Biogen Inc.

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Event Participants

Analysts 1
Paul Matteis

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Priya Singhal

Paul Matteis Analyst

Great. Good morning, everybody. Happy to be moderating my annual panel where Priya has to listen to me pepper her with questions for 40 minutes or so with Priya Singhal, Head of Development at Biogen. Thank you, Priya, for joining as always. I'm going to kick it over to you to just make some opening remarks on Biogen and give us a snapshot of the development portfolio, and then we can do Q&A.

So thanks again and take it away.

Priya Singhal Executive

Thank you, Paul. Thanks for having me. It's always a pleasure to join you. So before we begin, I'd like to point out that we will be making -- that I will be making forward-looking statements, which are based on our current expectations and beliefs. These statements are subject to certain risks and uncertainties, and our actual results may differ materially.

I encourage you to consult the risk factors discussed in our SEC filings for additional detail. So really excited to be here, Paul. As you may know, that over the last 2 years, we've really focused on efforts to augment the pipeline. And the main goal has been rebalancing the risk profile and investing to win in key areas of expected future growth. So in 2024, I think we made a lot of progress in our pipeline, where we've prioritized key programs, internal programs, where we believe that we have the opportunity and potential to win such as Alzheimer's, where we were able to amend our Phase II study, CELIA for BIIB080 and accelerate a potential proof-of-concept readout next year in 2026.

We also got a positive Phase III outcome with our dapi Phase III trial. And then we also focused on external innovation. And we had one M&A with HI-Bio, and we have felzartamab

now in our portfolio, poised to have 3 Phase III starts in 2025. And then in addition, we did the collaboration with Stoke Therapeutics and brought in access really to zorevunersen. And that's very exciting because we have the ex U.S.

region and also poised to start Phase III in 2025. We've also advanced LEQEMBI. We continue to focus on SKYCLARYS pediatrics, which is really the next very important milestone that we are ready to get going on as well as SPINRAZA high dose, where we had a filing already in both Europe and the U.S. So a very exciting year. And I think as a result of this progress, we've been able to focus now our development efforts on a set of really high conviction -- high scientific conviction mid- to late-stage assets.

And if we're successful, we could set up franchises in very key areas like Alzheimer's, lupus as well as rare disease. And these, we believe, are really core areas of expertise and capabilities. So we are harnessing that low volume, high-value sort of portfolio here. So very excited.

Paul Matteis Analyst

Yes. Okay. Great. Well, we're going to try to take time and go through each of the assets you mentioned and a couple of the key questions. But maybe one more forward-looking question for you just in terms of the whole where is Biogen going?n And I guess it wouldn't be a Biogen panel without the token business development.

We super cool like anti-LINGO-2 program. And it feels like Chris now talks a lot more about rare disease and immunology as key areas. So just as it relates to CNS specifically, is this an area you think you'll continue to build out and take on risk in? Or is it an area where you feel like your portfolio is full and you're trying to continue to shift elsewhere?

Priya Singhal Executive

Yes, it's a great question. And I think overall, what I would offer are 2 important thoughts here. One is that neuroscience continues to be a core capability. It's an area we've succeeded in. We've often broken the ceiling there.

We'll continue to invest and keep our capability in neuroscience, but we've diversified. So we're not just going to go after high-risk neuroscience programs that will be a decade to kind of get to proof-of-concept. We are balancing that with immunology and rare disease, both areas which we -- I also believe we have deep expertise. So with rare disease, we've had one of the best launches in projects with SPINRAZA. We're continuing to build on that momentum, and then we brought in SKYCLARYS.

And you can see that we brought in SKYCLARYS where it's rare, but also neuroscience. So what the distinction here is, is being confident in the data, being confident that when we get to late stage, we've derisked and we have a significantly higher POS and a probability of technical and regulatory success and payer success than we have maybe in the past. That's what I will offer is the key change. And then immunology, I think I would say that it's really foundational. With multiple sclerosis, everything that we've been doing, immunology has been in focus.

