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REGN.OQ - Regeneron Pharmaceuticals Inc Roundtable Lynozyfic

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OVERVIEW:

Company Summary

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PRESENTATION

Operator

Welcome to the Regeneron conference call to discuss its Lynozyfic 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, Investor Relations

Thank you, Shannon. Good morning, and welcome to our Regeneron Roundtable Investor event, a series of presentations spotlighting key opportunities across our pipeline. Today, we will focus on our Lynozyfic development program in multiple myeloma and precursor conditions. Today's roundtable features key leaders from Regeneron, including Dr. George Yancopoulos, Board Co-Chair, President and Chief Scientific Officer; Dr. Andres Sirulnik, Senior Vice President and Clinical Development Unit Head, Hematology; Dr. Karen Rodriguez Lorenc, Vice President of Malignant Hematology Therapeutic Area Leader; and Justin Holko, Senior Vice President, Oncology and Hematology Commercial.

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 risks and uncertainties can be found in Regeneron's SEC filings. Regeneron does not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events, or otherwise. With that, I will turn the call over to George.

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

Thank you, Ryan. I will begin with a brief introduction to Regeneron's broad and diversified heme-onc pipeline. We won't be focusing on hematology today. Andres, who leads both efforts, will then discuss the current multiple myeloma landscape and our strategy for revolutionizing myeloma treatment with Lynozyfic or BCMAxCD3 bispecific antibody. Karen, who leads the malignant hematology clinical programs at Regeneron will review our ambitious Lynozyfic development plan, including our best-in-class data and ongoing development in relapsed/refractory multiple myeloma, our differentiated development plans in earlier line settings and our visions for addressing myeloma precursor conditions. Justin will then review the commercial opportunity for Lynozyfic, and Andreas will conclude by summarizing our development strategy and Lynozyfic value proposition. We will then open the call for Q&A.

Through decades of research and investment, Regeneron has built a broad hematology pipeline spanning multiple areas, including the hematological malignancies, coagulation disorders, transplantation and immunomodulation, complement and other emerging areas with assets across early, mid- and late stages of development. In our last round table we took a deep dive into our emerging [Factor XI] program, in the anticoagulation setting an exciting program that exemplifies the progress we are making in hematologic disorders using our differentiated technologies to provide innovative scientific breakthroughs. In heme-onc, our turnkey technology platforms have allowed us to be a leader in [monoclonal antibodies] and particularly in bispecifics.

Recall that we were the first to advance a flowing fully human bispecific antibody into the clinic and have continued to build on our knowledge and expertise over time. Today, we will focus on our cornerstone acid in multiple myeloma, which we believe has the potential to radically reshape myeloma treatment and potentially eliminate myeloma entirely to treatment of precursor conditions. Our differentiated and ambitious development plan positions us well to deliver on our vision, which [Andres] will now outline. [Andres]?

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

Thank you, George. I will begin with an overview of the existing multiple myeloma treatment paradigm and our strategy with [linvoseltamab]. Turning to slide 8. Today's myeloma treatment landscape is highly complex. With that complexity increasing as patients have progressive disease and move through lines of therapy. Standard of care for transplant eligible patients in first-line multiple myeloma includes triplet or quadruple combination regimens based on CD38 antibodies, followed by an autologous stem cell transplant and maintenance therapy until progression with monotherapy, doublet or triplet combinations.

Patients ineligible for transplant receive one of several toxic multidrug combinations until progression. As patients progress, the standard of care becomes increasingly unclear, with patients receiving a range of intense complicated combination therapies in hopes of achieving a response.

There is a clear unmet need for simplified effective options for -- that provide patients with less intense regimens that reduce the treatment burden and deliver simpler treatment optionality for physicians. A need, which we believe we will be able to meet as we progress our linvoseltamab development program. As discussed, we have leveraged our unique scientific expertise to identify and develop a highly differentiated BCMAxCD3 bispecific antibody which is the foundation for our strategy in multiple myeloma.

As we lay out on slide 9, our aim is to transform myeloma treatment with simplified regimens that deliver deep durable responses. With our recent approval, we are now establishing Lynozyfic in the late-line setting where we plan to build market share and generate positive patient and physician experience. We are advancing into early lines of therapy with a differentiated development plan and encouraging emerging data which [Karen] will detail shortly. And in the long run, we believe we have a unique strategy to treat myeloma precursor conditions to prevent progression to malignant disease potentially eliminating myeloma completely.

We believe this strategy supports our ambition to provide significant benefit to patients and establish linvoseltamab as the therapy of choice in the large and competitive multiple myeloma market. I will now pass the call to [Karen] to discuss our data and development plans in detail. [Karen]?

Karen Rodriguez Lorenc - Regeneron Pharmaceuticals Inc - Vice President of Malignant Hematology Therapeutic Area Leader

Thank you, Andres. I will begin our efforts in [late line] multiple myeloma before moving to our development plan in early lines of therapy, then to precursor conditions and [amyloidosis]. Noting that these are cross-trial comparison depicted on slide 11, Lynozyfic has demonstrated a differentiated profile compared to other BCMA bispecifics in relapsed/refractory setting.

