Edited Transcript of ARGX.BR presentation 9-Sep-19 2:30pm GMT
argenx SE at Morgan Stanley Healthcare Conference

New York Sep 10, 2019 (Thomson StreetEvents) -- Edited Transcript of argenx SE presentation Monday, September 9, 2019 at 2:30:00pm GMT

Presentation

Questions and Answers

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [1]

Yes. So I thought we'd start with efgartigimod, and there are a lot of FcRns in development. I think you guys have designed a few unique features to yours, so maybe you can just comment from a design standpoint, then we can talk about some clinical differentiation after that.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [2]

And the credit, of course, goes to the person who deserves that. So you know that at the foundation of every pipeline assets lies a great academic collaboration. And in this case, it's with Dr. Sally Ward. Sally's active at UT Southwestern and she, of course, wrote that seminal paper on the role of FcRn in IgG recycling but she also did a very smart phage display exercise to modify that natural like enter the C fragments for its interaction with FcRn. So these proprietary ABDEG mutations she identified are very clever because they can dramatically increase the binding in the acidified endosome for FcRn but you then outcompete wild-type IgGs. But once you recycle back to the surface of the cell, efgartigimod can still come off and continue to journey and bind again FcRn. And that's why we believe we have a unique PK-PD and biodistribution profile compared to the high-affinity monoclonal antibodies out there.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [3]

Okay. Perfect. And so I guess, how do you think that plays out in the clinic? Like, there are couple of things that we've seen with clinical assets, whether it's related to tolerability or your -- and I guess, tolerability related to your ability to dose to an appropriate level. So maybe you can just talk about how you think that plays out in the clinic.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [4]

I think you'll nicely start to see differentiation on all 3 fronts being safety, efficacy and those of convenience of dosing. So let's talk about safety. And first of all, this is a molecule which is enabled to bind Fc effectors -- cell receptors. Once it is docked on FcRn, it can no longer engage with Fc gamma receptors. So there is no hints for the headaches, the nausea, the vomiting, the diarrhea, which some of the other people have shown. It also is a perfect imitator of wild-type IgGs and that the cycling loop, it looks as if the system does not notice it's being hijacked by efgartigimod. There's no derailing of FcRn into the lysosome. It stays in the endosome, in the recycling path, available also to humans in serum albumin, the other protein which likes to recycle through FcRn. So there are no drops reported in serum albumin levels, which we think is also important. So that's from a safety point of view.

From an efficacy point of view, what we see is a dramatically fast onset of action. In our myasthenia gravis patients, after the first infusion, you already have a statistically significant separation from placebo, same in pemphigus vulgaris. I mean, after the first infusion, we basically see in our PV patients a dramatic response in terms of disease control. Maybe that is linked to that very fast traveling of the molecule to the tissues. Remember the very-high biodistribution I was talking about.

The third thing, which is convenience, is also easy to understand, right? It's just an Fc fragment. It's about 3x smaller than a full-size IgG. It has a beautiful manufacturability profile. You can concentrate it to very high concentrations without paying a price in stability or viscosity. So now have a very concentrated product with very low viscosity, which we can further equip with the Halozyme technology to now have a superb execution on the subcu front. So I think on all 3 fronts, safety, efficacy, convenience, we start to see meaningful differentiation.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [5]

And maybe I want to go on and talk about a bunch of other things, but just I think we've seen a lot of FcRns, which are sort of full-length antibodies and we can -- we sort of understand the profile. Alexion has in-licensed with Affibody AB compound, which is very small and maybe have some of the size features, et cetera, as an Fc fragment. So maybe you could compare and contrast what we know about that compound and what you see is the potential risk that, that compound poses or not.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [6]

Look, we know very little about this specific molecule. Of course, we've submitted the technology that they had in the past at Ablynx in the days of protein scaffolds were in fashion. There were more than 50 scaffold companies, including Affibody. There is limited clinical data available in the public domain. I think the only data we have seen on the Affibody compound is initial Phase I healthy volunteer data. So just in all fairness, I think we will have to wait for more data and check what the PK-PD profile is going to be and the immunogenicity in these patients. For sure, it's a smaller molecule. So in principle, if it's well behaved, we should be able to squeeze more material in milliliters than you can do with a full-size monoclonal.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [7]

Okay, okay. Good. So maybe I thought what we could do is let's go through progress on some of the clinical studies that you're working on, some of the key disease areas and talk through that. So first, ADAPT. Maybe just remind everybody where you are in enrollment, how the progress is going and if you remain on track for data in the second half of '20.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [8]

