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PRESENTATION

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Good afternoon, everyone. I'm Tyler Van Buren here, Senior Biotech Analyst at TD Cowen. Thank you very much for joining us for TD Cowen's 43rd Annual Healthcare Conference. For our next session, very pleased to have a fireside chat with Regeneron. And it's my pleasure to introduce Marion McCourt, Executive Vice President of Commercial; and Ryan Crowe, Vice President and Head of Investor Relations. Marion and Ryan, thank you very much for being here.

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

Thank you, Tyler, and thanks for hosting us here at the TD Cowen Conference. Before we get started, I just wanted 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.

With that out of the way, Tyler?

QUESTIONS AND ANSWERS

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Great. So if you guys have any questions in the audience, by the way, feel free to raise your hand, and we'll try to get it in there. But let's go ahead and start with EYLEA. So Marion, were you surprised by the June 27th PDUFA date? And why do you think that might have occurred?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Sure. So I'll tag team this with Ryan on some of the details, but I do want to say that from a commercial perspective, we're very pleased to have the earlier launch timings and certainly will work to make sure that we're in the market as quickly as possible. And obviously, over the next weeks and months, we'll share more detail on our plan, but it's a tremendous opportunity to bring aflibercept 8-milligram into the marketplace. Our aspiration, as many of you know, is to provide a new standard of care. We've realized that will take preparation, and it will take some time in the marketplace. But certainly, it's a market we know really well with the product today in market EYLEA as a standard of care.

And then with this extra element of disease control that's being recognized with aflibercept 8-milligram with the opportunity for similar great quality in terms of clinical aspects of visual acuity, safety, as we've seen demonstrated to date in the clinical trials, and also with this really important element of being able to give greater durability to patients and the physicians who treat them.

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

So yes, Tyler, to the question about the PDUFA date at the end of June as opposed to late August, which we had previously signaled. I think this was a nuance in the latest PDUFA guidelines, and the FDA has decided to treat this new BLA as one that is for a non-new molecular entity. And the PDUFA guidance actually isn't specific to the regulatory or the review time line for a non-NME BLA. We had assumed it was going to be the full 12 months. There is a 10-month review cycle for non-NME new drug applications, and we ended up getting the same treatment for our new Biologics License Application.

So it's great that we'll be able to reach patients earlier and sooner, we hope, with approval, but it also potentially moves up the timing for when we could receive a permanent J code. If we're able to complete our application for a new J code by the end of the month or July 1, we'd potentially be in line to receive a permanent J code at January 1 as opposed to sometime later, had we gotten an August PDUFA. So it's really important for multiple reasons, and we're really excited that it came a little sooner than we thought.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

So what's your confidence in getting that J code application out there by July 1?

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

I think Marion's team has been working very hard to make sure that, although the window is tight, that the application is complete on time, so that we are in line for that January 1 J code.

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Yes. I'd add, we do have a very talented and capable market access and reimbursement team and certainly the opportunity to have a permanent J code is something that we'll be focused on. But I also do want to share that even under a temporary J code, we do believe there will be strong interest in aflibercept 8 milligram, but obviously, we'll work in all the correct ways to make sure we have applications in on time and complete and certainly look forward to a PDUFA date and possible acceptance in the earlier time frame. It's very exciting.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Yes. I mean I feel like people have been making a bigger deal out of temporary versus [whole] J codes or permanent J codes, especially with the Vabysmo launch. But the doctors are essentially saying that if it's a temporary J code and you have confidence that you're going to get reimbursement, then it's not really going to make a big difference, right? And with a high-dose EYLEA and Regeneron, I would imagine -- and the similar total effect of annual price, I would imagine they're going to have pretty high level of confidence in that rate.