We have deep and durable responses with nearly double the complete response rate of otherwise specific, a similar follow-up and in general, manageable safety profile, including the lowest rate and severity of cytokine release syndrome or CRS. Lynozyfic has also offered patients shorter hospitalization requirements, a simplified step-up dosing scale, a convenient IV administration with the opportunity to extend to

monthly dosing for patients with a very good partial response or better, after only 24 weeks and at least 17 full doses. The strength of these late-line data from the LINKER-MM1 study in highly refractory patients give us confidence that linvoseltamab may be the best-in-class agent and that our approach can translate to profound efficacy in a [early-line] stage.

Moving to slide 12. We have continued to follow patients in this study and at 21 months of median follow-up the overall response rate reached 71% and the complete response rate reached 52%. Patients respond quickly to Lynozyfic with a median time to respond under one month and those responses are durable with a median duration of response of 29 months. Importantly, we have seen responses in these patients deepen over time, a very well-known phenomenon in myeloma treatment.

With an additional 10 months of follow-up, the complete response rate from linvoseltamab observed at 21 months was 52% versus 45% at 11 months of follow-up. The tendency for response to deepen was also observed in [teclistamab], although at 46% complete response rate reported at 30 months was in line with the complete response rate observed for linvoseltamab after only 11 months of follow-up. Linvoseltamab's [robust] efficacy and deepening of response over time in this setting, give us further confidence in emerging data in early lines of therapy.

We received accelerated approval for Lynozyfic in the United States in July 2025 based on the result of the LINKER-MM1 study and our confirmatory Phase III, the LINKER-MM3 study is now fully enrolled. This study includes approximately 410 patients comparing the [linvoseltamab monotherapy] against a standard of care, elotuzumab, pomalidomide, and dexamethasone combination, or [EloPD], which has historically shown an overall response rate of 50%, a complete response rate of approximately 8% and a progression-free survival of approximately 10 months in third-line patients.

Importantly, because the study allows the inclusion of patients who were previously treated with [anti-CD38] antibodies such as daratumumab, we have selected a comparator in this setting that does not include CD38 therapy. Over 50% of patients enrolled in this study are considered refractory to daratumumab, meaning they progress while on therapy.

We believe using the comparator helps to ensure linvoseltamab will be clearly able to address the many CD38 exposed and refractory patients in this setting. We look forward to the results of LINKER-MM3 study, which are anticipated in 2027. Moving to slide 15 on our efforts in early lines of therapy. Emerging data in the first line and second line setting has demonstrated profound response rate for patients in Lynozyfic monotherapy or in simplified combinations even with limited follow-up.

I will first detail second-line data for the differentiated linvoseltamab combination with carfilzomib, a [proteasome] inhibitor, which included patients who had progressed after at least two lines of therapy and were double class refractory or triple class exposed, which was reported early this year at the ASCO conference, along with our plans to advance into Phase III studies.

I will then review the data we have generated in the first-line setting with linvoseltamab monotherapy, which was just presented at the ASH conference this past week and detail our differentiated development plan in first-line patients. On slide 16, you can see the encouraging early data we reported at the [ASCO] conference early this year for a [differentiated] combination of linvoseltamab with [carfilzomib]. The combination demonstrated an overall response of 90% and a complete response of 76% across all linvoseltamab doses with responses continuing to deepen with additional follow-up.

Notably, at 200-milligram dose, three of the five patients have already achieved a very good partial response or better with less than six months of median follow-up which we expect will continue to improve over time. We've also observed a strong early MRD-negative results with five of the seven patients [evaluable] achieving MRD negativity at 10 to the minus-5 sensitivity.

Patients respond quickly to this combination with a median time of partial response or greater of less than two months. Responses have also been durable with 87% of the patients maintaining a response at 12 months. Safety was generally consistent with expectations based on the known profiles of each of the drugs and no new safety signals have been observed. Cytokine release syndrome was the most common nonhematologic treatment-immersion adverse event and most [cytokine release syndrome] occurred prior to the patients starting carfilzomib. There was no Grade 3 or higher cytokine release syndrome observed.

There was one patient with a Grade 4 thrombocytopenia at the 100-milligram dose during tumor lysis syndrome in a patient with a very elevated baseline serum free light chain. This fully resolved and the treatment was resumed at the same dose. This exciting data is informing our Phase III LINKER-MM5 study with the plan to initiate at the beginning of 2026, comparing this combination to linvoseltamab monotherapy and physician choice standard of care. Pivotal data from this study are expected in 2028.

We believe this [differentiated] combination will provide patients and physicians with an important new treatment option in the setting that does not rely on an anti-CD38 antibody, making it a valuable option for many second-line patients who are CD38 exposed or refractory. Moving now to first-line setting on slide 17.