We're really the only company now with 2 different mechanisms of action, both in Phase III for

lupus as well as systemic as well as cutaneous for litifilimab. So I think that's how I would think about it. It's not a departure. It's a building around, it's a diversification.

Paul Matteis Analyst

Yes. Okay. Fair enough. As it relates to taking on risk, what gave you and your team conviction about executing the Stoke deal before Phase III?

Priya Singhal Executive

Yes. Excellent. So I think overall, just stepping back, Dravet is a very serious disease, high unmet need, no disease-modifying therapies. The other piece, I think, to keep in mind here is that these children are often cycling through 4 to 7 anticonvulsant therapies. And they really -- we know that from the evidence we've seen and we've kind of evaluated, we don't believe these really impact what the decline is from a cognitive functional behavioral perspective as we've seen kind of in scales like Vineland 3.

So what we're excited about with Stoke and with zorevunersen is that we saw the data -- although it's a small subset, we saw that in this population that had the background of 4 to 5 anticonvulsant therapies, including fenfluramine, 50 -- more than 50% of the patients who are on background fenfluramine, we saw an 85% reduction in anticonvulsant therapy and then out to 6 months, still durable with about 75%. That itself is very powerful. Well, we didn't just look at that. We looked at the natural history that also Stoke ran. They have a 3-year natural history data set.

And then we looked at what were the trends on behavior and cognition on the Vineland 3. And we believe that this product can actually impact that the developmental kind of milestones and the behavioral milestones that are so important for Dravet. And then, of course, it's generically -- it's grounded in genetic evidence, right? Because we know that 85% of Dravet occurs due to a haploinsufficiency of the [SCN1A] gene. And that then results in the sodium channel Na(V)1.1 reduction, which then leads to an impact on the inhibitory interurons and the interplay causing seizures.

So we think that there is not only mechanism of action belief here, but there's a potential data that we've seen in the early phase studies that setrly phase studies that set us up for Phase III. Now of course, Phase III studies, you do need to get regulator buy-in. And that was the other important pivot and anchor for us that Stoke had already discussed their Phase III program, had obtained agreement with regulators in the U.S., Europe and Japan on what the Phase III program would look like, how it would be powered. So we had a lot of data going in.

And it kind of goes back to your first question because I wanted to say that what's changed is we are not -- it's not like we wouldn't take a risk. The question is how calculated can that risk be? And are we confident that we've derisked some things that we would want to with POC. That's the distinction.

Paul Matteis Analyst

Yes. So I mean this is a tremendously interesting program. And just as it relates to epilepsy more broadly being kind of going through like it's not a shift because I don't think it's ever

going to be broadly like this, but like a subtle shift towards precision medicine. We felt like one of the key questions with this program, and obviously, given the mode of administration, this would be a big commercial swing factor to the upside, right, if this is successful, is the cognition piece. And I was curious how you think about this question and whether you think this question is relevant.

But if you were developing a drug for cognitive impairment in schizophrenia, right, you'd be pursuing a population that is not acutely psychotic, right, because the FDA wants you to decouple cognitive benefit and benefit on psychosis. As it relates to the Stoke asset, do you look at that data and think this impact on cognition is independent of seizure reduction? And I guess as you think about getting like a label for this and a claim for this and marketing this, like does that matter? Like how should we think about that?

Priya Singhal Executive

Yes. Another great question. I think it does matter. And I think it matters because we -- based on our current understanding and all the data that we've evaluated; I don't think it's been demonstrated that just simple seizure reduction will lead to that cognitive improvement. We think there could be some effect, but we think you need to be doing more really in terms of the mechanism of disease.

So addressing mechanism of disease is going to be very critical. And that's why we're excited because this is not just anticonvulsive therapy. It's actually going for more than 85% of what we know is causative biology. Plus, I mean, just having that data isn't enough because that's what you know from disease understanding. But then we saw in the small data set, granted it's small and its open label.

