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REGN.OQ - Regeneron Roundtable gMG & C5 Complement Program

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OVERVIEW:

Company Summary

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PRESENTATION

Operator

Welcome to Regeneron's conference call to discuss its C5 Complement Development Program. My name is Shannon, and I will be your operator for today's call. (Operator Instructions) Please note that this conference call is being recorded. I will now turn the call over to Ryan Crowe, Senior Vice President, Investor Relations. You may begin.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Thank you, Shannon. Good morning, and welcome to our Regeneron Roundtable Investor Event, a series of presentations spotlighting key opportunities across Regeneron's pipeline. Today, we will focus on our C5 complement development program built around cemdisiran, an siRNA that targets C5, and pozelimab, an antibody that also targets C5.

Before we begin, I would 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. Now let's begin.

Regeneron has five key late-stage programs that are poised to deliver meaningful advances over the near, medium and long term across diverse therapeutic areas, including solid tumor oncology, myeloma, complement-mediated diseases, anticoagulation and obesity.

Additionally, our early-stage pipeline includes opportunity spanning inflammation and immunology, ophthalmology, cardiovascular metabolic disease and neurology. We anticipate featuring many of these programs in Regeneron Roundtables in the months and years ahead, reflecting the excitement we have for this next wave of innovation. We have used the Regeneron Roundtable series to provide focused program level deep dives on some of our most important late-stage development programs rather than trying to cover the entire pipeline in a single event.

Today's C5 roundtable follows the November 2025 Roundtable on the Factor XI development program for anticoagulation disorders and the December 2025 roundtable on the Lynozyfic development program in multiple myeloma and premalignant conditions. We believe these late-stage programs are all poised to deliver meaningful advances over the next few years, bringing value to both patients and shareholders.

Today's roundtable will cover our C5 development program and in particular, how cemdisiran and pozelimab can be utilized to treat multiple complement-mediated diseases by matching the right therapeutic approach to disease biology with the goal of optimizing efficacy while mitigating safety events and proximal nocturnal hemoglobinuria or PNH, the combination of cemdisiran and pozelimab is designed to deliver rapid, complete and uninterrupted C5 inhibition addressing persistent hemolysis associated with current standards of care.

Registrational data in PNH is expected in late 2026. In generalized myasthenia gravis, or gMG, the disease biology supports only partial C5 inhibition that can be achieved with some Cemdisiran monotherapy. We recently submitted an NDA taking approval from the FDA using a priority review voucher and expect a decision in the fourth quarter. And in geographic atrophy, we're exploring both monotherapy and combination approaches with initial Phase 3 lead-in data anticipated late this year.

Taken together, this program highlights the flexibility of our siRNA antibody approach and positions our C5 franchise for multiple meaningful near-term clinical and regulatory catalysts. Now let me introduce our speakers and the topics they will discuss during today's roundtable. This cross functional speaker panel consists of leaders across Regeneron's research, clinical development and commercial areas. First, Dr. George Yancopoulos, Regeneron's Board Co-Chair, President and Chief Scientific Officer, will provide a strategic overview of the C5 program including our siRNA with or without an antibody approach and how we believe it offers different levels of complement inhibition for different diseases.

Next, Dr. Andres Sirulnik, Senior Vice President and Clinical Development Unit Head for Hematology will discuss the ongoing PNH and geographic atrophy development programs, which are both in late-stage clinical development. Following Andreas will be Dr. Umesh Chaudhari, Vice President and Global Program Head of our C5 program, who will discuss generalized myasthenia gravis, where cemdisiran monotherapy has demonstrated robust efficacy with quarterly dosing, supporting a differentiated clinical and convenience profile. This follows yesterday's publication of results in the land set and data presentation at the American Academy of Neurology for positive Phase 3 NIMBLE results were presented for the first time.

And finally, Soma Gupta, Vice President, Commercial New Products, will lead the discussion on the commercial strategy and outlook focusing primarily on the upcoming potential of cemdisiran launch in gMG. We will then use the remaining time for Q&A. With that, let me now turn the call over to George.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

Thank you, Ryan. Our pioneering C5 program is the first time an antibody and an siRNA that target a single pathway have been combined, in this case, to inhibit complement. Pozelimab, a fully human antibody, which was derived using our VelocImmune technology was FDA approved in 2023 for the treatment of Chaple disease, an ultrarare indication. Cemdisiran is an siRNA designed and initially developed with our collaborator, Alnylam. Regeneron has licensed and distant for use as both a monotherapy and in combination with pozelimab.

Each of these reagents serves a different role in inhibiting complement. Cemdisiran reduces C5 production in the liver, where the majority of C5 is synthesized while pozelimab neutralizes any residual C5 protein in the circulation that was not already blocked by cemdisiran. This combination completely blocks the C5 pathway. There are several advantages to this dual approach compared to other complement inhibiting therapies.

First, having the two reagents gives us the flexibility to treat different diseases that require different levels of targeted inhibition to maximize efficacy. We also have data suggest that the combination approach will provide complete rapid and durable C5 inhibition that is not achievable with other therapies even at higher doses.