We report exciting new data last week at ASH annual meeting for our LINKER-MM4 study in newly diagnosed multiple myeloma, the first study to evaluate a BCMA bispecific as monotherapy in this setting. In the study, newly diagnosed patients with no prior multiple myeloma treatment who received linvoseltamab monotherapy at 200 milligrams achieve an overall response rate of 86% and a complete response rate of 43%, with only nine months of follow-up with response deepening over time as expected.

Across all dose levels, over 70% of patients achieved a very good partial response or [better] despite limited follow-up. [Depth of response] response is also confirmed by the encouraging MRD negativity with all nine patients dosed at 200mg with available samples who have a very good partial response or better, achieving MRD negativity at the 10 to the minus-5 sensitivity. Across all dose groups, 95% of evaluable patients with [VGPR] or better achieve (MRD-negativity status). Similar to what was observed in both the second line and late line setting, patients responded quickly to the treatment with a median time to partial response or better of just over one month. The safety profile of linvoseltamab remains generally manageable with no new safety signals identified.

The incidence of adverse events were similar across those levels, and there was no dose-limiting toxicity or grade 5 treatment emergent adverse event. [Cytokine release syndrome] was the most common nonhematologic treatment emergent adverse event of which, most cases, [occur] are during the step-up dosing and all were grade 1. These results support initiation of 3 Phase III trials in first-line setting, LINKER-MM6 in transplant ineligible patients [LINKER-MM7 and 8] in transplant eligible patients.

Slide 18 depicted Phase III LINKER-MM6 study in transplant in eligible patients which is sponsored by the European myeloma network and is now enrolling. The study will evaluate linvoseltamab monotherapy after a short course standard-of-care debulking therapy compared to CD38 based standard of care multiple-combination data that is commonly used in this setting.

Our goal is to simplify front-line therapy and provide patients and physicians with options for a less intense monotherapy regimen following a limited debulking treatment regimen that remains a strong efficacy while potentially improving upon safety. Linvoseltamab is the first and only BCMA bispecific being evaluated as monotherapy for transplant ineligible patients rather than a combination approach, which is supported by the remarkable results in newly diagnosed patients reviewed previously.

Pivotal data from this study is also expected in 2028. Moving to slide 19. We are also advancing a differentiated strategy from online patients transplant DC locations, where standard of care consists of an intent CD38 based triplet or quadruple combinations, followed by a burdensome autologous cell transplantation and maintenance therapy.

Our strategy in this setting aims to give physicians increased flexibility to provide patients with convenient, less intense regimen that will not compromise efficacy. In the [LINKER-MM7] study, we are evaluating linvoseltamab monotherapy in the post-transplant maintenance setting with a differentiated approach to potentially enable a longer treatment pre-period for patients significantly reducing patient burden while maintaining efficacy. The [LINKER-MM8] study will evaluate simplified and less intense [linvoseltamab] combination both with and with an alternative to transplant as compared to standard of care [autologous stem cell] transplantation treatment, including standard of care induction, consolidation and maintenance regimen.

First, we will evaluate less intense potential combination in conjunction with transplant using this combination in the induction, consolidation, and maintenance setting. We will also evaluate the potential for a simplified the linvoseltamab combination as [an] alternative to transplant, which may significantly reduce burden. Together, this regimen could enable significant improvement physician optionality with

less intense treatment, both with transplant as an alternative to the transplant. Both studies are expected to initiate in the first half of 2026 and if successful, have the potential to dramatically reshape the treatment paradigm in front-line setting.

Moving now to our development strategy in amyloidosis and precursor conditions. We have pioneering treatment of amyloid light chain amyloidosis and precursor conditions like high-risk smoldering in multiple myeloma and monoclonal gammopathy of underdetermined significance or MGUS. Early data that we have generated suggests significant potential for linvoseltamab in this setting, where there has been limited progress developing new treatments. Our differentiated approach supports our long-term vision to potentially eliminate myeloma through early intervention, preventing progression to malignant disease.

As shown on slide 22, early data presented from the Phase II [LINKER-SMM1] study in high-risk smoldering multiple myeloma show linvoseltamab has a profound efficacy effect with very limited follow-up. With median follow-up of less than four months linvoseltamab 200mg monotherapy demonstrated an overall response rate of 100% with a complete response rate already reaching nearly 40%. This represents best-in-class potential compared to the approved [daratumumab] monotherapy, which achieved only 9% complete response rate in the same setting with a median follow-up of 60 months -- 65 months, sorry.

Through -- though there is a currently lack of head-to-head data in this setting. Based on the strength of this data, we plan to initiate a pivotal [LINKER-SMM2] study in the first half of 2026, comparing linvoseltamab monotherapy head-to-head with daratumumab monotherapy. Positive data would establish linvoseltamab at the standard of care in this setting, potentially placing linvoseltamab ahead of other BCMA bispecifics in the treatment algorithm. We are also evaluating linvoseltamab monotherapy in monoclonality of undetermined significance or [MGUS].

