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Akash Tewari *Jefferies LLC, Research Division - Equity Analyst*

PRESENTATION

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

Good morning, everyone. For those who just got back from ASCO, I feel sorry for you. I'm exhausted as well. But this is day 1 of our Jefferies Healthcare Conference, something that I am just really excited about, and I have the pleasure of hosting Regeneron, and I'm going to hand it off to Ryan for some brief introductions and forward-looking statements, and then we'll get into some questions.

Ryan Crowe - *Regeneron Pharmaceuticals, Inc. - VP of IR*

Thanks, Akash, and thanks for having us here at the Jefferies conference. It's always well attended, and I'm excited to be here. I'll start off with some forward-looking statement disclosures. I'd like to remind you that remarks made today may include forward-looking statements about Regeneron, and each forward-looking statement is subject to risks and uncertainties that could cause actual results and events to differ materially from those projected in such statements. A description of material risks and uncertainties can be found in Regeneron's SEC filings. Regeneron does not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

So we have Bola Akinlade and Brook Jennings here from Regeneron, both in the I&I space. Since they're probably new to most of you guys out there, I thought we'd have them do a little intro on their background and what they are responsible for at Regeneron. So Bola, why don't you take it away?

Bola Akinlade - *Regeneron Pharmaceuticals, Inc. - SVP of Clinical Development, Immunology & Inflammation*

Thank you very much, Ryan, and thank you very much, Akash. Good morning, everyone. I'm Bola Akinlade, and I'm Senior Vice President for Immunology and Inflammation Therapeutic Area at Regeneron. I've been at Regeneron now for over 8 years, joined in January 2015. I joined as a clinical leader for Dupixent that most of you probably are aware of. And I led the clinical team for the first approval in atopic dermatitis and have been involved with many of the other indications that Dupixent is approved for. So I lead late-stage clinical development. And my team runs the trials and also gets approval for our drugs that are in the pipeline. I'm also responsible for itepekimab, which is an IL-33 antibody that has shown proof of concept in asthma and COPD, and we are in very large trials, now 2 large trials for COPD with itepekimab. So I'll stop there for a little bit, and then I'll let Brook introduce himself.

Brook Jennings - *Regeneron Pharmaceuticals, Inc. - VP of Commercial Dermatology*

Thank you, Bola. My name is Brook Jennings. Like Bola, I've been with Regeneron now for a little over 8 years. I joined the organization to lead the marketing efforts across all indications for Dupixent. And now I lead the U.S. Dermatology business group. And just to give you a quick understanding of where we stand from an overall performance perspective in the United States.

As many of you are aware, we had our first quarter earnings relatively recently and approximately $2.5 billion in global sales for Dupixent, which puts us on an annualized rate of about $10 billion, and that is a 40% year-over-year growth, which is also a very healthy growth rate for us, and

we're pretty excited about that. If we look at the individual indications in atopic dermatitis, we are the #1 most prescribed biologic by dermatologists, and we are continuing to see robust growth in every age range for which we are indicated in atopic dermatitis.

In asthma, we are now the #1 product from a new brand prescription standpoint and the #1 brand being prescribed from an NBRx perspective by both allergists and pulmonologists. And as the fifth biologic to market, that is quite a feat as well. In the newer indications, chronic rhinosinusitis, we continue to be the market leader as we continue to build and expand that market. And if you look at the other 2 newest indications, over 11,000 patients have been initiated now with eosinophilic esophagitis. And our newest indication prurigo nodularis is continuing to grow as well.

If you look at the size of the business opportunity for us in the United States, there's about 3.5 million patients. Those 3.5 million patients would be across the 5 indications that we have. So we do have significant opportunities to grow in penetration to that group as well as new opportunities in expanded age ranges for our existing indications. And then finally, when you think about what we have in the pipeline, and specifically from a Dupixent perspective, and I know we're going to talk about it today, but the very exciting BOREAS data that dropped recently in COPD represents a significant opportunity and the potential for a significant advancement in a marketplace that has not had any advanced therapeutics literally ever.

And then finally, chronic spontaneous urticaria. We will be hearing back from the FDA in the fourth quarter of this year, which has the potential to add another couple of hundred thousand patients to our potential opportunity here in the U.S. So very exciting time overall and pleased to be here. Thanks for having us.