Additionally, our antibody plus siRNA combination may enable lower antibody dosing in a highly convenient subcutaneous formulation. We believe these advantages will be critical across these distinct diseases. Our C5 program's flexibility is reflected in the range of therapeutic areas and indications that we are pursuing because complemented media diseases require different levels of C5 inhibition, we can tailor the dose and the modality, siRNA alone, antibody alone or combination based on the disease biology and clinical need.

Chaple disease is an ultra-rare, life-threatening pediatric disease caused by CD55 deficiency, where pozelimab monotherapy at high dose has demonstrated clear clinical benefit.

In PNH, we believe that disease biology requires near complete uninterrupted C5 inhibition to prevent breakthrough hemolysis. The combination of the cemdisiran siRNA and the pozelimab antibody enabled deeper and more durable control of C5 ravulizumab, a leading C5 antibody on its own, supporting our dual mechanism approach.

In generalized myasthenia gravis, we have now demonstrated that robust and sustained efficacy can be achieved with only partial complement inhibition using cemdisiran monotherapy, which delivered strong clinical benefit in this disease, while preserving residual complement activity, supporting a potential best-in-class efficacy and safety balance with quarterly subcutaneous dosing.

In geographic atrophy, the biology and optimum level of complement suppression is still being explored. Thus, we are evaluating both cemdisiran monotherapy and the cemdisiran/pozelimab combination to identify the right balance of efficacy and safety in a large heterogeneous population. The key takeaway is that this is not a one-size-fit-all C5 program. We believe the flexibility of having an siRNA and an antibody allows us to match the treatment intensity to disease biology, creating a pipeline and a product opportunity across multiple disease settings.

Slide 10 illustrates the difference in C5 inhibition between cemdisiran monotherapy and the cemdisiran/pozelimab combination as well as why different complemented median diseases may require different levels of C5 inhibition to achieve optimal clinical benefit. The CS50 graph on the left was presented yesterday at AAN from the cemdisiran Phase 3 NIMBLE trial in generalized myasthenia gravis.

Cemdisiran monotherapy delivered rapid and durable complement inhibition, which reached 77% by week 24, but was sufficient to drive robust clinical efficacy in generalized myasthenia gravis. The combination of cemdisiran and pozelimab achieved near complete C5 inhibition as early as week 12. That's important in diseases like PNH that require near complete uninterrupted C5 inhibition, which is where the siRNA and antibody combination becomes critical.

In contrast, efficacy in generalized myasthenia gravis was achieved without full complement inhibition, supporting the concept of preserving residual complement activity may be both effective and potentially favorable from a safety perspective. This precision-based approach underpins our strategy, match the right level of C5 suppression to the biology of each disease rather than forcing a one-size-fit-all solution. Now I will turn it over to Andres to discuss PNH and geographic atrophy.

Andres Sirulnik - Regeneron Pharmaceuticals Inc - Senior Vice President, Clinical Development Unit Head, Hematology

Thank you, George. Paroxysmal nocturnal hemoglobinuria or PNH is an acquired life-threatening hematologic disorder driven by uncontrolled C5 activation due to loss of CD55, CD59 on red blood cells, resulting in chronic intravascular hemolysis, thrombosis and substantial morbidity. Current standard of care therapies improved survival but often fail to fully normalize ADH or prevent breakthrough hemolysis and patients with extravascular hemolysis remain inadequately served by existing C5 inhibitors or require a complex multidrug regimens.

The PNH landscape now spans multiple mechanisms, including inhibitors for complement Factor 5 Factor 3, Factor B and Factor D, yet no current approach consistently delivers complete sustained terminal complement inhibition with convenient dosing highlighting an opportunity for differentiation.

The cemdisiran/pozelimab combination is designed to address these gaps by reducing C5 production in the liver with cemdisiran and blocking residuals circulating C5 with pozelimab, thereby enabling continuous durable C5 separation with subcutaneous dosing.

The Phase 3 leading data, which I will review shortly, suggests this dual mechanism approach is needed to achieve potentially best-in-class disease control and improve on current standards of care.

Slide 13 is the trial design for the ongoing Phase 3 ACCESS-1 trial in PNH patients. This head-to-head study directly compares cemdisiran plus pozelimab against ravulizumab in cohort A and eculizumab in the registrational cohort B, enabling a rigorous assessment of disease control versus established C5 inhibitors that are considered today's standard of care for PNH. We are announcing today that enrollment in cohort B is complete, positioning the program for a registration-enabling data readout by the end of this year.

Taken together, the Phase 3 design, comparator choice and endpoint selection are intended to demonstrate that cemdisiran plus pozelimab can deliver more complete and consistent disease control than current standards of care, supporting best-in-class potential in PNH.

As a reminder, the exploratory cohort A from the registrational PNH trial read out in late 2024, supporting the combination's potential in this setting. Now let's take a look at the results of cohort A. Slide 15 showcases the 26-week data generated from this exploratory cohort. Patients treated with our C5 combination achieved greater disease control compared to the current standard of care, ravulizumab and nearly all patients on the cemdisiran pluz pozelimab combination were able to achieve normal LDH levels.

Through week 26, cemdisiran plus pozelimab combo leads to average LDH levels of 0.8 below the upper limit of normal with 96% of patients maintaining adequate control of hemolysis. This compares favorably to ravulizumab with average LDH levels of 1.2 times the upper limit of normal at week 26, with 80% of patients maintaining adequate control of hemolysis.