This study, and kudos to the study team, is running like a Swiss train. I mean it left the station on time, is going to arrive in the station on time. Remember, we gave the guidance of 22 months from start to data. That trajectory is perfectly on track. Also, the rollover into the open-label extension study, the 1 years, and ADAPT Plus study is going very well. So we're very pleased with how that study is being executed and we are on track to release top line data second half next year.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [9]

And can you talk a little bit about the study design there and how we should think about that? I mean I think -- well, I start there and then a couple of other questions, sorry.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [10]

Sure. I think we have been public on quite a number of features of the study. I think it's a low-risk design, this Phase III, because we have been staying very close to the Phase II patient population where we saw the black and white signal. And the primary endpoint is also powered on the patients with acetylcholine receptor autoantibodies. Remember, we are allowed to recruit some of the people that have other autoantibodies, but they will not be involved in the calculation of the primary endpoints. By the way, the primary endpoint will be calculated along the lines of the ADL score. That's clearly the preference of the regulators. It's also our preference. And again, I think that's a

low-risk choice because in Phase II, we saw a perfect correlation between knockdown of IgGs, including pathogenic IgGs, and improvement in ADL and QMG scores. So -- and the ADL the score is a perfect thing to do. It's also the score which -- or the scorecard which is being used these days in clinical practice increasingly frequently. We also took a pretty conservative approach to the calculation of the power of the study. The beauty today is that we know how the placebo arm in an MG study behaves. We saw it in our own study. We could learn from the REGAIN trial. We can learn from other people like the UCB Phase II study. So now we could take actually a pretty accurate guess on how that placebo arm response could look like and do a pretty conservative powering of the study.

So all in all, I think a very well-thought-through design. The only thing we have not spoken about yet in public is the actual dosing regimen. We spoke about the dose. How exactly we're dosing patients is something we want to disclose somewhat later. For sure, we're going to do that well ahead of the Phase III top line data. And the reason that we want to time the announcement around the dosing regimen is that it's all about the product positioning. How are we going to position this product based on the likely label we will be able to get and then effectively compete with the other therapies underway.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [11]

And can you just -- without disclosing what you don't want to disclose, but can you talk about what are the broad parameters there that may influence you to have a certain label versus a different label and how that could impact your view on the commercial opportunity?

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [12]

Clearly, we did quite some work with the patients, with the physician and with the payers. What we said in public in the past is that this is not a progressive disease. It's not because you stop medication that you will progress. Actually, what you need to do is you need to give the medication when the patient needs the medication. And it's along these lines actually that we have crafted the design of the Phase III trial.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [13]

Okay. And then I guess second question or one of the questions I get a lot around safety is chronic IgG suppression. And so given where you are in the study, I guess, what would -- if you were sitting in our shoes and we haven't seen anything, what would you say about the fact that you're maybe a year away from data, give or take, a little bit and the data that you've collected and how much that derisk that concern?

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [14]

The truth is that we need the data. I mean I can say whatever I like today. We will need Phase III data and also from the open-label extension study to talk intelligently about the safety profile of the drug in MG patients. Now there are other couple of factors I can share with the audience today to give you comfort on the likely chronic safety profile of such a drug. First of all, there is precedent in MG patients with chronic plasma exchange. So people are being chronically plasma exchanged. There is no increase in infection. And with plasma exchange, of course, we take out much more than just IgGs. We also take out other antibodies. So I think that's already one comforting factor.

And the other thing I want to say is that there is plenty of evidence from FcRn knockout animals or preclinical studies where you use an FcRn antagonist that these animals can mount the perfectly normal immune response, if and when they get charged with the pathogen. So we're not basically impairing the immune system to the level that you cannot mount an immune response from your memory B cells. Something our physicians find important is that we do not knockdown IgGs all the way down to 100%. That is the safety buffer left of about 25% of IgGs without, of course, touching IgMs or IgAs, which make up your first line of defense or which protect your mucosal surfaces. So a number of comforting factors but the jury is out. What I can say hand on heart today is that there

is no sign of increased rate of infection based on our safety database, which is the biggest available for any FcRn antagonist.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [15]

And have you talked about or would you be willing to talk about sort of what the criteria you've set out for the DSMB to look at? And what would trigger a concern in the study in terms of imbalance and infections?

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [16]

The only thing I can comment there is that the study is actively being watched, not only by our own patient safety people but also by an independent body as you say. I don't know by heart the rules for escalation, but infection is going to be an area of specific interest.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [17]

Great. So I guess, I want to talk about commercialization. But maybe before we do that, let's just talk about the path to subcu and what you're doing there. So maybe we could address your subcu as well as the Halozyme-augmented subcu.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [18]

So the key to understanding the different product presentations we're developing is that we want to serve patients across multiple indications, across multiple payer and physician systems. So depending on the indication, depending on the place where you are and which patient and physician you're dealing with, IV could be preferred or subcu can preferred.

