So I think it's only right that the market is focused on how's progress going with enrollment, what's the cadence there.

John Whittaker

Analyst, Citi

Okay. Great. Well, we all look forward to that. And you actually preempted my last question around Lisaftoclax around the competitive dynamic and sonrotoclax from BeOne obviously coming out as a second generation, those competitive dynamics that I'm sure will be very much in focus and your comments around where we might see the different Lisaftoclax versus sonrotoclax get used in these patients. It's obviously a large market. There's room for multiple therapies. Is that something that will – you'll be speaking about in terms of can we expect to see areas where Lisaftoclax will hopefully be the drug of choice, perhaps not all of them, but talk about those specific opportunities and patient groups where we can win.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Yeah without a doubt.

John Whittaker

Analyst, Citi

Okay.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

I think you'll see the narrative play more towards what we've been trying to set the stage for with the development programs...

John Whittaker

Analyst, Citi

Yeah.

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

...that we have right now. That's probably the best way to put it.

John Whittaker
Analyst, Citi

Yeah.

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

This company essentially started the work here with Lisaftoclax – if you go back to Bcl-2, this is a target that was first identified, I believe, in 1984, right. And wasn't until the two co- founders, Dr. Shaomeng Wang and our CEO and chairman, Dajun Yang, going back to 1996, 1997 when they first contemplated going after Bcl-2. So, I think this company – the other thing I think is not too well-known about this company is that the company is really focused a lot on the U.S. more than people think given that first INDs that were filed with the FDA as opposed to the CDE. That was certainly the case with Lisaftoclax. So, the company has always had its eye on the ball of being global. We're conducting trials outside of China, in Australia, Europe, India. So now it's more about – I think as approvals happen, registration studies read out, the differentiation is shown and physicians and families are more informed about the type of regimens and patient populations where these drugs, single agent or in combination, can be exploited. So, we're very excited about that because it's very much community disease categories as well as specialty categories as well.

John Whittaker
Analyst, Citi

Right. And your question, bringing me nicely to just a question or two around Olverembatinib around that globalization and obviously it's super encouraging to see the uptake and the utilization in China and obviously the opportunities to continue to see that grow. But maybe spend a minute just about the relationship with Takeda and what should we be looking for in terms of any updates on the global development?

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

Yeah. Absolutely. So, a few things there. One is we really appreciate the validation that Takeda provided. I mean, this is a company that has the third-generation – the other third-generation TKI, ponatinib, which they have been very successful in getting to the market, to patients. And of course, Novartis has asciminib, but that's a different mechanism of action, that's an allosteric inhibitor.

So, with Takeda, we didn't disclose obviously the full agreement, but what we've disclosed is that when we entered into the – when Takeda entered into the option agreement with us, that was associated with US$100 million upfront and a US$75 million equity investment. So, we appreciated that support, which provided good momentum into the Nasdaq dual listing. And Takeda, between the potential option exercise and milestones, that essentially totals US$1.2 billion, is what we disclosed, and a royalty ranging from 12% to 19%.

So, the relationship, to answer your question, we're operating almost as if we never even entered into agreement in terms of the resources that we ourselves are applying. We're assuming that in full faith and exploiting the potential of Olverembatinib, making all the necessary investments. I think that one of the trials that speaks to that in terms of

hard evidence is the GIST trial, where this company did a really good job identifying the SDH mutant patients and showing particular efficacy. And we're investing in China to run that trial as well. So, yeah, very close communication with Takeda. POLARIS-2, increasing number of sites, enrolling well. POLARIS-1, good discussion with the regulators here, including the FDA as it relates to giving more details on that one in Ph-positive ALL, which is obviously another I think catalyst that investors are going to be looking for, which we expect to deliver good news in terms of rolling that out.

John Whittaker

Analyst, Citi

Okay. Good to hear. I mean, it sounds like there should be some good data flow coming from the asset. I won't ask you for the specifics on milestones, but presumably after they are received, you'll be communicating about that.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Yeah. It's very important. Now that we have potentially three U.S. registration studies that are going to be active by year end –two of them already ongoing, it's going to be very important to give updates as it relates to the progress, and we fully intend to do that. It was important to get the financing done. I think it's given us now cash through 2027. So, it's given us another year and we're now it’s very much, not to sound too cliché, all about execution, right, the trials, commercialization, rolling out the protein degrader candidates. So, that's all in the plan, fully funded.