QUESTIONS AND ANSWERS

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

Great. Well, thanks so much for those intros. So why don't we start off with COPD? And I think that's where a lot of the investor focus is on for Dupi. And the question you've gotten a million times is, are you going to file with one study. And when you will make that decision, when we're really going to hear back from the agency. But I would ask you, maybe put yourself in the agency's shoes. And what do you highlight when you go to the agency and you say, you know what, this deserves to get on the market with accelerated approval. What do you think is clinically meaningful for the agency? What justifies an accelerated approval?

And then to add on to that, when I do talk to my colleagues on the buy side, there is kind of this view, oh, they may be able to show mortality data over time with the FEV1 signal. But can you also talk about how long it would actually take to show a signal like that and when a reasonable expectation for it even showing up would be from a data perspective?

Bola Akinlade - *Regeneron Pharmaceuticals, Inc. - SVP of Clinical Development, Immunology & Inflammation*

Thank you very much. A lot of questions in there. First of all, Brook did a really nice job in talking about Dupixent, which is really a flagship product in immunology. I mentioned to you that I was a clinical lead for the first indication, atopic dermatitis. And we've had several more indications since then, formal indications. So asthma, chronic rhinosinusitis with nasal polyps, eosinophilic esophagitis, and very recently prurigo nodularis. Dupixent is actually defining the way we look at and treat and diagnose type 2 inflammatory conditions.

Recently, as you said, we had extremely robust results from the BOREAS study in COPD. And I just want to remind you, I mean, we went into the study without a Phase II trial, okay? But based on the strength of the evidence we had, the genetics data that also guided us, and also some preliminary data that we had from patients who had COPD-like conditions in our chronic rhinosinusitis with nasal polyps studies, we went into 2 large studies, the BOREAS study and the NOTUS study. And you've all read about the extremely robust results from BOREAS, the first biologic to actually show significant clinical efficacy.

So 30% reduction in exacerbations, improvement in FEV1, about 80 mLs over placebo. Patients felt better when it comes to quality of life, the SGRQ. And then also, symptomatically, they felt better. And when you look at the magnitude of effect, p value is less than 0.001. It's so, so impressive. I mean no other biologic has done what Dupixent has demonstrated.

And remember, COPD is the third leading cause of death. So there's a really, really strong unmet medical need. Yes, we've approached the agencies. We'll see what they tell us. And it's not inconceivable that the agency approves a drug based on the strength of one data depending on the quality of the data and the strength of the data.

So we are hopeful, we are optimistic. And just remember, there is a huge unmet medical need out there for patients with COPD. Now you mentioned accelerated approval. This would really not be an accelerated approval, if it's granted, because we do have clinical outcome, okay? It's not an approval based on a biomarker, okay? This is actually real outcomes, okay? Patients had reduction in exacerbations, improvement in FEV1, and they felt better. So maybe you can argue with that, right?

Now you asked the question about mortality. And I think that's a really, really good question. Okay, we don't have long term -- our trials are 1 year in nature. We didn't see any -- there were fewer deaths on Dupixent compared to placebo patients. But we really would need much longer trial and larger patients to actually see if there is a mortality benefit with Dupixent in COPD on the chronic treatment basis. But we're hopeful, and we may be able to go into such a trial with our collaboration partner, Sanofi.

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

Okay. Understood. And I will say this. The body language read I have from your team now is there seems to be more confidence than, let's say, when the initial data came out. I think the initial data said, we'll see. Let's see what the agency says. It seems like your confidence on potentially getting approved with one trial has increased over the last few months. Is that a fair characterization?

Ryan Crowe - *Regeneron Pharmaceuticals, Inc. - VP of IR*

Let's just leave it at: we'll have the conversation with the FDA and we'll get our answer. And once we get it, we'll share it.

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

Understood. Now maybe on the size of the COPD market. Now there's that cutoff on 300 eosinophils. But the truth is, if you look kind of historically with COPD patients, very rare do they actually have elevated eosinophils for an entire year, right? So only about 20%, 30% of those patients can have sustained elevated eosinophils. So as we think about how this market eventually settles out, right, it's on top of triple therapy in this 300 cut-off on eosinophils. That's the way that I think the market would start to look at it logically.

But when you think about selling these -- penetrating this market, thinking about how clinicians would view it, is the 300 cutoff what really should be thinking about? Or is it really -- how do we define type 2 driven disease? And how do you think that will evolve?