The other thing we know is probably across different indications, we will want to play somewhat with different pricing. So market access has a strong voice in developing this optionality. For example, in ITP, we know that the bulk of the competition plays in a price for around $120,000, $140,000 per patient per year. That could or could not be different, for example, in MG, CIDP or PV. So by being able to offer different products, we can maybe start to think about different sharing from a market access point of view, especially if products are not interchangeable. And that's what we're pushing forward in our ITP study. We are going to test the IV induction, followed by the subcu maintenance approach, that subcu product not being able to replace the IV product. You're right, we're also developing that same subcu product now with the addition of the enhanced technology from Halozyme. Here, the idea would be that both IV and subcu could be interchanged. So -- and that will allow us basically to serve in different markets, different payer base. So that's the whole thinking behind that product optionality.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [19]

And for disease areas like MG where you don't have as part of the pivotal study, what's the path towards getting that to be a labeled option for those patients?

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [20]

Unlike the predecessors using Halozyme, we are not looking at the Halozyme technology as a life cycle management tool. We are really going to aggressively push the subcu product with enhanced technology forward.

Once we announce the Phase I healthy volunteer data where we have studied PK-PD bioavailability and assuming the study reads out positively, we will also announce how we're going to progress that product into patients. You're right, for MG, the strategy was speed to market. So we're going to go to market with the IV product first, but we will actively try to then bridge to subcu. What we will need for that are the data from the healthy volunteer trial and, of course, our conversation with or the consultation with the regulators, being the FDA, PMDA and the EMA.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [21]

Okay. Perfect. MG commercial and then ITP. So MG is starting to become a potentially more competitive market. Alexion has made significant progress, right? I mean I think they have over 1,200 patients or somewhere around on drug right now. Maybe just remind people where you see is the piece of the market where you see the most potential for efgartigimod and how you're planning to commercially go after that market.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [22]

So the label we're aiming for is a label which would allow the use of the drug upstream of Soliris and also across the entire patient population. Let me clarify that. The Phase III study done with Soliris is in MG patients, basically restricted to patients to the refractory patients, people failing at least 2 lines of therapy before they could get Soliris. The label the regulator gave to Alexion is a very broad label, but the payer is niching Soliris back into its refractory patient population because of the price. So the way we are actually developing efgartigimod is that we can dose the product on top of any standard of care as long as the patient stops responding to that standard of care. There's no requirements for having failed a number of lines of therapy. So in principle, that would allow you to go upstream in the treatment paradigm.

The second thing, we know that autoantibodies exert multiple modes of action at the neuromuscular junction, not just complement recruitment. And there is actually about 15% of patients where the autoantibody is not recruiting complement is doing other stuff. In these patients, of course, a complement blocker cannot play but efgartigimod should be able to play. So we're going to try and play across the whole spectrum of MG patients compared to a complement block.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [23]

Okay. Okay. Perfect. ITP, so you recently announced the study designs for the pivotal program in ITP. I think the biggest question I got was, what's the risk from dosing on top of standard of care? So maybe you could address that but -- and just remind everybody what the study design is as well.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [24]

Remember, we're building on the Phase II data. In our Phase II trial, we have been comparing head-to-head with placebo on top of standard of care. So very similar to the myasthenia gravis approach, we went into patients which were no longer controlled by standard of care. In the case of ITP, that means platelet count below 30,000. What we have shown in the Phase II convincingly is that regardless your background medication, you have the right to respond to efgartigimod. So whether you were on corticosteroids or immunosuppressants or TPOs, you could respond to the drug. So we're going to build on that success in Phase III, but we're going to expose the patients for a somewhat longer period of time to efgartigimod because we believe that we really pushed the envelope in Phase II by only getting a 3-week exposure in these highly refractory patients. So we're going to dose for longer periods, maximizing the chances to see response. And then in the dosing algorithm, we have a way to play with the dosing cadence to adjust the dosing to platelet counts. In the second study, we are going to introduce also the subcu maintenance concept. So after going for a maximum chance to induce the response with the IV induction phase, we will try to maintain response on weekly low dose of efgartigimod. That's the concept behind the 2 Phase III trials.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [25]

Okay. And I guess, TPOs have been relatively successful. Maybe just in terms of let's talk about revenues, let me put it that way. The penetration is maybe modest, but I guess, how do you think of

them as a competitive agent for you or not in terms of the added cost maybe of having dose on top of them with a label like that?