But I think we have great teams within Biogen and we're able to really dissect these data sets to see whether we have enough confidence that tips us over to know that could this have the potential if the Phase III is designed correctly to have disease-modifying therapy. And that's what gave us that confidence. So we're not just looking for an anticonvulsive therapy. We are looking -- definitely, it has to have impact on seizure reduction, and we think that will be contributing to outcomes. But we think it needs to have a distinct disease-modifying therapy, which we believe this product definitely has the potential.

Paul Matteis Analyst

Yes. Okay. Great. All right. Let's maybe just do hits around the whole pipeline.

So on lecanemab subcu, can you remind us of just the general time lines there? And as it relates to subcu initiation, how has the program evolved over time as it relates to doing more dose work? And what would you say the target product profile is, specifically as it relates to ARIA and whether you can get to a lower rate of ARIA?

Priya Singhal Executive

Yes. So overall, I think very excited about the intravenous LEQEMBI approval that we got just a couple of months ago because this was a big debate out there about whether this product has a dual action, can we actually have a label-enabling update on that. And I think that was

an important milestone because LEQEMBI is really the only product now where we say -- where we know that if you remove plaque, obviously, if you remove amyloid, you -- that translates to clinical benefit, but that, that benefit can continue and be durable beyond plaque clearance. So I think that was a very important milestone for us. The other is that you know we remain in review for subcutaneous maintenance, which I think is going to be very important, and we will get an outcome, and we have a PDUFA date in August this year.

And why is that important? Because this gives optionality to patients and prescribers, could potentially alleviate some of the stress in the health care system. But importantly, there's going to be this bolus of patients who are going to be completing their 18-month therapy or such where they have the plaque reduction and potentially, they could transition if we -- assuming we get approval for the subcutaneous maintenance. Moving to subcutaneous initiation what we've said, is that we will file that at some point this year and we expect an outcome a regulator an FDA outcome before the first half or within the first half of 2026. We remain on track for that.

Now the data, we try to be as driven by data in every program. So here, again, the data has driven us. Because we saw with the data that the 360 milligrams IV twice a week will actually lead to a higher plaque clearance and is much more than we potentially need. So the question here is, can we reduce that in some way to make it more optimized to reduce the initiation dose, which potentially could have an impact. We think efficacy will be maintained, but it could have an impact on ARIA.

Now ARIA, I think nobody has fully understood it. And I think what's important is 2 things. One is it has a window of susceptibility especially for a product that's not titrated. It happens early and you can capture it with monitoring. And most of it is asymptomatic and serious ARIA really remains below the 1% mark, at least for lecanemab, symptomatic less than 2.8%.

We haven't seen any differences with real-world data with more than thousands of patients treated now. So that gives us confidence, one, that it's kind of replicating what we saw in trials, physicians are able to manage it, and it's something that education really helps. Second is that if it's lower, that will be a potential advantage, but we're not there yet. So I think the data that we're generating is to really look at can a more optimized dose be adequate in terms of efficacy. And I think if it provides advantages in terms of ARIA, which we know with subcutaneous is more related to steady state, unlike the intravenous formulation.

So we'll see. But I think overall, we believe ARIA continues to be manageable and is replicating for lecanemab as we saw it in the clinical trials.

Paul Matteis Analyst

Yes. Okay. That makes sense, Priya. Chris, I've always appreciated his candor about this launch because I think he's not -- he hasn't tried to oversimplify it, right? I mean I think he's been pretty open that this has just been such a complicated launch and like there's so many factors that play in.

And I guess now where we are with lecanemab, how would you rank order the impediments to uptake? I would assume -- you tell me if I'm wrong, but I would assume subcu maintenance might have an incremental impact on uptake just because you have to be on the drug for so

long. For subcu initiation, like how much of a game changer is that? Or is it still more about everything else, seeing a neurologist, the MRIs, et cetera?