A common asymptomatic precursor condition to myeloma as well as in non-high-risk smoldering multiple myeloma. Initial proof of concept data is expected next year, and if successful, could represent a significant long-term opportunity for linvoseltamab as a prophylactic treatment to prevent progression to malignant myeloma.

Moving now to amyloid light chain amyloidosis. A related condition where abnormal plasma cell produced an excess of [misfolded] light change project, creating amyloid which deposit in the tissues and organs leading to severe complications. We have created compelling early data with linvoseltamab monotherapy in the second-line amyloidosis patients, a majority of whom previously received [daratumumab-containing] combination, showing profound reduction in [mean involved] free light chain to normalized level in just 15 days.

For comparison, [a daratumumab-based] quadruple combination in the first-line amyloidosis patients took approximately five months to approach [mean involved free light chain] normalization. The pivotal [LINKER-AL2] study is enrolling with [data] expected in 2029. If successful, this could allow linvoseltamab to address the disease where significant unmet need remains and continue to reshape the treatment of myeloma and related conditions. In summary, we have an ambitious, differentiated development plan spanning across lines of myeloma therapy and precursor conditions, which we believe has the potential to establish linvoseltamab as the therapy of choice in the treatment of myeloma and related conditions. I will now pass on the call to Justin to discuss the commercial opportunity.

Justin Holko - Regeneron Pharmaceuticals Inc - Senior Vice President, Oncology and Hematology Commercial

Thank you, Karen. Let's move to slide 25. I'll begin with our recent launch of Lynozyfic in relapsed/refractory multiple myeloma, where we have seen strong early momentum. Enrollment in the REMS program has been strong with more than 300 institutions now certified. We've also secured early formulary wins at key institutions with Lynozyfic now added to over 35 formularies and in some cases, with preferred status. Physician feedback and adoption in the late-line setting has been favorable, not only because of Lynozyfic's differentiated clinical profile, but also because of its patient-centric hospitalization requirements and dosing. However, the late line setting is just the beginning for Lynozyfic.

As you can see on slide 26, there is significant opportunity in the estimated $30 billion multiple myeloma market. A market, which we expect to continue to grow in the coming years. While we are excited about the opportunity to provide profound benefit to late-line patients, the more significant opportunities will come as we advance into earlier lines of therapy. Today, the first-line and second-line settings represent the largest share of this opportunity with each setting representing an estimated market of over $10 billion.

Our strategy is to generate a firm foundation of positive physician and patient experience in the late-line setting and then advance with approvals in earlier lines where the market opportunity is significantly larger. We believe upcoming pivotal readouts from the first and second line trials detailed by Karen will be key catalysts for unlocking this value. We also believe our differentiated strategy in precursor and related conditions could add meaningful additional commercial opportunities for Lynozyfic. [Smoldering] myeloma and ALA represents significant untapped commercial markets. And that early data suggests the potential for Lynozyfic to have a differentiated efficacy in these settings. We look forward to data readouts and potential launches in these settings in the coming years.

Additionally, as Karen mentioned, successful proof-of-concept data in [MGUS] could open up another long-term commercial opportunity. In summary, we are making encouraging progress with our launch in late-line myeloma and Lynozyfic's paradigm-changing potential represents a major commercial opportunity for Regeneron, both in early lines of multiple myeloma in ALA and in precursor conditions such as smoldering myeloma and MGUS. I'll now turn the call back to Andres for some closing remarks.

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

Thank you, Justin. We previously reviewed the complex and confusing treatment algorithm in myeloma. But our vision is to significantly simplify this treatment landscape. We believe linvoseltamab provides a clear and differentiated value proposition in every line of therapy with the potential to provide better outcomes and convenience to patients and increase optionality to physicians. As [Karen] reviewed, we have generated data across the treatment landscape, and we have been pleased with the consistently remarkable efficacy across lines of therapy. We have taken a bold approach in our development, moving to early lines and precursor conditions with monotherapy or simplified and less intense combinations.

The data we have generated has been remarkably consistent and profound with as high as 100% molecular remissions achieved very quickly across different lines of therapy as well as in high-risk smoldering myeloma and amyloidosis. The data generated to date supports our ambitions to establish linvoseltamab as the backbone therapy for treatment of myeloma as well as precursor and related conditions.

Finally, we continue to advance our comprehensive development plan. With 8 registrational studies underway or anticipating to initiate in the next six months, spanning across lines of therapy and into precursor and related conditions. We look forward to a steady cadence of data in the coming years, particularly as we leverage the surrogate endpoint of MRD negativity with the goal to pull forward time lines and provide these options to patients and physicians as quickly as possible. I will now turn it back to Ryan.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

Thank you, Andres. This concludes our prepared remarks, and we will now move to the Q&A session of the call. To ensure we are able to address as many questions as possible, we will answer one question from each call before moving to the next. We also ask that you limit questions only to the scope of the content covered in this call. Shannon, can we please move to the first question?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Tyler Van Buren, TD Cowen.