Bola Akinlade - *Regeneron Pharmaceuticals, Inc. - SVP of Clinical Development, Immunology & Inflammation*

That's a good question. So we would not be the first biologic that would use eosinophils as a cutoff or as a biomarker for treatment. Remember, anti IL-5 biologics use eosinophils as a cutoff for the treatment of asthma. And they've been fairly successful in showing a treatment benefit. We also know that -- and we see this with Dupixent also, that the higher the threshold of eosinophils, the more of a treatment benefit you have because the patients are more type 2 skewed in terms of the inflammatory milieu.

Now about 40% of patients with COPD will be characterized as eosinophilic COPD. Yes, eosinophil counts may fluctuate. But once you declare yourself to be eosinophilic COPD, I think you stay that way. I don't think you turn around to become a non-eosinophilic COPD patient.

So we chose the threshold of 300 based on our experience with our asthma trials, based on competitors and what they did with their own COPD trials, and also based on a genetic data where we have really strong data that correlates COPD and baseline eosinophils. And we see that the strongest association is with the patients who have elevated eosinophils. So we're very confident that using the thresholds that we've had in our trials will actually be very relevant in practice. And now I turn to Brook and see what his thoughts are.

Brook Jennings - *Regeneron Pharmaceuticals, Inc. - VP of Commercial Dermatology*

Thank you very much, I would certainly agree. This is a subset of the overall COPD population. And when you think of the size of that population, we estimate that in the G7 markets to be about 500,000 patients. And that's going to be patients who have eosinophil counts that are 300 or above. The other thing that Bola gets to play with on a daily basis is our IL-33 molecule as well. So we have a different mechanism of action that may have a broader remit in the COPD space in addition to what dupilumab will have.

The 1 thing I'd throw out there as well, and Bola touched on this, is the experience in pulmonology and allergy offices is the 2 areas that will be treating COPD most aggressively. They have broad familiarity with the use of biomarkers, specifically eos, because they're doing the testing right now as part of the regular routine testing from a blood test perspective, where they get eos results now. So it's not going to be an added burden for them to check that, and it's going to be a very easy way for them to figure out what patient population will likely be the patient population to more likely respond to dupilumab.

Bola Akinlade - *Regeneron Pharmaceuticals, Inc. - SVP of Clinical Development, Immunology & Inflammation*

And I just want to make another comment about eosinophils, okay? So the earliest biomarker approach for eosinophils with asthma and COPD was actually looking at sputum eosinophils, right, where they had a cut of about 2%. And getting sputum from patients is actually very difficult, okay? So researchers in the past said, "Look, what is a good surrogate, okay, in terms of an easily acceptable way of assessing whether a patient has elevated eosinophils in the airway?"

And they actually came on using blood eosinophils, okay? And it correlates really well with sputum eosinophils. And the pulmonary community and folks that treat patients with asthma and COPD are very comfortable now with using blood eosinophils as that surrogate marker rather than having to induce sputum and have a measurement of sputum eosinophils.

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

So you mentioned something about COPD is, I was surprised, third or fourth leading cause of death in the U.S. I don't think that's something everyone wakes up and thinks immediately. And do you think about the bolus of demand that might be out in the COPD market? Because you're going for a well-treated patient population, right? There is a mortality potential benefit to be had. There is this kind of lung -- your lung function starts to worsen. After a certain point, you may not be able to recover.

So when you characterize the kind of bolus of demand you had for asthma versus what you would perceive the bolus of demand would be for COPD, how should we think about that, right? Could COPD potentially have even more demand out of the gate?

Bola Akinlade - *Regeneron Pharmaceuticals, Inc. - SVP of Clinical Development, Immunology & Inflammation*

I think that's a commercial question. But I'll give you -- I'm a physician, I am an internist and board-certified internist. So I have seen COPD patients, okay? So let me just characterize the patients we enrolled in our trial. These were patients who were still symptomatic, still exacerbating despite the best standard of care. They were on triple therapy, okay. So LABA, LAMA and ICS. So they were optimally treated, and they still had symptoms and exacerbations and felt bad, felt ill. So there is an unmet medical need there, okay?

And unlike in asthma, where we had other approved biologics before Dupixent, there's really no biologic that has demonstrated the robustness of the efficacy that we're seeing with the BOREAS trial. So I'm thinking to myself as a physician, there's really nothing out there for those patients who are still exacerbating despite the best standard of care. And I'll let Brook answer it from more of a commercial perspective.