Priya Singhal Executive

Yes. I think you're right. I think Chris has articulated that exactly right as well. It's a multitude of factors. Some are related to the product, but a lot are related to the infrastructure and the fragmentation of dementia care in the United States really.

And I think that we believe there are several catalysts. And to your point, I do think subcutaneous maintenance could be just incremental. But if we really see a blood-based biomarker hitting the ground in terms of an IVDR in 2025, so FDA approved, that could really be quite important because I think the biggest hesitation neurologists have is that they have to go through so many steps to even confirm amyloid, right, before they can put a patient on drug. So I think that with the advent and sort of upswing that we see on digital cognitive tools, if IVDR comes along, like I think the combination of that, the potential of optionality for patients with a subcutaneous formulation, all of this could be really powerful. And then if we can sort through some of those things and we come along with a subcutaneous initiation possibility in 2026, well, I think that could really be a very important.

But I think, yes, you're right, it's going to be a series of catalysts of continued education for prescribers.

Paul Matteis Analyst

How would you think about the probability of success for a credible blood-based biomarker coming to the market in the next 1 to 2 years?

Priya Singhal Executive

I think it's high. I think...

Paul Matteis Analyst

What should we be looking at -- do you want to just help people what should we be looking out for?

Priya Singhal Executive

Yes. So we know that Fujirebio is already in review. I think as of September '24 in the public domain. And I think this is going to be important because the one thing that people need to remember and prescribers also need a lot more education on this is that there are lab-developed tests, which are not FDA approved and then there are IVDRs, which are potentially FDA approved. Fujirebio is definitely in review.

There may be 1 or 2 more players who will get in there. I think that will be good momentum to have. The difference is the sensitivity and the specificity. And this is important because this is a serious diagnosis, high unmet need, but a serious diagnosis with implications for both the patient, the caregivers and the prescriber. And so I think that prescribers are looking for concordance with PET amyloid as well as CSF.

So that's going to be important, which I think the specificity of an IVDR is poised to deliver. That's number one. Number two, it needs to get reimbursed. And I think having IVDR status is likely to potentially garner, I hope, a reimbursement, which is pretty important. It's not big dollars in the big picture.

I think it's just about getting the data right. And then finally, they need to scale up.

So I think that's going to take the entire infrastructure. But I do think that next 1 or 2 years, this is likely. And I think it could be a game changer along with all the other momentum because on its own, a diagnostic test doesn't mean much if you can't do anything for the patient. Now with the advent of products like LEQEMBI, we believe the physician actually has something to offer. So there's a lot of momentum in the future.

I think PCPs could be using the blood-based biomarker, but I think that might take a little bit of time. But things move fast when you get to this stage, there's a tipping point.

Paul Matteis Analyst

Yes. Yes. Okay. Very interesting. Let's talk about the tau program.

And I think the natural question -- and you guys have some data to address this, but the natural question for me for any of these intrathecally administered products, be it antisense oligonucleotides, RNA, gene therapy is, are you getting enough target engagement across the key areas of the brain? And I think it's like complicated, but I think as we've tried to bridge from the early successes in spinal muscular atrophy to other diseases, right, like the success rate has been very mixed. And again, it's nuanced, but one of those -- if -- one of the reasons, I think, is biodistribution. And so to that point, can you just review for everybody the target engagement data you've generated and your level of conviction that you are reducing tau levels in the brain areas that matter in Alzheimer's?

Priya Singhal Executive

Sure. And I think there's 2 lines of evidence I'm going to offer. One is preclinical data. And I think tau has been a long-time focus for Alzheimer's drug development. We know a lot of attempts have failed.