Patients on ravulizumab were then switched to the cemdisiran/pozelimab combination in the extension study. At the start of the extension study, 13 out of 19 patients treated with ravulizumab had adequate control of LDH. After switching to the combo, all but one patient achieved LDH control, including four of five patients who had failed to achieve LDH control while on ravulizumab.

Our novel cemdisiran/pozelimab approach enable complete rapid and interrupted and durable inhibition of terminal complement. And as I mentioned before, enrollment in cohort B is complete, and we now anticipate reporting data from this registration cohort in the fourth quarter of this year.

And Regeneron is still pursuing additional agents for PNH patients given the high unmet need. We recently initiated a first-in-human study of our siRNA targeting complement Factor B initially intended for 20% to 30% of patients who remain anemic despite optimal C5 therapy due to extravascular hemolysis with the potential to expand to a broader PNH population. We hope to share data from this ongoing program in the near future.

And now to geographic atrophy, starting on slide 19. Geographic atrophy is a late-stage irreversible form of dry age-related macular degeneration that leads to progressive vision loss and has a meaningful impact on daily functioning, including reading, driving and recognizing faces. A substantial body of evidence implicates the complement system in GA pathogenesis, including genetic associations, histopathology and preclinical studies validated further by the fact that both approved GA therapies locally inhibit complement.

However, despite two approved products, there remains significant unmet need in geographic atrophy as these approved therapies have slow lesion growth, but have not prospectively demonstrated preservation or improvement of visual function.

Also, current intravitreal therapies require frequent intravitreal injections and carry meaningful ocular safety risks. Cemdisiran plus pozelimab is being evaluated as a differentiated systemic approach with the goal of delivering meaningful disease modification while potentially avoiding the ocular safety issues associated with the intravitreal administration.

Slide 20 depicts the trial design of the ongoing Phase 3 GA trial, which is a global randomized, double-mask placebo-controlled study in patients with GA secondary to AMD that will evaluate whether systemic C5 inhibition can deliver a meaningful disease-modifying effect while potentially avoiding ocular safety issues seen with intravitreal approaches.

For this study, there will be a total of approximately 975 patients in the trial, which is designed as a seamless two-cohort program similar to how we structure the Phase 3 PNH program. While Regeneron has not previously generated clinical data in this indication, we have decided to go straight to a Phase 3 program given our deep understanding of disease biology and data generated in other complement mediated diseases.

As we have previously stated, cohort A is fully enrolled, and we expect interim data in the fourth quarter of 2026. These results from approximately 225 patient cohorts will guide with a systemic C5 inhibition demonstrates sufficient therapeutic effect in GA, whether monotherapy sufficient or combination therapies required and will inform future trial design parameters. Note, the cohort A is not powered for statistical significance and is not a regulatory readout but rather reserves as a decision enabling checkpoint.

Systemic C5 inhibition offers a fundamentally different treatment paradigm compared to today's treatment options. Regeneron's approach moves beyond intravitreal only therapy by enabling systemic administration, which may allow treatment of bilateral disease without separate injections in each eye, addressing a key burden of current GA care.

Approved GA agents will require every month or every other month intravital injections often in both eyes, a systemic subcutaneous option with meaningfully reduced procedural burden for patients and retina specialists, especially for those patients who may be co-treated with anti-VEGF therapies.

In terms of safety, current intravitreal therapies have reported ocular safety events, including occlusive retinal vasculitis, which has caused catastrophic blindness in some patients. The systemic approach is anticipated to reduce localized ocular risk, representing a potentially important safety advantage. We also have an opportunity to go beyond slowing of lesions growth and prospectively demonstrate a functional benefit.

Regeneron's program aims to show greater reduction in GA lesion growth alongside preservation of visual function, raising the bar on meaningful clinical outcomes. Further, today's therapies require frequent in-office administration by retinal specialists.

Regeneron's approach introduces the potential to self-administration via subcutaneous dosing, reducing clinic visits and improving patients' quality of life. The C5 program leverages with Regeneron's deep experience with complement inhibition and established ophthalmology presence, positioning us to pursue a differentiated scalable opportunity in a large and growing GA market.

In parallel, Regeneron has also initiated development of an intravitreal pozelimab formulation aimed at longer durability, potential safety advantage from a nonpegylated reagent and potential to co- formulate with anti-VEGF therapy, providing strategic flexibility across patient segments.

Now I will turn it over to Umesh our Global Clinical Head of C5, who will discuss generalized myasthenia gravis.

Umesh Chaudhari - Regeneron Pharmaceuticals Inc - Vice President Global Program Head (C5)

Thanks, Andres. First, let me give a bit of background on generalized myasthenia gravis, starting on slide 23. gMG is a rare chronic autoimmune disease where pathogenic autoantibodies, most commonly against the acetylcholine receptor activate the complement cascade, leading to a formation of the membrane attack complex at the neuromuscular junction. This complement mediate injury disrupts the neuromuscular transmission, damages postsynaptic membrane and ultimately drives the muscle weakness and fatigue that characterize this disease. Importantly, this is not simply an antibody-mediated signaling issue, it is a complement-driven structural injury, which is why inhibiting C5 has proven clinically effective.