Unidentified Participant

This is [Nick] on for Tyler. For me, J&J presented the results from the [Majestic 3] trial at ASH yesterday. However, 95% of patients were [dara-naive]. What do you think your linvo plus [dara] suggests about the potential efficacy in a more real-world dara-exposed patient population?

Karen Rodriguez Lorenc - Regeneron Pharmaceuticals Inc - Vice President of Malignant Hematology Therapeutic Area Leader

So thank you for the question. So your question is in reference to the data from [Majestic-3] with more like naive patient population to anti-CD38 versus the data that we are currently generating. So it's difficult to compare because of the patient population from the two different studies are not exactly the same. What we are trying to do in our clinical trials is to involve patients who are representing the patient populations are going to be treated in the future with our monotherapy or combinations and we are encouraged by the observations that we have on efficacy and safety. And some of those combinations are going to move forward to pivotal Phase III trials as the one that we previously discussed with (carfilzomib).

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

Thank you, Karen. Next question please.

Operator

Alexandria Hammond, Wolfe Research.

Alexandria Hammond - Wolfe Research LLC - Equity Analyst

So I think there's a lot of growth with many community centers still not using bispecifics. As you try to kind of expand into the community, what have you been hearing as the reason for reluctancy on their part to use as bispecific? And how do you think linvo will be able to kind of address those concerns? And just lastly, how difficult is it for these centers and their patients to adhere to the REMS program?

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

Thanks Alex. [Justin], maybe you want to take that one?

Justin Holko - Regeneron Pharmaceuticals Inc - Senior Vice President, Oncology and Hematology Commercial

Sure. I would say the first thing is that we are seeing significant more utilization of bispecifics in community. Clearly, this class is being used in multiple myeloma, in lymphoma as well as in some solid tumors. And so it is a bit of an inevitability that more and more physicians would want to get their hands on these really important and powerful treatments. What has typically held some of these groups back historically is that you have hospitalization requirements, in which case there may not be appropriate monitoring in place. And there's also just capacity constraints when considering those types of requirements.

When you look at the profile of Lynozyfic, whether a patient is going through step-up dosing in an academic center or in community, what's clear is that having only those two days of hospitalization and monitoring is an advantage compared to some of the more laborious requirements for some of the other bispecifics. So in the end of the day, we are seeing utilization grow within community, and it's through the help in part as a result of the -- again, the patient-centric dosing and the less hospitalization requirements that we have for our step-up dosing.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

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

Operator

Salveen Richter, Goldman Sachs.

Unidentified Participant

This is [Shrunatra] on for Salveen. At [ASH] we also saw some late-line disease data from AbbVie and AstraZeneca's assets, pretty limited, but also interesting. Just your thoughts on how that data compares against the [linvoseltamab] profile and how you think those assets might impact the late line competitive landscape in the future if they're approved.

Karen Rodriguez Lorenc - Regeneron Pharmaceuticals Inc - Vice President of Malignant Hematology Therapeutic Area Leader

So your question is in reference to the other assets that were also presented in relapsed/refractory multiple myeloma. Can you please confirm?

Unidentified Participant

Yes.

Karen Rodriguez Lorenc - Regeneron Pharmaceuticals Inc - Vice President of Malignant Hematology Therapeutic Area Leader

So we are very encouraged by the data that we have in late line therapy with our depth of the response for 52% of the patients reaching CR and also the depth based on margin activity. So we understand that there are also other players that are are coming, but also our data in initial lines of therapy with monotherapy are very encouraging with not only the efficacy, but also the safety that looks even better than in the relapsed refractory. So for us and there is a room for getting into early lines of therapy coming with combinations that are less burdensome and providing this optionality for the treatment. I think that all in all, we are very happy with the linvoseltamab information that is generated because again, it's not only the efficacy and the safety profile, but also the convenience, the shorter hospitalization of relapse refractory. think that all in all, is providing a good option for physicians and for patients.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

Let's move to the next question.

Operator

Cory Kasimov, Evercore ISI.

Unidentified Participant

This is [Josh] on for Cory Kasimov. What does FDA feedback been like in regards to MRD negativity as an endpoint. And then I'll squeeze it extra one here. When can we see a subcu formulation for linvoseltamab?

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

So we are currently -- this is [Andres]. We are currently working on a subcu formulation. So eventually, we will be generating data. We are generating data, and we'll be presenting the data in due course. In terms of the feedback from [MRD] as an acceptable surrogate endpoint for an accelerated

path for potential approvals, I think that at the moment that has been the case and accepted following the [ODAC] that took place now almost a year ago. And in many of our pivotal studies that we have described today, MRD is our primary endpoint for which we plan to potentially submit in the future.