John Whittaker

Analyst, Citi

Is it fair to say, as we look at the way you're developing just in China and expanding those indications there that we will look to see a similar framework followed for the global development as well?

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Exactly. Like, China and also other countries as well, like India and Australia. This company has been very good at de-risking in multiple ways. Now, obviously, on the commercial side. And as you know, we're going after solid tumors as well with three of our disclosed pipeline assets. So, we get a lot information as it relates to patient populations, which actually is applicable in other countries, including the US. And as long as we develop the later stage trials, according to what the regulators want in terms of balance, in terms of population and country representation, these are the lessons that we've learned along the way that we will apply going forward.

John Whittaker

Analyst, Citi

Right. Makes a lot of sense. And obviously, significant efficiencies to include Chinese sites and patients in any global registrational trial. And it does seem like the way you've generated the clinical data to-date, getting some of the approvals in – perhaps in some of the later line heavily pre-treated patients, continuing to see opportunity to expand the addressable population as we think about pulling this forward. And then that's true on the Lisaftoclax side too.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

And also the combo of Olverembatinib and Lisaftoclax. So, as you all know, this is particularly exciting because we've got two drugs that got approved on a single agent basis and it's important to understand that for younger patients with ALL, Ph-positive ALL, we have generated data. Yes – and it's small, but the response rate very high, including complete responses. The combination of the two in a particularly young pediatric population, that's meaningful. And it's really what that particular segment wants. So I think that's an important area to point out as well. In addition to also in that same population showing strong efficacy in venetoclax refractory patients.

John Whittaker

Analyst, Citi

I know something that we talk about – you talk about is the ability to spare some of these patients from chemotherapy and just the burdens that come along with that. To-date I believe most of the combination data is in the relapsed/refractory patient group, right. Is it appropriate to think that there could be an opportunity to bring that into a frontline Ph-positive ALL setting at some point?

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Yeah. So it's interesting, like, these patients – I think we have enough data where the combination of Lisaftoclax plus low intensity chemotherapy, very much suited for a pediatric population. So we can go straight to that. And then as it relates – it's kind of a barbell, right, where there's also the elderly unfit AML population as well. So, as it relates to the combo of Olverembatinib and blinatumomab and by the way, these patients also take ponatinib as well. So, they go through the wringer.

John Whittaker

Analyst, Citi

Yeah.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

No question about it. But fortunately so far, we have to prove this out in the long run. We may have an effective approach for the elderly unfit as well as it relates to the blinatumomab. And then as I mentioned, the combo with Lisa and Olverembatinib as well. So, thankfully we have some interesting menu of alternatives here on the ALL side.

John Whittaker

Analyst, Citi

Yeah.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

So, yeah. we have a number of active pipeline programs here. These types of decisions need to be made as it relates to combination approaches.

John Whittaker
Analyst, Citi

Well, it's clear with the two – two now approved products, there's a real depth of expertise on the hematology side. Maybe shifting a little bit to the solid tumor side. You mentioned the GIST study. But I think at the outset, you talked a bit about APG-2449 and maybe just spend a minute. I'm not sure we have time to talk about the entire pipeline, but if there are couple assets that we should make sure people are focused on where we have the opportunity to do something that is first-in-class, best-in-class. I started with APG-2449, but feel free to start with another if you prefer.

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

Yeah. Absolutely. Happy to start there. So, APG-2449, very interesting because more and more – I think there's increased awareness as relates to – so. APG-2449 is our triple kinase inhibitor, for the listeners. It's a FAK, ROS, ALK inhibitor. We're carrying out a study in China in NSCLC in ALK resistant patients. I think the awareness now the RAS pathway can be heavily exploited. Lots of companies, variations on pan-RAS, G12C, G12B, etc. No matter what the particular RAS candidate is, I think there's increased view that this should be combined with a FAK inhibitor.

So, this is going to be, I think, exciting for us to prove that out because both the RAS and FAK pathways, eventually they converge into the programmed cell death downstream pathways, but FAK particularly upregulates the YAP proto-oncogene, which has a blocking effect on programmed cell death. So, in order for RAS to really realize its potential, you need to have a strong FAK partner. And so far we've shown, the data we've amassed, very strong activity with our FAK inhibitor, even compared to companies that have FAK inhibitors currently approved, not to name names, but that's kind of...

John Whittaker
Analyst, Citi

Yeah.

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

... exciting on our end.