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

So I think that many of those comments are correct that there's comfort, that reimbursement would be achieved for a product like our aflibercept 8-milligram. And certainly, as time goes forward, we'll give more information related to launch strategy and information related to pricing strategy. We've not shared any of that information at this time. But certainly, we'll be working forward to be very connected to the market in terms of our understanding, the sophistication of our audience, the multiple stakeholders. And I think also for Regeneron, it's always been an element of being very responsible with our pricing.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Is it fair to say that the overall plan is still to have the same total effective annual pricing for patients, and that's something that you'll refine as you get more data?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

It's certainly, Tyler, an important element that we look at, but we have not given any specific comments yet at all related to pricing. So I'm deliberately being vague on that more because we haven't given information not to give you any conclusions of what our pricing strategy is yet. I promise that will come just not yet.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Fair enough. And -- in terms of the HD EYLEA launch strategy, on one hand, you're defending against Vabysmo, right, as a new entrant. And on the other hand, you're trying to convert the existing EYLEA patients as quickly as possible. So is it really a two-pronged approach? Or how do you see this playing out?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

So Tyler, I would share that when we're thinking about the market opportunity and patient unmet need and what prescribers, key opinion leaders and other prescribers are telling us what they need, it's the profile that aflibercept 8-milligram has, based on the clinical data we've seen so far that's most exciting. So it's an opportunity to participate in the entirety of the anti-VEGF category. Certainly, EYLEA is a product in that mix. There's a couple of other branded products, there's lower cost Avastin as an alternative. And I'll use as a bit of a benchmark today. As you know, we have about 50% of the anti-VEGF category with EYLEA.

Other products have smaller percentages. What we would seek to do is over time, appropriately working with our stakeholders and our prescribers and understanding use of aflibercept 8-milligram in the marketplace, our goal is to become the standard of care in the anti-VEGF category. I wouldn't though position us versus a particular newer launch entrant that might have modest uptake to date. It's more about how do you move the entire opportunity for patients and treating them with the best possible product in terms of clinical outcomes, their visual acuity, safety, all aspects of efficacy and then also this notion of durability, which is incredibly important when you think about how individuals, of course, will have injections in their eye to save their vision, but it's not something that anybody looks forward to.

So doing that less frequently and potentially, over time, extending the dosing intervals out to 12 weeks, 16 weeks after appropriate loading doses is a very important aspect of aflibercept 8 milligram's profile.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Understood. And with respect to protection and exclusivity, what do you expect for HD EYLEA and with respect to the IRA since it's a new BLA, will that clock start from 0?

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

Yes. Let me -- Tyler, thanks for both of those questions. They're kind of separate and distinct, but I'll start with the exclusivity question. So part of the decision by the FDA to treat this as a non-NME BLA makes it fairly unlikely that we'll get any regulatory exclusivity for this product, which is not unexpected, of course, aflibercept is aflibercept. Same goes for a composition of matter patent. That was originally patented under the 2-milligram formulation. So we won't have the benefit of regulatory exclusivity or a composition of matter patent. However, I'd note that there are other means for protecting this asset, and we are being very thoughtful in how we pursue the patent estate for 8-milligram aflibercept.

And we've already actually received a patent related to the formulation, which has expiration in 2039. There are other patents that cover other aspects of the formulation that are currently pending. And there are other patents that -- for methods of treatment using 8-milligram aflibercept that are also pending. So we certainly have -- and we believe this is a novel formulation and certainly a much higher concentration and only a little bit more volume.

But notwithstanding all of that, I think there's actually a natural moat for aflibercept 8-milligram. If a biosimilar were to try and create a biosimilar version, but they'd need to essentially start from scratch, and they'd need to reverse engineer the formulation. They'd need to generate the preclinical data. They'd need to generate the CMC data required for it. They'd need to run the clinical studies and they'd need to go to the FDA and ultimately seek approval before they could launch. And we think that's at a minimum of a several-year period, for which we'll have marketing exclusivity naturally. And then, of course, we would hope to extend that with those patents that I mentioned.