Despite advances in treatment, there remains a clear unmet need. Many patients experience incomplete, fluctuating responses waning between doses, safety trade-offs and high treatment burden, particularly with chronic IV or frequent dosing regimens. Our goal with cemdisiran is to address this by delivering sustained targeted C5 inhibition that aligns with gMG biology, providing rapid efficacy, durable disease control and meaningfully reduce treatment burden.

Slide 24 outlines the Phase 3 NIMBLE trial, which was designed to evaluate cemdisiran and cemdisiran plus pozelimab combination in patients with symptomatic generalized myasthenia gravis. NIMBLE is a randomized, double-blind, placebo-controlled study, enrolling acetylcholine receptor positive patients on stable background therapy who have initiated meningococcal vaccination reflecting real-world clinical practice.

This study includes a 24-week placebo-controlled double-blind period, which is the basis for the primary and key secondary efficacy analysis, followed by a 28-week double blind extension and open-label treatment period and then long-term post-treatment follow-up.

The primary endpoint is the change from baseline in myasthenia gravis activities of daily living, or MG-ADL total score at week 24 and with a key secondary endpoint of change in quantitative myasthenia gravis or QMG total score at week 24. During the 24-week double-blind treatment period, all patients -- all treatments were administered subcutaneously with cemdisiran dosed every 12 weeks, highlighting the convenience of a quarterly regimen.

As shown in the efficacy data presented subsequently, cemdisiran monotherapy met the primary and all key secondary endpoints, demonstrating rapid, deep and durable clinical benefit without weaning across the dosing interval.

Now let's describe the results from this registrational study. With this -- with quarterly subcutaneous dosing, cemdisiran met the primary end point delivering a 2.3 point placebo-adjusted improvement in the MG-ADL total score at week 24, which is clinically meaningful and statistically significant. The magnitude of benefit compares favorably to historical C5 inhibitor data, which have generally shown 1.6 to 2.1 placebo-adjusted MG-ADL improvements in their respective pivotal studies at similar time points.

Importantly, efficacy emerge rapidly with clinically meaningful improvements seen as early as week two continue to deepen over time and was sustained without any evidence of waning across the full dosing interval. The key secondary endpoint, QMG, was also met with a 2.8 placebo-adjusted improvement, reinforcing the consistency between patient-reported and physician-assessed outcomes.

While the combination arm also met the primary and key secondary endpoints, it did not provide additional benefit over cemdisiran monotherapy in gMG, demonstrating that complete complement blockade is not required to achieve robust clinical benefit in gMG. Taken together, these data suggest that cemdisiran delivers rapid, deep and durable efficacy with markedly reduced treatment burden, positioning it as a best in -- potentially best-in-class C5 targeted therapy for patients with gMG.

Safety also appears to be a differentiating factor for cemdisiran in this indication. Overall, safety profile was favorable and consistent with expectations for the C5 class with no new or unexpected safety signals observed across treatment arms. Cemdisiran monotherapy was generally well tolerated with no serious infections, no meningococcal infections and no treatment discontinuations during the 24-week double-blind period.

Rates of adverse events, serious adverse events and severe adverse events were numerically lower with cemdisiran versus placebo and combination therapy, supporting the safety of partial C5 inhibition in gMG.

It is also worth noting that only 1% of patients in the cemdisiran cohort experienced the adverse event of myasthenia gravis compared to 17% of patients randomized to placebo, further reiterating the treatment of effect of cemdisiran in this setting. Taken together, these data support a differentiated benefit risk profile, pairing strong efficacy with a generally manageable safety profile suitable for chronic use.

Slide 27 summarizes what we believe is a clearly differentiated clinical profile for cemdisiran in generalized myasthenia gravis. From an efficacy standpoint, cemdisiran delivered clinically meaningful improvements within the first two weeks with depth of response that compares favorably within the C5 class and remains durable across the full dosing interval.

Importantly, that efficacy is sustained without waning, supporting a quarterly dosing regimen that meaningfully reduces treatment burden for patients managing a chronic disease. From a patient experience perspective, subcutaneous administration and infrequent dosing differentiates cemdisiran from both IV-based C5 inhibitors and more frequent cyclic daily or weekly options.

On safety, through 24 weeks, cemdisiran demonstrated a generally manageable profile with no treatment discontinuations, no serious infections and lower rates of severe adverse events relative to placebo.

Taken together, these attributes position cemdisiran as a differentiated potential advanced therapy option, balancing strong clinical performance with convenience that is highly relevant in real-world gMG management.

This slide highlights how cemdisiran differentiates within the C5 class, specifically, compared cross-trial to ULTOMORIS an infused C5 inhibitor. Cemdisiran achieved rapid, deep 2.3-point placebo-adjusted MG-ADL improvement with only two subcutaneous injections over a 24-week treatment period. ULTOMORIS requires four infusions over a 26-week treatment period and demonstrated a 1.6-point placebo adjusted MG-ADL improvement. We believe cemdisiran has the potential to offer a best-in-class profile, combining strong sustained efficacy with a substantially reduced treatment burden through convenient, quarterly subcutaneous dosing.

Now compared cross-trial to Viyvgart, the leading FcRn inhibitor, which have grown the advanced therapy market for gMG, we believe cemdisiran can offer a differentiated clinical profile. A key distinction is durability as cemdisiran maintains efficacy throughout the dosing interval without the cyclic waning of efficacy that can be seen with Vyvgart and the other FcRn-based approaches.