Operator

Evan Seigerman, BMO Capital Markets.

Unidentified Participant

This is [Conner McKay] on for Evan. I guess following some of the LINKER-MM4 data you presented this week at ASH, can you maybe share a little bit on how you're thinking about the use of bispecifics in earlier lines of therapy? In the context of these data and also maybe how you're thinking about sequencing versus CAR-T.

Karen Rodriguez Lorenc - Regeneron Pharmaceuticals Inc - Vice President of Malignant Hematology Therapeutic Area Leader

So we consider that, as you know, currently, the treatment paradigm for patients in initial lines of therapy is quite cumbersome as we were discussing in the case of [Transplant-eligible patients] are receiving triple or quadruple combinations, high-dose chemotherapy followed by autologous stem cell transplantation and then consolidation and maintenance. So it's quite a heavy treatment. And what we see is that probably the bispecifics can contribute on decreasing the intensity of the therapy and providing even better efficacy and with a good safety profile.

So I personally think that these patients are going to transition into early lines of therapy with a very good option for physicians and for patients. And in reference to the use of CAR-T or if there is a sequencing as what we know is that, yes, [bispecifics] are also working well in that setting. So yes, I think that they are more like a maintain for the treatment of these patients. But I think that we need to also highlight that the bispecifics are providing an off-the-shelf option for many more patients are for a broader group of patients. So I think that all in all, it's like a good optionality of tools for physicians in the future to treat these patients in early life setting.

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

Yes. I mean maybe we should just give a little bit of a bigger picture, and it's a little hard to probably take in all this data and put it into context. And understand the opportunity, and we were just hearing in the early line with or without transplant-eligible, ineligible and so forth. I think the thing that's really stunning about the data, I mean, it starts with how differentiated this bispecific is. I mean we got to all remember, I mean, this is the history of Regeneron. We have many programs where we create the best-in-class agent, the best-in-class antibody because we have technologies.

We don't just take any one antibody, any one bispecific and move forward. We've screened thousands and thousands based on our technologies, which nobody else has access to. So for example, [dupilumab] which is one of the, if not the largest, most highly prescribed antibody in the world. It succeeded where other companies, including Amgen, failed against the same exact target. Why? Because all the antibodies are not the same and bispecifics are even more complicated. I think the big picture here is it's cross-study comparisons, but these data stands up pretty much historically over time. In the last-line setting, what these guys are telling you is they have double the complete response rates with similar times of follow-up. That says that this bispecific is perhaps very different, just like [Dupi] was very different than the failed molecules from other programs.

This is perhaps very different bispecifics than all the other BCMA. And what you're seeing in monotherapy, and it doesn't matter which setting that they're looking at. They're looking at it in the first line [setting], you're looking at the premalignant and you're looking at it in the later line setting in the second line. They're producing MRD negativity rates that have really never been seen before. And now the challenge is figuring out how in this very complex landscape with all these different lines of therapy and all these so forth to take advantage of something that by itself I mean the data went by pretty quickly. But for example, by itself in many of these settings, the data as a monotherapy delivering molecularly negative disease, MRD-negative disease exceeds that of complex triplet and quadrupled regimens. That is really stunning. And

this is why you see a very complex, large development path because we're trying to take advantage of it in all these settings. In almost all of these settings, what we're trying to do is simplify the regimen. The regimens are so complicated right now. People don't even know what to do.

They do various triples, quadruplets and so forth. If you could simplify these things with single agents [or] simple double combination that the data suggesting might have even higher rates of producing molecularly measured negative disease, it can really change the treatment paradigm. And what we're also seeing is the earlier you go, this bispecific behaves even better. So not only are we talking about going into the first line setting, but we're talking about going to the premalignant settings where, as you've seen stunning results in two weeks. You're making disease disappear in light chain amyloidosis, whereas with other approaches, more complicated and so forth, it takes months to get even close to that level. Same thing in small [during], we believe it's going to be even better in [MGUS] where we may have the opportunity, for example, to do prevention, eliminate a very prevalent, pre-existing condition that people are constantly dreading.

Oh, I have (MGUS), when might it convert to myeloma? If you have a safe and effective treatment that can essentially eliminate the disease safely in a large percentage of the patients, you can potentially eliminate the threat of this disease. So we got to understand this is very complicated. We can look at each individual study and try to look at the data, in particular. But the big picture message is when you look at the data in the last-line setting, as a monotherapy, it looks impressively different than anything that's ever been tried before in terms of any other bispecifics.

You go to early line therapy as a monotherapy, it's still outperforming much more complex regimens, and the opportunities that we're now seeing with very simple doublets are also incredibly impressive. And so this offers enormous opportunity to simplify regimens and go earlier and earlier in the disease course and maybe even eliminate the threat of disease in the premalignant sets.

Operator

Brian Abrahams, RBC.