Related to Inflation Reduction Act, we have said that this is going to be a new BLA. We have now had an accepted BLA filing. And while the law is still new, and it's -- we don't know exactly how we implemented or interpreted ultimately when the rubber meets the road, we believe that a new BLA creates a new reference product. And therefore, it would not be an eligible -- 8-milligram aflibercept would not be eligible for negotiation until its 11-year period had lapsed.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Thanks for all those details. I want to move to Dupi, but before we leave ophthalmology, I wanted to just get your latest thoughts on the attractiveness of the geographic atrophy space given the recent Syfovre approval.

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Sure. I'll start. We'll give you a little bit of our perspective. Certainly, it's really early days, would be the first -- and certainly, it's not an area of expertise, for me as the commercial lead in Regeneron. But I would say it's going to be very interesting to watch. Certainly, the market characteristic is where you're creating a market and establishing a new treatment course potentially in the marketplace and also considering the fact that patients are doing this in order to prevent a subsequent issue in their vision. But we will study this space very carefully. And certainly, to comment Ryan will, we have individuals who are actively involved in studying this particular indication and disease area with Regeneron [Science].

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

Yes. We have an active C5 development program, albeit in different disease areas. And we're looking very closely at whether or not it makes sense to pursue something in geographic atrophy with either pozelimab monotherapy or in pozelimab in combination with cemdisiran. Those are all things that we're looking at very carefully and does it make sense to have intravitreal administration or systemic, and our scientists are hard at work evaluating what this is, and I'm sure on the commercial side, the same analysis is being done as this launch unfolds.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Interesting. Okay. So Dupixent COPD, the Phase III BOREAS trial readout, a lot of people are looking forward to it. Are we still thinking potentially in the April time frame or sometime next month? Or what can you tell us?

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

Well, I have -- I'd say this, that the official guidance from us and Sanofi is first half of the year, but we can -- what we've learned is that from Sanofi is that the enrollment was completed in February of last year, and we know that it's a 52-week study. So I think it's fair to assume that we can expect results in the next month or 2.

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

I'll just add. It's an exciting potential opportunity because of the number of patients in the U.S. alone, it's about 300,000 patients. In the top 7 markets worldwide, it's about 500,000 patients. We obviously will have to wait and see what the clinical data reads out, but there is significant unmet need. And I think all hope that there's a possibility of Dupixent being able to help these patients.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

And how should we think about the level of efficacy that was required to successfully pass the first interim in that trial?

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

Great question. We've been getting that one a lot recently. I'd say first of all, we're still blinded to the results. And we don't know what the results of that interim were. All we know is that it exceeded -- met or exceeded the bar -- the prespecified bar that we set. And I'd characterize it almost as something between a futility analysis and a Phase II result. And a typical futility analysis, you're looking at whether or not the active arm has a chance to be statistically significant versus the control, whereas a Phase II result would inform whether or not to move forward into Phase III. That's exactly what this interim analysis did, and it informed that a second Phase III study should be initiated. And I'd add that, that decision was taken knowing the resources and the money was going to take to fund a second large Phase III study. So we thought the bar that we set was sufficiently high to warrant triggering that second Phase III, and that's where we stand today, with NOTUS currently enrolling and BOREAS readout in the next couple of months.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. That's helpful. And as we think about the top line data, what level of exacerbation reduction is clinically meaningful per KOLs?

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

I think KOL opinions range a bit. But for Regeneron, I think our view is that mid- to high teens in terms of annual reduction in rate of exacerbations would be clinically meaningful, but that will be on the low end of the range of clinical meaningfulness. And I say this because there's been really no innovation in the space. There's no approved biologics for these patients. It's been decades since a new mechanism has been introduced for COPD. So even a high-teens reduction would be clinically meaningful in our view. Of course, we're aiming for higher, but that's where we sit right now.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. And what about FEV1, how should we think about that?