Unlike Vyvgart, which is dosed cyclically, cemdisiran provides deep and continuous improvement in MG-ADL scores with only two injections over 24 weeks. That durability enables quarterly subcutaneous dosing, which meaningfully reduces treatment burden compared with frequent cyclic administration schedules. This is particularly relevant in a chronic disease like gMG where patients require sustained symptom control rather than episodic relief.

And finally, slide 31 highlights how cemdisiran differentiates relative to the newly approved B-cell depleting agent, particularly in speed of response and durability. From an efficacy standpoint, cemdisiran delivers rapid placebo-adjusted improvements in MG-ADL, with clinically meaningful benefit observed within weeks rather than months.

Also, the mechanism matters. By directly targeting complement mediated damage at the neuromuscular junction, cemdisiran provides symptom control without relying on broad immune cell depletion. While B-cell depleters may offer a potentially longer dosing interval, that does come with prolonged IV infusions that require premedication and post-infusion monitoring requirements.

In summary, the gMG market is very competitive, and we believe cemdisiran has the potential to offer a differentiated alternative to currently approved advanced therapies with strong efficacy, generally manageable safety and quarterly subcutaneous dosing.

With that, let me turn the call over to Soma, who will now discuss the commercial opportunity.

Soma Gupta - Regeneron Pharmaceuticals Inc - Vice President Commercial New Products

Thanks, Umesh. We believe our C5 program represents a late-stage multi-indication, multibillion-dollar opportunity, spanning gMG, PNH and GA. Today, these markets combined generate about $9 billion in annual globalized sales and continues to grow rapidly, supported by strong underlying prevalence dynamics. gMG represents the first and largest near-term opportunity with an FDA decision and potential product launch in the fourth quarter of 2026.

As Umesh has highlighted, we believe cemdisiran's clinical profile, including quarterly subcutaneous dosing and strong efficacy, has the potential to position it competitively in the rapidly expanding advanced therapy market.

PNH represents another potential large commercial opportunity with current annual worldwide sales of around $3 billion. The cemdisiran and pozelimab combination targets patients who require complete and uninterrupted C5 inhibition, offering a differentiated option versus the standards of care. And then rounding it out, geographic atrophy provides the largest population with over 1 million diagnosed patients in the U.S. alone. Currently approved agents have started to build this space, delivering just over $1 billion in annual worldwide sales today, reflecting the early stages of disease modifying agent adoption.

A systemic approach could differentiate meaningfully here versus chronic intravitreal injections if efficacy can be demonstrated. Two important commercial considerations for our C5 commercial strategy I'd like to highlight. First, Regeneron are solely responsible for development, manufacturing and commercialization for cemdisiran monotherapy as well as for the combination and pay modest royalties on net sales to Alnylam. Secondly, our commercialization strategy is highly indication-specific, allowing us to optimize value and access in each market, independently which allows us to align pricing and access to the underlying disease biology, market size and competitive dynamics.

We believe this C5 franchise presents a long-term growth opportunity for Regeneron given this derisk program, multiple shots on goal and staggering launches.

Now let me focus on the near-term gMG commercial launch and strategy. The gMG market is undergoing a structural shift driven by rapid adoption of advanced therapies as treatment goals move beyond symptom control towards durable disease modification. Advanced therapy penetration is relatively low today at just 15%, but is expected to grow materially closer to 40% over time, creating a multiyear growth category. Both FcRn inhibitors and C5 targeting agents are expected to account for the majority of incremental sales as patients cycle through earlier lines of therapy more quickly.

Despite increasing competition, the market is expanding faster with total US gMG net sales expected to more than double over the next several years to over $12 billion in annual net sales by 2032, supported by newly approved agents, higher treatment rates and longer durations of use.

Cemdisiran is expected to enter this market at an inflection point as the first siRNA in gMG offering a differentiated mechanism quarterly dosing and a profile well aligned with physician and patient preferences for durability and convenience. Importantly, this expansion in the use of advanced therapies broadens the treated population, potentially allowing differentiated agents to succeed without having to displace incumbents.

Our objective with cemdisiran in gMG is very clear. We plan to position cemdisiran as a differentiated and convenient targeted therapy for gMG patients. Cemdisiran represents a first-in-class siRNA approach targeting C5. This will require education to ensure stakeholders understand how this differs mechanistically from antibodies, FcRn inhibitors and B cell depleters. To establish cemdisiran in this market, we look to drive adoption by leading with cemdisiran potential best-in-class clinical profile highlighted by its efficacy, safety as well as dosing convenience.

The Phase 3 data show rapid, durable symptom improvement with no waning between doses, which clearly differentiates cemdisiran for cyclic or infusion-based therapies. Just as importantly, quarterly subcutaneous dosing meaningfully reduces treatment burden with potential to improve predictability and adherence for patients living with a chronic neurological disease.

As we move into launch optimization, the focus shifts to maximizing long-term adoption and value. We are actively working to evolve from HCP administered vials to patient self-administration, further reducing treatment burden and improving persistence. We also plan to expand beyond the US into key international markets where the combination of strong efficacy and quarterly subcutaneous dosing is also viewed as highly differentiated there. As the use of advanced therapies for gMG expands, self-administration options are introduced, and we expand into additional geographies, cemdisiran is poised for sustained growth.