We ourselves have failed with BIIB092 or gosuranemab, which was an antibody. And I think what we've learned from everything that we've done and evaluated is that you need to be able to knock down intracellular and extracellular tau. And I think that's the beauty of the ASO platform. That's what it's given us the opportunity to knock that down. And when we looked at really our preclinical models, we saw that we were getting sufficient exposure across the key brain regions, and that really is the most direct evidence of target engagement for BIIB080.

Now we've looked at BIIB080s effect on tau expression in brain tissue of mice, rats, nonhuman primates. And consistently, we've seen a robust reduction of the MAPT mRNA or tau protein levels in brain regions where BIIB080 was detected. Now that's not enough, right? So you've got to do the human experiment. And we converted that Phase I study into a Phase Ib study.

We opted in early. So this was our wholly owned now Biogen program, where we saw effects

on tau pathology and clinical outcomes. This was more than what we might have expected, right, which is more than just PK data. And I think what is most attractive about BIIB080 in and in terms of how do you kind of get to proof-of-concept and what gives you the confidence to continue to invest or invest to win as that's the category the programs in. And it's the fact that we saw a confluence of the fluid biomarkers tau PET, which we believe is very critical to observe.

Paul Matteis Analyst

Can I clarify something with you? Have any of the antibodies that have failed shown an effect on tau PET to your knowledge?

Priya Singhal Executive

No. Not to my knowledge. Not to my knowledge.

Paul Matteis Analyst

Not to mine either.

Priya Singhal Executive

Yes. That's the piece we're always looking for. In fact, it's become very simple for us to look at exciting programs because we're looking for that piece of data.

Paul Matteis Analyst

Yes.

Priya Singhal Executive

Yes. So that's critical. And also -- so I would say, unexpectedly, we saw an emergence of clinical outcomes that was very exciting. Granted, it's a small data set. It's a MAD study, but we saw that these were durable several weeks after drug.

And that was another very exciting piece of information. So that's the confluence that gives us excite -- gives us the impetus to kind of keep going. So we looked at that data. Our CELIA study, which was our Phase II study was already ongoing. We went back.

We reevaluated what was the power we needed for CELIA. We actually cut that study in half. And yes, like you, I was concerned about intrathecal delivery and acceptance, right? But you'll be surprised to know the study enrolled very fast. We completed enrollment in 2024 ahead of our sort of expectations, I would say.

So very exciting. And it's anecdotal, but when I've talked to investigators, they say that patients really want to try it. They really want to try it. The patient today is really well educated. This is also targeting MCI and mild.

They have an understanding of the Phase I data. They've seen the information. So I think they want to give it a shot. And so it's been very exciting. And yes, I'm excited.

We'll get a readout in '26.

Paul Matteis Analyst

Yes. No, I'm very excited about that program, too. Can you -- maybe some of the other just biological questions that I think come up with tau. I mean one is the right time to intervene or the right window for intervention. So maybe you can comment a little bit on that when we think it plays a role in the disease?

And then the second is just tau, if you just read about it on a base biology level, right? I mean it's evolutionarily conserved. It's talked about an important cytoskeletal protein. Like how confident can we be that knocking it down is not going to have some sort of safety down?

Priya Singhal Executive

Yes. We looked at this question very carefully, and I'll offer a few points here. So first one is that the current understanding of the biology of tau is that there are lots of redundancies in the biological processes that tau participates in, such that the tau knockdown has an impact on the pathologic gain of function, but not on physiologic function. This has been published, and I think it's an important line of evidence. The other is that when we looked at animal models in mice, we looked at complete knockout of tau.

And we saw that, that's tolerated, and animals are viable. So that's like -- it's not a very high bar, but animals are viable. And multiple tau -- different tau knockout mouse lines have been generated and phenotypically characterized in these lines, the complete tau knockout had normal development and cognition with a minor motor phenotype developing later in life. So potentially mitigating the safety concern that it would be a devastating outcome, right? So that's 1 -- 2 pieces.