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

I think FEV1 is important, but I don't think it's as important as the reduction in exacerbation. I think the exacerbations are what drive the hospitalizations and all the costs, the health care -- to the health care system. The primary endpoint is a reduction of exacerbations. We'll find out if there is an improvement in lung function because they are key secondaries at week 12 and week 52. And it would be great to have both, of course, but I think that the reduction in exacerbations is probably the more clinically -- the more important endpoint for us.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Yes. Okay. That's fair. Marion, maybe stepping back with the Dupixent franchise. Can you give us the latest in terms of what the breakdown is per indication in sales? And where you're seeing the most growth, what areas you're seeing the most growth?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Yes, Tyler, I'll give you an overview. We've never given specific breakdown by indications, but I can give you a framework that I think would be helpful. Certainly, our largest indication is atopic dermatitis. It's been amazing over 6 years to see the uptake in adult patients, then adolescent patients, pediatric patients and now our youngest patients from 6 months to 5 years. Truly remarkable in terms of the ability to help patients and families, who are suffering with atopic dermatitis.

As we go forward into some of the other indications, obviously, next launch in the area of asthma, very important in biologic asthma, and they're more crowded category, but very proud to share that the Sanofi-Regeneron teams in market have the lead in terms of number of new scripts coming into the biologic asthma space with Dupixent. Nasal polyps was also a very important launch and indication.

Most recently, I mentioned the youngest patients for atopic dermatitis, I'll mention that one again only because it has such an important aspect of confirming the safety of product and ease of use of the product when you see such young patients doing so well. And then as we go further, just even more recently, we look at launches for eosinophilic esophagitis. Now again, allergists and gastroenterologists now added into the group of specialists treating with Dupixent. So very really tremendous early days in the launch. There's been thousands of patients who've been treated with Dupixent already for eosinophilic esophagitis. And we do look forward to having potential approval for pediatric patients with that very difficult condition and one of the leading causes of patients, children failing to thrive because they're suffering from eosinophilic esophagitis.

We also, just towards the end of last year, launched prurigo nodularis, which many of you know is a condition that impacts probably about 75,000 patients in the U.S. alone, incredibly high burden to patients. They have these very, very distressing nodules, and it's the intensity of itch that becomes absolutely debilitating to them. So we're really exciting to have that indication in the market now as well. At the same time, I focused a little bit more on U.S. We've had a lot of these same indications rolling into international markets. We have started our international commercialization and target markets with Sanofi, so it's really been incredibly exciting to watch Dupixent unfold on the world stage.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. That's a helpful overview. Maybe we could just double click on...

Unidentified Analyst

Just a follow up. Do you see off-label use, and were you able to monitor off-label use (inaudible) area?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

We do have an opportunity to use what's available in terms of market insights, analytics and market research, and the use of Dupixent is on label, primarily. I can't say in every situation, but on label. And I think as an example, I'll reflect in our U.S. marketplace, it's based on work and coverage we have with payers and aspects of making certain that the correct patients are being treated.

Unidentified Analyst

And the price, is (inaudible)?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

The price is similar by indication. One exception would be rather than every 2-week dosing on eosinophilic esophagitis, the dosing is weekly. But I'm very pleased to say that we've had very strong relationships with our payer stakeholders and the reimbursement has moved with the expansion

of indications. Keep in mind that at the start, Regeneron with Sanofi priced Dupixent at a very appropriate level. And I think we benefit from that today as the product has become obviously larger, used more broadly. It's a specialist product, but certainly, there is recognition that patients are helped in a very meaningful way.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

On AD, where is your confidence level in terms of continued growth for Dupixent? And with lebrikizumab on the horizon, how do you think about that potential competitor?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Sure. And one thing I'll add because it relates to [Lilly] bringing a product into the atopic dermatitis space. As everyone probably knows with DUPIXENT, we have a dual mechanism of action, IL-4/IL-13, and it's really important in terms of allergic cascade or type 2 disease. So as I just rattled off all those indications, where Dupixent has an indication today and you know many other areas where we're either awaiting data or there's future indications. The product profile is such that it's not just the indication, but it's also the potential to help patients that suffer from other allergic cascade, type 2 diseases.