Now I will turn it back to George for closing comments.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

Thanks, Soma. Let me briefly summarize this roundtable discussion. C5 program is not a single asset story, it's a differentiated pipeline and a product opportunity with blockbuster potential. Cemdisiran used either alone or in combination with pozelimab enables different levels of C5 inhibition, depending on how much complement suppression each disease requires.

We've shown that partial C5 inhibition is sufficient and optimal in generalized myasthenia grabs while complete uninterrupted blockade is required in diseases like PNH. That flexibility is the core advantage of our siRNA and antibody approach.

Moreover, while our C5 program has achieved clinical validation in its two leading indications, we expect to generate proof-of-concept data later this year in geographic atrophy, potentially derisking yet another significant commercial opportunity for complement mediated disease with significant unmet need.

In summary, with near-term pivotal data and planned upcoming launches, we believe the C5 program represents an undepreciated opportunity for long-term growth, not currently reflected in Regeneron's valuations. And with that, let me turn it back to Ryan.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Thanks, George. This concludes our prepared remarks. Thank you for your attention. We will now open the call for Q&A. (Event Instructions) Shannon, can we please go to the first question?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Evan Seigerman, BMO Capital Markets.

Evan Seigerman - Bank of Montreal - Analyst

Hi, guys. Thank you so much for taking my question. Really appreciate you doing this. So regarding the geographic atrophy opportunity, can you walk me through some of the rationale why you think your approach will be better than the currently available assets? I know that there's limitations and most physicians are not thrilled with those. I'd love to know how you think you can improve on those given that this is a pretty tough indication? Thank you.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

Well, in one case, in terms of being better, our studies are powered to pick up a potential functional benefit, which the other studies did not actually pick up. But our major advantage is going to align in the setting of both convenience and safety, as we outlined. Right now, patients often suffer from bilateral disease. And as you probably know, treatment often triggers a requirement for anti-VEGF therapy as the patients progress from dry AMD to wet AMD. So the treatment burden is very substantial for many of these patients with bilateral injections targeting complement as well as additional injections for their wet AMD.

What we hope to be doing here is using a subcutaneous systemic treatment approach that will dramatically decrease the treatment burden. It will allow simultaneous bilateral treatment from the systemic approach. And if the patients then require anti-VEGF therapies, those will be the only intravitreal injections they'll need. They won't need to also be continuing their C5 injections.

We also mentioned, of course, that we do have a follow-on intravitreal approach where we're developing a co-formulated form of what we hope to be a long-acting antibody combined with our long-acting anti-VEGF agent, which would be a completely independent way of addressing the profound treatment burden that these patients suffer from, the need to have these simultaneous treatment approaches going.

And so these will be two important separate distinct opportunities that could dramatically address the biggest problem that these patients suffer from, which is the treatment burden and also obviously, the safety consideration with the occlusive vasculitis that unfortunately is seen with the current intravitreally administered agents. We would expect not to see that obviously, either with our systemic approach or with our dual antibody+EYLEA approach.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Thanks, George. Let's move to the next question, please.

Operator

Alexandria Hammond, Wolfe Research.

Alexandria Hammond - Wolfe Research LLC - Equity Analyst

Thanks for taking the question. So what does the path forward look like for moving from the subcu administration and the clinic all the way to that self-administration option, such as I'm assuming with an on-body injector at home without a health care professional? Thank you.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

Soma, would you like to take that?

Soma Gupta - Regeneron Pharmaceuticals Inc - Vice President Commercial New Products

Sure. Happy to take it. So we believe that the auto-injector will be an important -- self-administration option will be important for patients. However, as we start, we actually think that the currently C5 are given as infusion therapies, and this is going to be a subcu in the office every three-month administration, which aligns with those schedules that patients visit anyway. Many patients visit anyway.

So we've heard that this is not going to be a barrier out of the gate. But ultimately, this was really a launch sequence that was designed to avoid delaying entry while still enabling a convenience step up post launch.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

I'd just add that the timing for the self-administration option is going to be largely dependent on upcoming regulatory interactions, and we'll certainly keep you informed as those evolve over time.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

But certainly, having a subcutaneous treatment regimen every three months, which as Soma said, is aligned with patients visits to their physicians is a substantial difference compared to the much more regular large volume infusion having to visit often infusion centers and so forth that these patients have or even the weekly infusions that some patients have with some of these therapies.

So obviously, we think it's a very differentiated approach that offers, of course, two important features. One is dramatic decrease in the treatment burden; two is potentially best efficacy in class, but also an efficacy that is very rapid and durable and sustained without cyclical variations. So we believe that it offers a very advantageous profile for patients and physicians to consider from the convenience but also from the treatment benefit side.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Okay, let's move to the next question, please.

Operator

Chris Raymond, Raymond James.