Brook Jennings - *Regeneron Pharmaceuticals, Inc. - VP of Commercial Dermatology*

Thank you, my friend. So I think Bola touched on it, right? So when you think of the asthma space from a biologic standpoint, as Dupixent was the fifth biologic in the marketplace, that bolus had already come and gone in the market, right? So you had the IL-5s in the market, you had the anti-IgE in the marketplace. So it wasn't as though there was a huge unmet need of patients who had never had the opportunity to have an advanced therapeutic.

Now there was a whole host of patients in the asthma market who had failed something that was already there, another one of the advanced therapeutics, and then had the opportunity to experience what Dupixent had as well. So COPD, I look at kind of as a quasi piece between those 2. Are those patients out there that are maximized on standard of therapy right now and not having the results that they would like? The answer is unequivocally yes.

But are all of those patients going to be able to rush out tomorrow and gain access to a biologic if it were indicated? The answer is unequivocally no. So what we do know is we will be working very closely with the allergy and the pulmonology communities to make access as easy as possible for those patients and for those HCPs to be able to access the brand if and when that time comes, which will allow them to more quickly get through that list.

So will there be a bolus? Yes. Is it going to be what other markets have seen where you've got hundreds of thousands of patients literally waiting on day 1, not likely?

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

And in terms of step edits, because it sounds like these patients are coded, they're identified, doctors know exactly what this subset of patients looks like, when you think about ease of access, how would that compare to, let's say, you were launching an indication where you didn't have an in-built sales force, you didn't really have a relationship with these doctors and some level of rapport with the insurance companies.

Brook Jennings - *Regeneron Pharmaceuticals, Inc. - VP of Commercial Dermatology*

So from an access perspective, I think that's probably one of the unsung situations that has led to the success from a dupilumab perspective. If we think about where we are today in the space for atopic dermatitis from a commercial insurance standpoint in the United States, over 99% of patients have access to the drug. Now access and no step edits are not the same thing as we know, but they have access to the product. Across the other markets, we see very similar, very high rates of access. And because we have such great access for existing indications, we would expect there to be a rapid uptake from a payer perspective to allowing patients to gain access to the brand.

Now what hurdles they would put in the place and what step edits they would put in place, we fully expect there will be some. We don't know what they would be. We'd have to work through them with that when the time came.

Bola Akinlade - *Regeneron Pharmaceuticals, Inc. - SVP of Clinical Development, Immunology & Inflammation*

Yes, Akash, I just wanted to kind of touch on something you asked about approval based on 1 study, right? Okay. And I know Ryan said we will get back to you, and thanks, Ryan, for that. But I just want to remind everyone, okay. I mean this is probably the first biologic that has been approved for children as young as 6 months of age, okay? This speaks to the unparalleled safety that Dupixent has demonstrated, okay?

It also has been tested in thousands of patients in clinical trials. And as our commercial colleagues remind me and tell me, we've had hundreds of thousands of patients treated with Dupixent, perhaps 600,000, perhaps. And this is an incredibly, compared to most biologics, safe drug. So when the regulatory agencies evaluate, it's not a new drug. So remember that, okay? This is a drug that has an established safety profile that the regulatory agencies are very aware of. When regulatory agencies look at approving drugs, they look at the risk and benefits. So I just want to kind of throw that out there.

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

I really like that. All right. Now I was going to ask on IL-33, but I think we're running out of time. Let's hit on atopic derm, and I get this quite -- the question you'll often get is, what's your Dupi number. And I've always said it's kind of whatever you want it to be. I mean, I'm not going to sit here and tell you atopic biologic derm penetration is going to be 12% and not 10%, and it just seems kind of silly. But there is a question about -- Lilly is -- it's 1 of the best executing companies from a commercial perspective out there. They do have a very solid product profile that is competitive versus Dupixent.

And let's not think maybe about percent growth, but in terms of just net patient adds for atopic dermatitis, as you get lebrikizumab on the market, and now you do have a meaningful biologic threat from a very savvy commercial organization. Should we expect net patient adds for atopic derm to change in any way? Whether it slightly go down, flatten or actually start to increase?