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [26]

The truth in ITP is that the long-term response on TPOs is 130%. The way we look at TPOs is that maybe they're not just a competitor, they're maybe also the friend. Because if you dose efgartigimod with this mode of action on top of an agent which is stimulating platelet production, maybe you see synergy between the 2. And the first TPOs will be going off patent by the time we will be launching. So from a cost point of view, there could be a case to be made that you dose the premium-priced innovator on top of our generic TPO. So that's one way to look at that space. Now we want to win on response rate. We want to come with an unprecedented response rate and become the agent of choice when you go into this difficult-to-treat ITP patients because of the maximum chance to induce response.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [27]

Okay. Perfect. So a couple of other things to talk about. Maybe let's talk about the CIDP. Large indication for IVIg. So outside of potential market, why did you pick that as one of the next indications? And then -- yes, let's start there maybe.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [28]

It's a logic execution of the beachhead strategy. Remember, we picked MG, ITP and PV as the 3 beachheads into what we believe to be the vast supply of opportunity. So now we are building adjacencies around the beachheads. In neuromuscular, the first but not the last indication we announced is CIDP. I think we're taking an incremental risk on the biology access because there is less known about these autoantibodies. We know these are IgGs, but we don't always know the autoantigen they bind. But there's plenty of evidence out there that when you reduce autoantibody levels, that you put CIDP patients in remission. And we believe that the feasibility of doing clinical trials is proven. The SCIg players showed it when they compared with IVIg. And as you correctly point out, the commercial opportunity is sizable. So for us, it's a logical continuation of the beachhead strategy.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [29]

And maybe help us think about when we can understand what your clinical program is to attack that and how we should be thinking about the time lines for you to get some initial data to derisk some of those points that you made?

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [30]

So far, for every indication, we have organized a KOL event where basically we educate our shareholders on the disease, the burden of disease, the management of the disease today, the unmet need. Then we present the data, showing our conviction about the biology. Why do we believe pathogenic autoantibodies drive the disease? And then we typically end by explaining the trial design of the Phase II study. So you can expect a very similar pattern for the KOL event, which we will do here in New York before the end of the year, likely early December. And then you will also have an insight and you know what the scope and duration is going to be of that study.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [31]

Okay. Okay. Good. So before we talk about some of the newer molecules that you introduced at your R&D Day earlier this year, maybe we should just touch on PV. So maybe just give us an update on PV and the progress you're making there.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [32]

It's a high conviction indication. I mean the biology of the disease is exquisitely well understood. We have made public the data from cohort #1, that's monotherapy, pretty spectacular data. So we know we can bring these patients very quickly in disease control. The key outstanding question is how fast can we, if we can, bring PV patients into complete remission, into clinical remission. That's the data point which we are waiting for and which we're going to announce together with all the other data first half of next year. So I think it's a very exciting indication from a biology point of view. It's a very high unmet medical need, and there is a tremendous need for more tools in the toolbox to treat these pemphigus patients. So let's see but high conviction indication.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [33]

Great. So then in the last 2 or 3 minutes here, some of the new pipeline assets. So maybe complement or...

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [34]

They follow the same pattern. So an academic collaboration tapping knowledge, which we could never have developed in-house on complements. This professor has now 3 complement products on the markets. He knows complement inside out. We explained in the R&D Day why we think C2 is not just a novel target but also a very exciting target. The molecule we presented is a highly differentiated molecule. That sweeping antibody can basically knock down C2 in a spectacular fashion. And again, we have a number of high conviction indications where we think we can credibly execute proof-of-concept studies and potentially also Phase III studies. So we look at ARGX-117 as a successor of ARGX-113. ARGX-118 is again coming out of that mold, super exciting signs. Here is an antibody which can dissolve a crystal but has never been published before. We can go after crystallopathies, in this case, a crystallopathy involved in allergic asthma, severe asthma. We're again niche indications where we think we can credibly execute the proof-of-concept work. So I think 2 pipeline assets were to argenx.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [35]

Well, great. I think maybe just before we finish, just remind people cash, cash runway and your sort of outlook on the financials.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [36]

Thanks to the follow up we did last September and then the deal with J&J, the cash position has grown to just over $1 billion. That's what we announced on August 1 when we announced the half year results. So this company is solidly financed to execute its business plan into 2021.

Matthew Kelsey Harrison, Morgan Stanley, Research Division - Executive Director [37]

Okay, great. Tim, thanks for being here. Appreciate it.

Tim Van Hauwermeiren, argenx SE - CEO & Executive Director [38]

Thanks for the conversation.