Unidentified Participant

This is [Joe] on for Brian. I wanted to touch on the safety profile in the newly diagnosed patients. So just wanted to hear your view on the rates and severity of CRS and [ICANS]. You saw how manageable these would be for [centers] in earlier line in presymptomatic setting. As I imagine, there would be much higher volume patients versus later line and what this means for patients duration of hospitalization, if any. And I wanted to just quickly touch on dosing frequency as well in earlier lines in the presymptomatic patients given those patients seem to be responding to the therapy.

Karen Rodriguez Lorenc - Regeneron Pharmaceuticals Inc - Vice President of Malignant Hematology Therapeutic Area Leader

So you're asking about the safety profile and then that is going to be correlated with hospitalization requirements. So in the case of linvoseltamab, in the case of the LINKER-MM4 study, we tested the two patient populations, transplant eligible and transplant ineligible. And the results in safety are very encouraging. In reference to cytokine release syndrome, we observed very few cases. and all of them were only grade 1, which means like only fever.

There were no patients with a 2 grade 3 cytokine release syndrome. We have a single patient with [ICANS] that was also a grade one and all the events recover and the patients continue with the therapy in the same dose that they were previously receiving. So we hope that this enables us to have monitoring in the future instead of hospitalization because of the better safety profile that we are observing in initial lines of therapy compared with our existing data in relapsed refractory. So in reference to the regimen, the regimen is starting with the weekly doses and following four biweekly doses and then monthly doses and what we are trying to do in the initial lines of therapy, also trying to see to evaluate fixed duration therapies.

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

So by the way, a lot of people are focused on CRS and so forth. But obviously, one of the biggest problems that these patients are suffering from our infections. And you guys now have some experience in the newly diagnosed setting, treating with your BCMA bispecific where we know these patients are prone at baseline because their marrows are so compromised and so forth to severe infections. So maybe you guys can describe what is your experience now why you're dosing as patients are responding, what remarkable things are you seeing in terms of safety and infection rates there?

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

Yes. What has been remarkable when we looked at relapse refractory multiple myeloma with our bispecifics. One of the notable findings was that infections decrease over time. Everybody thought that as you continue treating them with bispecifics, infections were going to increase over time. But actually, we saw that after approximately 6 months the rate of infections decreased. So there are many ways of thinking, why that would be possible. One of them is you have reconstitution of the marrow, you have a healthy individual and a better immune system. -- as we move into early lines of therapy. And the data that we just generated in newly diagnosed show us that actually the rate of infections decreased even earlier. So now we went from a decrease in infections on the first 6 months in the last line of therapies to a decrease on the rate of infections after three months. Again, showing that as you clear the disease patients are better off and infections actually go down instead of coming up. So I think that that's also speaking to the safety and how important it is to bring to patients potential therapies that are not burdensome that are potentially toxic and why we are taking the bold approach of thinking of monotherapy in first line or less toxic combinations that may afford a better risk-benefit profile without compromising efficacy.

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

And as you say, [Andres,] I mean, it probably is about taking a sick bone marrow, a [bone] marrow that's been infiltrated that doesn't have the capacity to create, for example, all the white cells that you need to respond, neutrophils and so forth, by getting rid of the disease, you allow the bone marrow to recur. And as you said, the evidence suggests in the later line patients because it's been a more long-standing disease, and the bone marrow [is sicker] takes longer for the bone marrow recover, whereas you're seeing in the early-stage patients much quicker apparent recovery of immune function as measured by the decrease in rates of infection. So that's a really, really important feature.

While everybody is focused on CRS the fact that you're actually almost paradoxical, but it actually makes sense now in retrospect, you're actually decreasing infections. I mean, that is actually quite stunning. And quite unlike the other therapies, we got to remember, drugs like [daratumumab] the CD38 targeted agents, they're actually compromising neutrophil function, and they actually increase risks of infection on their own. So these are very important differentiators and reasons why it's important to pursue these minimal regimens that are using a drug that might actually not be harming in general, the rest of the immune system, while it is eliminating the myeloma cells.

Operator

Simon Baker, Rothschild & Company Redburn.

Simon Baker - Redburn Partners LLP - Analyst

Just wanted to dig a little bit deeper into early feedback on Lynozyfic use. If you could give us some idea of the characteristics of patients and prescribers at this stage, particularly the split between community and academic center prescription, that would be really helpful.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

[Justin], do you want to?

Justin Holko - Regeneron Pharmaceuticals Inc - Senior Vice President, Oncology and Hematology Commercial

Yes, happy to take that. So as you would expect, the majority of use right now really across the class is happening in the academic centers. And it's a bit of a mix in terms of patients seeing all of your dosing taking place there. There are some instances where patients come from the community. They get their step-up dosing within the academic then go back to the community. You do have, in some cases, some community sites that are equipped and doing step up. That's still probably the minority right now.