Chris Raymond - Raymond James - Analyst

Hey, yes, thanks. Just a question maybe from slide 10. Kind of intriguing, the phenomenon you're seeing that the different diseases may require different amounts of complement inhibition, I think that's pretty interesting. Do you have any plans to maybe more systematically study the biology behind this phenomenon? Or do you think you'll maybe just gradually learn what amount of complement inhibition is needed as you run these trials?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

We agree. This is a fascinating scientific question. We are honestly interested in trying to understand it. But as you said, the very first step is to just define how much inhibition you need in the various diseases. We have to admit that although we did the study, as shown on this slide, that showed partial inhibition compared to complete inhibition, that partial inhibition was if anything, at least as good, if not better, was very surprising to us and I think to the entire field.

It really opens up a whole new set of questions, which you're highlighting, and I think it's going to be something that we're all going to be very interested in studying. But the implications obviously are huge from the safety perspective.

Obviously, in a disease where patients have risk of breakthrough hemolysis, thrombosis and death and so forth, such as in PNH, you really want to do what's best to prevent those really bad outcomes in those patients. And there, we believe you do need the complete C5 inhibition that the combination affords.

But in myasthenia gravis, the opportunity to be actually seeing, if anything, better efficacy with less complete blockade really raises the possibility that these patients will have a much more favorable infectious risk profile. Now we did see it that in the small study when you compare the adverse events, but we're going to do additional follow-up studies to follow up and see whether that really can hold up to further scrutiny. But that would be a huge advance for the field and for patients.

All the other therapies are much more substantially immunosuppressive. We've seen now even with the FcRn therapies that they can be associated with serious reactivation and even fatal infections from EBV. We all know about complete inhibition with C5 leading to meningococcal infections and so forth. So this offers a very important different opportunity from the potential safety perspective. But as you said, it's a fascinating scientific question.

We did not predict this. And it certainly is a question of when. I think the whole field is now going to be very interested in following up.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Okay, thanks, George. Let's move to the next question, please.

Operator

Mohit Bansal, Wells Fargo.

Mohit Bansal - Wells Fargo Securities LLC - Analyst

Hello, can you hear me?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

Yes, Mohit.

Mohit Bansal - Wells Fargo Securities LLC - Analyst
So yes, very much -- and I want to double click on the geographic atrophy strategy a little bit. So I mean that systemic administration and whether or not it does cross the blood retinabarrier. And then the C5 that goes in, would it have similar or more benefit than the intravitreal C5. So how do you see that? Do you see the C5 as the bar? Or do you think a benefit in visual equity would also bewill also be need to be seen here for you to move forward here?

Thank you.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

We're really sorry the reception on your call was not very good, so we couldn't get the whole question. But certainly, it seems as if, by blocking C5 where it is made, there is very little actually almost no evidence that C5 is made anywhere other than the liver. It does not appear to be made in the eye. So blocking it at its site of production if it anything likely be more effective than trying to block it at the very last point in the eye. That said, we think that our major advantage will not necessarily be in further slowing down the progression of the disease.

But because we have larger studies planned and ongoing that we will actually be able to show a functional benefit that was not shown in the other programs. But the first hope in our first study is merely to show a very similar rate of slowing of geographic atrophy with the differentiated and potentially better and potentially safer certainly from the local injection safety perspective of the systemic approach.

And that should offer, assuming it's a well-tolerated and safe systemic approach, a huge benefit to patients. Many of these patients are not taking this treatment. There's -- even though there's over 1 million patients in the United States who could be eligible for this treatment, there is very slight penetration into this market probably on the order of 1% or so.

Most patients are not taking these therapies, why because they require injections directly into the eye, multiple injections, even trigger anti-VEGF injections on top of that and the injections themselves can actually cause catastrophic immediate blindness in rare cases because they cause occlusive vasculitis.

So the problem is there is a treatment approach that can help these patients. It's just not widely used because of the treatment burden and the safety risk of the intravascular injections. We hope to open up this entire field and all these patients for a much more convenient treatment approach and allow many more of them to undergo an approach that could slow or prevent progression of their geographic atrophy disease.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Okay, thanks, George. Let's move to the next question, please, Shannon.

Operator

Salveen Richter, Goldman Sachs.

Unidentified Participant 1

Hey, good morning. Thanks for taking our question. This is Elizabeth on for Salveen. We wanted to get your thoughts on targeting C5 specifically in GA and why inhibition at C5 is optimal within the complement cascade for this disease versus upstream or potentially downstream? Thank you.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

Well, so far, approach is targeting either C3 or C5 have been shown to be similarly effective. There's no evidence to suggest that going higher up would be more effective. Of course, going higher up blocks more of the pathway and has higher risks in terms of infections and so forth associated with it. And so we thought that the C5 approach has the opportunity to have as good efficacy and potentially better safety once again.

Once again, we have in our pipeline other programs to both address other targets, both in the complement pathway, but elsewhere in this entire pathway as well in the upcoming years that we may be able to bring forth as well. But right now, we thought that the C5 was the best known and available target from the safety and efficacy perspective and that we had this differentiated approach that could make the treatment much more convenient and hopefully safer for the patients.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Okay, let's move to the next question, please.

Operator

Geoff Meacham, Citi.

Unidentified Participant 2

Hey, good morning. This is Nishant on for Geoff. On G&G, given the competitive treatment landscape, at launch, do you expect uptake to be driven more by switching from existing C5 or by new starts that might otherwise have gone to and how should we think about that mix evolving over time? Thank you.