Brook Jennings - *Regeneron Pharmaceuticals, Inc. - VP of Commercial Dermatology*

So thanks for not asking the penetration question and we will give 1% extra. That's one we typically hear. But what I think of the marketplace overall in atopic dermatitis. First and foremost, I would say that the most recent entrants, the JAK inhibitors, came from 2 companies that are also very well established and know exactly what they're doing in AbbVie and Pfizer. So the market has certainly seen additional entrants come. They have certainly seen additional entrants that came with fanfare and additional dollars to spend on helping to grow the overall marketplace. And quite frankly, I actually am very excited about Lilly coming to market with lebrikizumab because I think that, that will help to expand the market further.

When you think of the overall marketplace as an example in the biologic market in psoriasis, that market is significantly more penetrated today than it would have been many, many years ago. And quite frankly, since dupilumab launched in 2017 with the first atopic dermatitis indication, we were the only ones working to expand the market. So with Pfizer having come to the market, with AbbVie having come into the market, with LEO having come to the market, the growth rate in the atopic dermatitis advanced therapeutic market has increased. I think Lilly will only add to that.

I think that the benefit from a Dupixent perspective is when you have the lion's share of the market, you get a disproportionate share of that growth. So while a rising tide will lift all boats, I think we will continue to find ourselves in a leadership position.

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

Understood. So maybe stepping back and maybe for Ryan, just more generally speaking, people's obesity numbers just seem to keep going up in models. I think it's probably implying around $120 to $150 billion at this point. You guys are renowned drug discoverers. You have the AstraZeneca collaboration, and you've looked at areas that are adjacent in the past. What does Regeneron think about the obesity market? If they were to get involved, where would they try to differentiate? And what could be some time lines we should be thinking about where that story might play out?

Ryan Crowe - *Regeneron Pharmaceuticals, Inc. - VP of IR*

Yes, sure. Thanks, Akash. It's definitely not lost on us that obesity is a rapidly expanding category with extremely high commercial potential. As you mentioned, I think in 2021, Regeneron discovered the GPR75 gene, where we've seen small -- 650,000 exomes that were screened, only about 1 in 3,000 had

-- didn't have a copy of the GPR75 gene. And they had 54% lower risk of obesity and were, I think, on average, 12 pounds lighter than those that had a complete GPR75 gene. So we've found a very solid genetic marker and we're exploring that through a couple of different ways.

You mentioned the AstraZeneca collaboration, and we're working on finding the right small molecule for that. But we also are looking at it from an antibody standpoint internally, and then we're also working on an siRNA approach. So a couple of different ways of looking at the GPR75 opportunity. But even beyond that, I think in our pipeline, we have some other mechanisms that are of interest where they could potentially pair with a GIP or a GLP to maintain weight loss and also potentially shift the ratio in terms of fat versus lean muscle loss when you have these weight losses. So some things to watch perhaps starting in the second half of this year as we get organized around our obesity approach.

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

Okay. Understood. If I can sneak in maybe just one more question on high-dose EYLEA, which at least give me credit I did not go there.

Ryan Crowe - *Regeneron Pharmaceuticals, Inc. - VP of IR*

We've got 25 minutes in.

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

Yes, just one more. So like, just 2 things. A, the question that I do get from people is, hey, let's say that you have someone who is on low-dose EYLEA and they look at the data set that you put out with high dose. How does that kind of inform a switch? And how does that maybe impact a label that you could theoretically get with high-dose EYLEA? Is that a fair way to characterize it?

Because to be clear, when I look at the faricimab study, it's not like that teaches me how to get people per se off another VEGF agent as well. So any comments on what labeling could look like? And that question I'm sure you're getting from investors right now in terms of the switch.

Ryan Crowe - *Regeneron Pharmaceuticals, Inc. - VP of IR*

Yes. I think we're not going to comment on potential label, but the review remains on track. We expect a decision by the June 27 PDUFA. In terms of how physicians end up using the product, we think it brings a best-in-class profile, and will become the new standard of care with hitting non-inferiority on extended dosing intervals of Q12 and Q16 versus EYLEA at Q8.

We think that's a meaningful advantage for patients, for practices and overall for the health care system. We do see statistically significantly higher proportion of patients that had no retinal fluid in the center subfield at week 16 as well as at week 48 in the wet AMD study. So we're seeing an impact on drying. Overall, I think the product profile is extremely strong, and we're going to go after the entire category, not just patients currently taking EYLEA.

Akash Tewari - *Jefferies LLC, Research Division - Equity Analyst*

Understood. Thank you so much.

Ryan Crowe - *Regeneron Pharmaceuticals, Inc. - VP of IR*

Thank you.