Now for humans, the way we've tackled this is we have had access to the U.K. biobank samples. And our team, our translational medicines and translational sciences team did a lot of work on this question. And they saw that these really genomic data that was available showed us that heterozygous loss of function of tau in humans is actually very lightly tolerated and highly compatible with life. And that tells us that about a 50% reduction in tau may not be associated with gross neurological defects.

So -- and we see that also in the data that we saw. Now in the BIIB080 trial, granted, it's a small trial and small number of patients, we have seen that we saw dose-dependent and sustained reductions in tau, reducing it to about 50% in CSF, and we have an acceptable safety profile. So we think that this supports ongoing development. You can never be sure, so you need to continue to test it. And that, I think, is something that we are looking at very carefully in Phase II.

But so far, all the lines of evidence tell us that this is really compatible. And the other question you had is what's the right time for intervention? Well, as you know, I mean, everything we know about Alzheimer's tells us that you've got amyloid buildup for years, probably decades. And then you've got this penultimate sort of tau buildup.

Paul Matteis Analyst

Yes.

Priya Singhal Executive

And then you kind of have that tipping point a few years later of getting into symptomatic zone. And so we are targeting that same population, the MCI and mild, but we continue to look at the spectrum and think about are there other areas for intervention with that. But we're being very systematic about what do we want to first prove and then what does that unlock and in terms of development because I think BIIB080 could be really powerful in so many other avenues, right? Primary tauopathies, potentially moderate AD. These are all areas we are exploring, and we remain very focused on how do we accelerate once we get that confirmatory POC, which hopefully will have a readout.

It will tell us; we'll learn a lot because we've got tau PET. We've got all these markers in the CELIA study.

Paul Matteis Analyst

Yes. Yes. Okay. Great. What are you power for from an effect size perspective?

And do you think the effect size for something like this, given the IT administration has to be bigger? How do you think about the clinical hurdle?

Priya Singhal Executive

Yes. So I think one big thing to kind of keep in mind is we are looking at 3 doses and 2 dosing paradigms. We built this based off of the data that we had from Phase Ib. So that's the #1 thing. We're thinking about burden and we're thinking about adequate PK/PD sort of exposure and all of that and biodistribution, as you rightly pointed out.

And we saw durability of tau reduction. So that's going to be important for us to nail. The other thing is, yes, we're going to look for effects on fluid biomarkers. We're going to look for tau PET. We're going to look for clinical outcomes.

And we have the same primary endpoint, which is CDR sum of boxes, because we want to anchor it on a validated registrational endpoint. Now obviously, we have a lot of other secondary and exploratory outcomes. So we'll be looking to learn deeply, but we are anchoring this on what we know has evolved with the anti-amyloid space. So we are anchoring it on CDR sum of boxes. What do we need to see?

I think it depends a little bit. I mean we believe we powered it to see an effect. But I think it depends because remember, tau is not necessarily, or we hope it's not going to be associated with ARIA. So what's the benefit risk? How does that change?

And I think a lot of these factors will be part of our overall framework as we think of developing a go no-go framework for -- and go no-go means are we going to go beyond AD? Are we going to do more other exploratory trials? What are we going to do? Or are we going to double down just in AD, mild AD, MCI. So I think all these things will matter.

But overall, I think we're powered on -- we believe we are powered on CDR sum of boxes, and we've got a bunch of other things we'll be learning. We'll be looking at tau PET very carefully. We believe it's very critical and the fluid biomarkers.

Paul Matteis Analyst

Yes. Yes. Okay. Last question here, and it's really just on the oligo brain space in general. Do you have a view on the brain shuttle approaches?

I think we've seen -- we've seen these approaches in the brain validated with antibodies, proteins, enzymes. And then in the muscle space, right, also with transferrin, we've seen that oligos are a viable target, you can deliver to the right part of the cell. And I know there's interest with this tau target specifically with brain shuttle approaches, which, again, super early, higher risk, but could be IV. Is this something that Biogen has on its radar?