John Whittaker
Analyst, Citi

Understood. And just to confirm the registrational studies that are ongoing are currently in China. How do we think about potential globalization of the product over time?

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

Yeah, I think we can get there. Just a matter of I think find the right partner as it relates to candidates. But yeah, , it's our full intention to – we're happy with the progress. That's why we have a disclosed pipeline here. I think that we will be talking more about in time.

John Whittaker
Analyst, Citi

Okay. Great. Well, clearly, opportunity – first-in-class opportunity there., right. And it sounds like we're getting increasingly focused on who the most likely patients to respond are. So, hopefully, we're going to see that play through with higher probabilities of success going forward. Being mindful of time, I had jotted down a question or two around APG-115, but maybe it would be helpful to provide a little bit of background on that asset. If there are other pipeline assets that you want to make sure to highlight, by all means, take us to those as well.

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

So. I'll mention a few things about APG-115. It's an intriguing approach, right, because as it relates to MDM2-p53, it's now kind of been proven out through prior attempts that one of the issues is when you knock out MDM, you get a feedback loop with p53 upregulating MDM. So, a degrader approach actually could actually solve that. But as far as our current APG-115 program, we've shown that it's shown strong bioavailability, it's been highly selective, and we've gotten six orphan drug designations from the FDA just on that compound alone and two RPDDs as well, pediatric disease designations.

So, we're evaluating this actually in multiple tumors, melanomas, T-PLL, or NHL, liposarcoma, neuroblastoma and also adenoid cystic carcinoma, that's also part of the targeted population here. Very good disease control rates demonstrated so far kind of in the 80 to 100 range in particularly with ACC and also shown good activity in combination with PD-1 as well. So, still more kind of refinement to do with that asset, but we like the profile of it so far.

John Whittaker
Analyst, Citi

Great. It clearly sounds like an exciting opportunity.

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

Yeah.

John Whittaker
Analyst, Citi

Another demonstration of the efficiency and the innovative nature of what the R&D team is...

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

Yeah. We're very excited.

All these targets, right, like MDM, Bcl, Bcl-xL, I mean, these are I think now the last – go back to the 1980s to now, these have proven to be very difficult to drug targets and just a real testament to the co-founders going back to Georgetown, University of Michigan intellectual property leading to this. It's a real pleasure to see this saving lives and getting drugs approved.

John Whittaker
Analyst, Citi

Yeah. I was going to ask one more question, but if there's anything else on the pipeline that you think we should certainly be attentive to and be on the lookout for updates over the next several months or quarters, go ahead and flag them. My last question for you is, I know you mentioned about cash runway after the recent financing into 2027. Maybe just clarify what your current message is on that as it relates to does that include milestones from Takeda? Does it not include milestones and how we should be thinking about your capital formation strategy going forward?

Veet Misra
Chief Financial Officer, Ascentage Pharma Group International

Yeah. Absolutely. So, I'll get the most important point out on the table right now, which is that it does not assume option exercised by Takeda. So, we're independent of that. We got cash through 2027, which is where we want to be, right, to invest in our – potentially, like I said, soon to be three registrational studies in the U.S. The global trials we got ongoing. We got close to 40 trials ongoing globally. So I'm happy to say that our current cash runway takes into account all of those activities without any sort of other overhang or anything like that.

So, yeah, we are really appreciative of the following of investors that we've had over the years. Hopefully they feel like we've delivered and we did the raise not too long ago and the stock is up meaningfully since that point. We think it's through execution and smart deployment of capital, but at the same time, prioritizing where to spend and taking advantage of an efficient cost structure overall in China, that's all across the supply chain. And obviously, very strong overall global clinical R&D to translational, to discovery, all the way to the clinical ops team here in the U.S. where we've hired from big pharma and see all of this come together in a global effort. As a company, we are always, of course, looking to be opportunistic as it relates to raising capital and partnering. And we have, I think, a world-class team here that's doing all the right things now.

John Whittaker

Analyst, Citi

Great. Well, It's really been exciting to see the progress to-date. Congrats on the strength and the execution. It's nice to see the stock price showing and recognizing the execution. As you noted, it's a rare bright spot on the biopharma radar to see the IPO performance over the course of the year. So, it has been an exciting year. We certainly look forward to an exciting year ahead for Ascentage and thank you very much for the time today.

Veet Misra

Chief Financial Officer, Ascentage Pharma Group International

Thank you, John. Really appreciate it. Appreciate your support.