It's not at all uncommon for a patient with atopic dermatitis to have an element of asthma or use the examples in your mind. I mentioned it because as other companies, and there's actually IL-13 in the marketplace today, the level of efficacy to date hasn't been seen to be as strong. We'll have to await some of the data and the launch information on Lilly's product. But here too, it's a more limited mechanism of action, which could have some potential impact into not only efficacy in atopic dermatitis, but also the ability to help patients with other disease areas.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Great. Let's get into oncology, starting with the bispecifics. At ASH, you guys showed some follicular lymphoma data that the presenter called foundational, looked better than Roche's Lunsumio, and it leads us at least to believe that maybe when we get longer follow-up in DLBCL in myeloma later this year, that we could see some nice improvements there. But I'll ask you a commercial question, naturally. I guess in general, how do you expect to compete against large pharma in this space, given that they're first to market.

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Sure. So I think that you've seen Regeneron, not only the commercial organization has the opportunity to commercialize this exquisite science. And what I would share is that I hope over several years now, many years now, we've been able to demonstrate our ability to be competitive in the market with large pharma, midsized companies, and it's based on the attributes of the products that we bring into the marketplace, but then also our ability to build organizations, whether it's our oncology team, a future hematology team, some of the other areas we've discussed. So I think that will be highly competitive, we'll also practice best launch preparation activities, understanding our audience, building relationships in the marketplace. So we have confidence in our ability to bring the products into the market.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Maybe on the costims. The early PSMA data is pretty intriguing, right? The 3 out of 4 patients, PSA levels going to 0. So what can we expect -- or near 0. But what can we expect from the Phase I update in the first half of the year? And what are the next steps for that program?

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

So we had a poster at ASCO GU that kind of formally presented the data that we had initially top line back in August. There's a little bit of incremental information in that poster related to RECIST in a couple of patients, RECIST criteria and response rates, and baseline characteristics and things like that. But I think the more meaningful update for the PSMA by CD28 program will come in the second half of the year when we're going to look at patients with longer follow-up, patients that have been subsequently dosed post that top line report in August and also patients that are getting co-administered with sarilumab, an IL-6 antibody that Regeneron has developed, to hopefully mitigate some of the grade 3 immune-mediated adverse events that we saw in responders of this PSMA by CD28 bispecific.

And that's important to note, it really shifts the benefit risk when you only are getting these grade 3 or higher immune-mediated adverse events in responders, but we still hope to tamp that down to make it a more manageable safety profile for these patients.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay, on Libtayo. How are the early innings of the chemo combo launch going?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

So we obviously are in somewhat early days since we launched the chemo combo indication in November. Very important for Libtayo to add the chemo combo indication for lung. We obviously had monotherapy earlier, but it is a larger indication with chemo combo. And in speaking with our oncologists and KOLs, the optionality of chemotherapy is something that is important to them with Libtayo. Early days, we are seeing some steady upticks in performance, whether it's in numbers of prescribers, numbers of patients with lung cancer being treated with Libtayo. We're seeing inclusion in order sets, formularies, pathways, things of that sort, which are the early indicators of performance to come.

So we do think it's a really important opportunity for Libtayo. We continue to perform very well on the prior indications in skin with CSCC, basal cell carcinoma where Libtayo has become the standard of care, but we equally realize that the lung cancer indication, chemo combo specifically, is a very important opportunity for physician choice and for patients. So we're working hard on it.

I'll add that it's also important because Libtayo, now entirely owned by Regeneron, which we're really pleased with, is part of what you were talking about a few moments ago in terms of our future oncology portfolio, the combinations, things of that sort. So -- and we think there's a lot of excitement in the future for Libtayo, not only today's indications, but future as well.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Great. So as we think about another indication or combination with fianlimab and LAG-3, you guys showed some pretty compelling data at ESMO. And I believe you're going to have top line results next year from the Phase III? If not, you could, I guess, correct me on that if I'm wrong, but what do you need -- when will it come out? And what do you need to show to be competitive?