The patients that we're getting are probably typical to what you would see across this fourth and fifth line plus they've been through a lot. And thus far, the feedback that we have is actually quite strong. Certainly get a lot of feedback on the -- as I mentioned, the convenience of the dosing and the ability to go out longer with good responses, but we really see strong feedback on the on the safety and the efficacy as well. So early days, but a lot of our metrics that we're tracking are at or ahead of where our competition was at a similar point during launch.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

Thanks, Justin. Shannon, we have time for two more questions.

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

Before we go on to your question, I was just -- a question came up before about late-line relapsed/refractory and the use of other bispecifics and combined bispecifics, and people are excited about that data. And I didn't want to say because I just wanted to look up and remind myself of the numbers. But everybody is very excited about this combination, for example, of a [GPRC5D] and a BCMA, which together in the late line setting with about 12 months of follow-up, are giving you about 79% overall responses and 53% complete responses, and people are excited about because it's doubling the rate of BCMA bispecific by itself or at least in that BCMA bispecific base.

So I just want to remind you, again, if you're excited about that combination data, which comes with a lot more toxicity. I mean severe, much more toxicities there. Remember, the Regeneron bispecific which, as I said, different technology fundamentally different is delivering pretty much those numbers at a similar follow-up as a monotherapy.

So I think we have to understand why we should be excited. Other people are excited about adding more stuff to the point that we are already -- and I think this is, I think, a really big take-home message. I mean this is behaving fundamentally different and it's approaching the numbers that you see when you start mixing other things together and layering on toxicity. So the big picture here is impressive efficacy as a monotherapy or with very limited combinations and hopefully, safer combinations. So I think that, that's an example. People are excited about that bispecific combo. Well, you should be more excited about a monotherapy bispecific that's delivering very similar results.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

Okay. Shannon, two more questions for us, please.

Operator

Geoff Meacham, Citibank.

Unidentified Participant

This is [Nishant] on for Geoff. So following up on the earlier question in terms of sequencing in myeloma, (where some physicians) would prefer CAR T and then see bispecific. So would it make sense at some point to include a cohort of CAR-T as patients in the study given CAR-Ts are moving

Karen Rodriguez Lorenc - Regeneron Pharmaceuticals Inc - Vice President of Malignant Hematology Therapeutic Area Leader

Sorry. So your question is if we are exploring data with post CAR-T with -- yes, we are -- okay. So we are already including cohort in 1 of our studies with (post-CAR-T) data. And yes, that is being generated, and it will be released probably next year.

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

Once again, the big picture is, I think we have to start realizing or recognizing -- and I'm sorry, CAR-T is largely yesterday's news. I mean it's a very -- once again, a complex therapy it's also a combination therapy. You have to give chemotherapy before you can give the CAR-T, that probably explains the incrementally slightly improved numbers that they get with a very complicated therapy. There is really little evidence to suggest that they're actually giving better results and long-term results than you can get with the best bispecifics here.

So I don't think we're talking about a future world where CAR-Ts and all their toxicities and problems with giving them so are going to be moving to the early lines of therapy, okay? You're talking about were bispecifics and particularly the best bispecific is going to be moving to the early in therapy and to premalignant disease, and probably made CAR-Ts either obsolete or for late-stage salvage patients if they still have activity in that setting. So I think eventually, the whole thing is going to be reversed. CAR-Ts are going to become yesterday's news. They may have some late line salvage opportunities. But there is no way that they're going to actually be competitive in the early line settings in the premalignant settings.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

All right. Shannon, one last question for us, please.

Operator

Mohit Bansal, Wells Fargo.

Mohit Bansal - Wells Fargo Securities LLC - Analyst

And I think my question is also a little bit big picture. So oftentimes, we have seen in competitive markets. I mean, the drug could be better, but at the same time, I think the development strategy could be more important. And it does seem like that there is a lot of emphasis on early-stage myeloma here. Can you talk a little bit about the strategy there? I mean how do you think you are differentiating the key parts of differentiation versus a competitor from J&J and all other bispecifics, which are also trying to do the same. But how would you think that you could be differentiated on the development side of things?

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

I mean I think the team did a good job in a very complicated setting to try to communicate this. I mean the point is that other people are pretty much looking at adding their bispecifics on top of existing regimens and so forth, creating even more complications. And why are they doing it? Perhaps as we just showed you, in the last-line setting, you have to combine somebody else's BCMA with a [GPRC5D] to get to where our bispecific is by itself. When our bispecific is so active, we're thinking that we can now be using that either as a monotherapy. We've already told you the incredible response rates and MRD negativities that we're seeing in the first-line setting. We think that we can be doing that either in a monotherapy or with very limited combinations. That's the great differentiator here. And the fact that we can also go with this monotherapy into the premalignant settings and essentially remove the threat of myeloma disease.

Ryan Crowe - Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations

Okay. Thank you, George. Unfortunately, that's all the time we have for today. Thanks to everyone who dialed in for your interest in Regeneron and our Lynozyfic program. We look forward to seeing you at our next event. Thank you very much, and have a great day.

Operator

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