Priya Singhal Executive

Very much. So Jane and her organization, and we are partnering on this, we continue to believe that the brain shuttle delivery to the brain is a primary goal. So yes, the short answer is yes, this remains very exciting. We've got a lot of work internally. We believe we've made headway, and we have some real important areas that we think we're making rapid progress.

So yes, it continues to be very important, and we're continuing to work on it. It's really the third pillar for us.

Paul Matteis Analyst

Yes. Okay. Okay. All right. Let's talk about lupus a bit.

So -- and then we can maybe talk about felza and IgAN and the transplant space as well. But just as it relates to lupus, it's interesting, right, because I feel like Biogen's stock doesn't get much credit for dapi or litifilimab. And I think the things that hold investors back, one is that in the dapi Phase III, right, the study was positive, but the p-value was close, right? So there's a question on how much margin is there for the next study? Can we be confident in the replicability of it?

And then just the second question more broadly is that it's weird. On the one hand, lupus feels like it's this big unmet need. On the other hand, it feels like it's a competitive space, right? I mean there's a lot of stuff in development. And I think it's hard for people to kind of figure out where different assets fit in.

So I realize that there's multiple questions there, but it would be great to kind of get your snapshot on both the clinical risk side and then just the positioning side as well for your 2 assets.

Priya Singhal Executive

Yes. You're exactly right. I mean I think 2 points that you made, I'll reiterate is very high unmet need, extremely high and a lot of competition, absolutely true. But I think that when you look -- when you step away from those 2 points, you realize that there have only been ever 2 products that have been approved. It's been a graveyard for trials.

I think a lot of people did not expect dapi to be positive. We believe that the broad mechanism was going to be impactful on the T and B cells. We understand the area really well. We've worked very closely with UCB on the partnership, and we believe that the modality and the

target are very important. And so we were really delighted normally with the primary endpoint, but Paul, I want to call your attention to the fact that 50% reduction in severe flares, steroid sparing.

I mean these are the problems that these patients face every day and then really having that positive primary endpoint on BICLA, and this was a global trial. So I think that's the other piece. Do I think that we have a good chance of it replicating? Yes. We are working very hard before we -- actually, when we announced results within literally months, we were able to dose our first patient.

So we were already behind the scenes very bullish on it. That should tell you because we didn't lose any time in getting going on our second Phase III. Now the piece that I think we have appreciated over the past many years, and we've called in a lot of patients. We have patients who advise us on trial design, what matters to them as well as sort of we are on a lot of private public consortia and such for lupus. What's really become very clear is that only 20% of patients are treated today.

All modalities are important, very few biologics are available, and patients need more therapies. One of the key points that we've learned from our patient engagements is what patients tell each other. And they tell each other that this is heterogeneous, your lupus is not my lupus. And so we actually keep this in mind, and that is why we're so excited about dapi attacking from a B and T cell perspective, high upstream mechanism and then litifilimab going up after the sort of BDCA2 type 1 interferon signature. So I think that's what's making us really excited.

And you see that now we're in -- we are, I think, the only company -- the third product ever to have a Phase III positive is dapi. And then the only company with 2 programs with different mechanism of action in Phase III. It is competitive, but our teams are doing a fabulous job keeping us on track with enrollment and everything. And we'll have a readout with SLE in 2026. We put that up at JPMorgan about the fact that we expect to read out in '26.

Paul Matteis Analyst

Yes. Okay. Great. We only have a couple of minutes left. So I just want to try to cover felza and anything else to close.

But just as it relates to the H bio deal, there's data in IgAN, there's work going on in AMR and PMN. I think, again, like we think about what holds investors back from ascribing value of these assets. I think people have a hard time understanding like in what area is this the best drug, right? Or like which indication is the flagship indication? How would you answer the question about where you're most excited for this?