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

I think what we've already shown has been competitive when you consider the response rates that we've seen with the fianlimab-Libtayo combination in the low to mid-60% compared to Bristol's LAG-3 combination with OPDIVO around 43%. And even on PFS in the pooled cohorts of fianlimab plus Libtayo, we had 24 months versus 10 over the Bristol combination. So I think already, we've had a test and retest of this fianlimab-Libtayo combination that has held up extremely well and has been very consistent, and I think has shown early signs of differentiation versus Bristol.

To your question on data for the Phase III program, we're currently enrolling a metastatic melanoma study that could have data in 2024. We're also enrolling an adjuvant melanoma study, and we're also looking to kick off our lung program, starting in a Phase II environment in both all-comers

and high expressers with and without chemotherapy. So a lot to come from fianlimab plus Libtayo. I think there's other tumors we may be exploring as well with more to come on that later this year.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. I want to touch on the Regeneron Genetic Center briefly. So again, people to try to focus on the oncology pipeline more, right, and still very low visibility on the genetic center. But I guess what program should people be focusing on most there as we think about the next year ahead?

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

Maybe I'll start, I don't know if Marion has anything to add. But I think what we -- the collaborations that we currently have underway with Alnylam, I think the next readout is going to be in the APP, the ALN-APP program in early onset Alzheimer's. This will be a program that could potentially demonstrate proof of concept of an siRNA penetrating the CNS, which will be the first time that's ever been done. And it sort of opens up the door to a lot of other opportunities for neurodegenerative diseases and exploring them with an siRNA intervention. If we can get strong target knockdown and safety. So that's one to watch, certainly.

Of course, we have the NASH programs underway, one of which we're managing on our own, one of which we're managing with Alnylam. And then I'd also throw in Intellia, which we have a program in TTR amyloidosis underway and have shown a really robust and durable knockdown of that target. And then finally, Decibel. I think Decibel is the other one that people tend to overlook, but is an otoferlin gene therapy that is in a condition pediatric patients that have deafness, genetic deafness. So that's one that I believe will start dosing in the first half of this year and hopefully have an update there for you either later this year or in '24.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Great. On cash, you guys have $14 billion of cash. You continue to generate more each year. Does that mean you guys might be more aggressive on the business development front? Or what is your current focus and strategy?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Yes. I'll take a start. I think one of the things that as I know, have spent 5 years at Regeneron a month ago or so is that to understand how different our company is from some others in terms of how we look at business development, we have commitments, the talent and the science at Regeneron, so it makes it much less likely, highly unlikely that we would ever be a company seeking to acquire at a very high price, usually a late-stage asset.

That's just not our business model. So I think that investment in technology, platform, the kinds of things you've seen us do with CytomX or some of the other collaborations that Ryan cited or we've announced over the last year or so that's very much in keeping with Regeneron. But in terms of what you might think of as more traditional large pharma business development, that's not our strategy.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Okay. Fair enough. Yes. So to end, Marion and Ryan, I'll ask you both, what do you believe is currently the most underappreciated aspect of the Regeneron story by investors?

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

I can start. I think the genetic medicine business really has a lot to offer and there's nothing in the valuation for it today. As I mentioned, we have numerous opportunities that are going to begin to generate data. And I think it's time for people to start to pay attention to some of these partnerships that we have and hold significant economic stake in. And that's really where I think there's upside -- material upside.

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

I think Ryan answered it beautifully, and I would maybe just also in addition to that double down on oncology and our future more broadly there. But I also want to commit to everybody that we have a lot of work to do, obviously, in the ophthalmology space. We're really excited about the coming aflibercept 8-milligram launch once we have an FDA approval. And certainly, some of what we talked about today on Dupixent is very exciting as well with more to come.

So Tyler, thank you for having us today. Thanks, everyone.

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

Thanks, Tyler.

Tyler Martin Van Buren - Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst

Welcome. Thanks for being here.