Soma Gupta - Regeneron Pharmaceuticals Inc - Vice President Commercial New Products

Yes. So we're very -- we're excited about what we think this differentiated profile can do and potential best-in-class efficacy, dosing convenience, we think it will position as a very differentiated advanced therapy in the space. But the launch is really expected to capture a mix of switch and new patient starts. And the plan is really to compete for both because we think that there's certainly people who are on certain things, whether they're on infusions, whether they're on these cyclical based therapies and we think they are perfect candidates for switch.

But also, there's so many patients coming into this advanced therapy filter that are going to look for new agents that we think there's also a really good opportunity for new patient starts. So we think it's going to be a little bit of both, but not to underestimate the competition, it's a competitive space. It will take time. And so we do expect that as well.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Thanks so much. Shannon, we have time for two more questions, please.

Operator

William Pickering, Bernstein.

William Pickering - Sanford C Bernstein & Co LLC - Analyst

Hi. Thank you for taking my question. So in geographic atrophy, what read-through do you see from the fail Soliris trial, given that it's also a C5 inhibitor? And could you comment on why you initiated the intravitreal pozelimab trial? Thanks.

Andres Sirulnik - Regeneron Pharmaceuticals Inc - Senior Vice President, Clinical Development Unit Head, Hematology

Hi, this is Andres. So when you look at the Complete study, I think it's important to understand that this was an investigator-initiated study relatively small study. I mean this is 30 patients randomized 2:1. And there are a few, I think, points that are important. One is eculizimab, which was used in that particular study was dosed at 900 milligrams, which compared with our approach does not provide full suppression of terminal complement activity.

I think that that is an important point that we should bear in mind. And also the way the study was designed with a very small number of patients looking at a large magnitude of an effect. Now we have a better understanding of what to look for. And when we are looking at our particular study with a larger number of patients, and I want to remind you that we are planning to do an interim analysis with approximately [225] patients, we are looking for a 20% treatment effect, which is commensurate with what we have observed with IVT infusions. So I think that there were early days when the Cmplete study was performed.

And I'm not sure that had the best and enough power to really detect a significant improvement at that point.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, Director

Yes. I mean let's just emphasize what Andres said. We are not expecting to get a bigger slowing than the intravitreal agents. We're just expecting to do it in a much more convenient and safer manner. That slowing is about 20%.

A 30-patient study was -- had an 80% power to pick up a 75% slowing. So obviously, with 30 patients, you would not have seen a 20% signal. So you have to just ignore that study. It's like it was not done, plus it was done with an inferior agent. So of course, we would not be taking a study that has no informative value at all into account into our thinking because it literally taught us or the world nothing except maybe it misinforms some people who aren't paying very close attention.

Andres Sirulnik - Regeneron Pharmaceuticals Inc - Senior Vice President, Clinical Development Unit Head, Hematology

And you asked a question about the IVT formulation. Why are we doing that? I think that one important component is the fact that we recognize that maybe potentially one may need reduction of C5 or complement activity locally. So we understand that, that might be necessary. But I think what is important is our approach.

And the approach that we are taking is a co-formulation with anti-VEGF because as you probably know, the -- when you treat we complement, you may actually worsen the situations with wet AMD and so forth. So that is one important approach. the other is that our antibody will not be pegylated, which has been potentially associated or speculated that is what induces the complications, the ocular complications with intravitreal administration. So we recognize that we have multiple short-term goal.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

Okay, thanks, Andres and George. Let's move to the last question, Shannon.

Operator

Tyler Van Buren, TD Cowen.

Unidentified Participant 3

Hi, this is Sam on for Tyler from TD Cowen. Thanks for hosting this roundtables are very helpful. So just one question from us on the Phase 3 PNH pivotal data later this year. What are your expectations for the performance of the control arm? And what does poze/cemdi to achieve to reach statistical significance on percent change in LDH?

And then maybe what does it need to show to be viewed as having best-in-class efficacy?

Andres Sirulnik - Regeneron Pharmaceuticals Inc - Senior Vice President, Clinical Development Unit Head, Hematology

I think that the data that give us confidence on the outcomes of the study is what we presented during the roundtable. And that is that when you compare with ravulizumab, which is another standard of care -- a considerable standard of care today in the treatment of PNH, a larger proportion of patients that were treated with the combination of pozelimab plus cemdisiran achieved LDH control. Furthermore, a significant larger population of the patients have a normalization of LDH, which we think really represents the level of ongoing intravascular hemolysis. So we feel very comfortable.

Furthermore, when we looked at patients that were not well controlled or never achieved control with ravulizumab in that cohort, okay? There were five patients that never achieved control. When they were switched to the combination, our combination, four out of those five patients were able to achieve control of their LDH. So we feel confident that we have more profound, sustained uninterrupted inhibition of C5 activity that will lead to better control of intravascular hemolysis. So I think that, that is the data that encourages us and makes us believe that we have a positive study.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President of Investor Relations & Strategic Analysis

And we won't have to wait much longer to get that data, should be coming in the fourth quarter. Thank you, Andres. And thanks to everyone who joined the call today. Unfortunately, that's all the time we've got. Thank you for your interest in Regeneron and our C5 development program.

Everyone, have a great day, and we can now disconnect.

Operator

This concludes today's conference. Thank you for your participation. You may now disconnect.