Priya Singhal Executive

I want to say that I actually am excited about all 3. And I'll tell you why. Because it's rare to have the same product with an established mechanism of action with 3 POCs simultaneously. That's what excited me personally a lot when we were doing the diligence. And I'll just give you some snapshots of the data that was so compelling and really made me an absolute believer.

One is the anti-CD38 in the specificity that felza has to protect sort of immune protection with going after the plasma cells that are releasing these autoantibodies. And in the AMR data, this is like a serious situation. They've got orphan disease designation. So they've got a lot of external validation, which is also very important and not to be, I think, minimized. I think it's very important.

And in Phase II, they saw 2 things that I don't think other products have shown. One is 9 doses over 5 months, resulting in a greater than 80% AMR resolution by biopsy at week 24, and then 20% for placebo. And 67% of responders remained resolved that 52 weeks. That's pretty compelling, published in NEJM, as you know. IgAN is an important area because it is competitive.

But this mechanism of action is unique. And I think that's the other piece that this is the only product that offers you that UPCR sort of reduction, which we know leads to durable EGFR stabilization. And importantly, you have durability out 18 months after the last dose out till 24 months. I mean, how important would that drug holiday, could that drug holiday be for patients? I think it should be pretty powerful.

And then finally, with [indiscernible] yes.

Paul Matteis Analyst

Is that the counterpoint to when investors, I think, make a table of these drugs and they just compare a percent change in proteinuria, like this doesn't rank at the top of the list. So is it more about the dosing holiday that got you comfortable with that or got you excited about this in [indiscernible]?

Priya Singhal Executive

Well, I think it's both. So I think it's 50% UPCR, 50% UPCR, that is important because I think they're all in that range. These are small studies, the variability that could be there. We know it's distinctive, right? So we know it heralds the EGFR outcome.

That's one good thing. I mean this is a wonderful space to be in because for once I find that the accelerated approval endpoints, surrogate endpoints are all established. So it's exciting. Number two, yes, the durability is pretty powerful, right? I mean think about it.

And in the future, I think there's also this potential of combinations and other things where we believe this is going to be a unique mechanism. So I think it's important with PMN also poised to start Phase III in '25. And I think that we observed rapid partial and complete immunologic responses in both newly diagnosed and relapsed patients. And as you know, as well as people who were on immunosuppressive therapy. And as you know, PMN is the largest cause of nephrotic syndrome.

I mean this is really high unmet need.

Paul Matteis Analyst

Yes. Yes. Okay. I am just looking at a couple of questions that came in because we only have a minute left. One asking for -- we'll see what we get Priya, but a comment on anything Sage,

right?

And then just any updates on development work with SPINRAZA and then we can close.

Priya Singhal Executive

Yes. I think Sage, I will just say that ZURZUVAE, I remain really excited. We see a lot of momentum in our launch in how patients and prescribers are responding to the option that ZURZUVAE offers women with PPD. So I think it's really been a wonderful story, and we have so many stories I could spend in the next hour. So that's what I'm going to comment on.

I think very excited teams continue to work very closely together on this launch, which we think is really important. On SPINRAZA, high dose, very excited. We've submitted both in Europe and the U.S. We're working through -- we'll soon be in that review period. We have a PDUFA date of September in the U.S.

So we remain on track for that. We think this is going to be very important. I mean I think that the data that we've seen is very compelling, and I'll draw us to the neurofilament data that we observed at day 64. We think this is really, really important. And coupled with the data that we've generated from RESPOND, which is post gene therapy and all of that, we think SPINRAZA remains a cornerstone for spinal muscular atrophy patients across all age groups.

And so we are very excited about what this does for SPINRAZA.

Paul Matteis Analyst

Great. All right. Well, we're 1 minute over. I want to be respectful of your time.

Priya Singhal Executive

Thank you, Paul.

Paul Matteis Analyst

Thank you, Priya. This was an awesome discussion. I think we covered a lot of interesting stuff. So I appreciate you joining us.

Priya Singhal Executive

Thank you for the great questions. Take care. Bye.