Content

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Good afternoon, ladies and gentlemen. Welcome to the joint webcast between Nordic Nanovector and APIM, where we would like to discuss the proposed merger between our 2 companies. My name is Jan Egberts, and I'm the Chairman of the Board of Nordic Nanovector.

Together with me this afternoon are Malene Brondberg, our Interim CFO; as well as Kostas Alevizopoulos, who is the CEO of APIM Therapeutics and the proposed CEO for the combined entity; as well as Fredrik Haavind, our internal Chief Legal Counsel.

Over the past couple of weeks, frankly, since before the announcement of the proposed merger, we have spoken with many of you. We received a lot of different e-mails, but we also had one-on-one meetings, in particular with the largest shareholders, where we basically heard that particularly APIM is not very well known, and people like to hear more about it, and that's the objective of this call to tell you a little bit about more about APIM and also explain to you a little bit about the proposed transactions.

But I really want you to know that we have spoken extensively with many of you, and we have tried to, as much as possible, include in our presentation many of these open questions.

Going to the next slide, I'd like to make aware about our forward-looking statements, and I really urge you to carefully review this document on this page and take it into consideration.

And next, I'd like to go to the agenda. I really like to focus on the questions many of you have had and we've heard over the past couple of weeks from our shareholders, in particular, both of the large shareholders, those were mainly in-person meetings, and from some other smaller shareholders very often by e-mail, but also other means of communications.

So what we try to -- we'll want to plan to discuss with you today, first of all, a top line of the rationale for the merger and the process we pursued. Secondly, I want to tell you a little bit more in detail about APIM Therapeutics, because many of you mentioned you don't know much about the company. So I think that's very important. Then I'll make some concluding remarks, and I'll explain a little bit about the process for the Extraordinary General Meetings of Shareholders and the voting process associated with it. And in the end, there will be a Q&A.

We also realized that a lot of the Norwegian speakers prefer to speak in our native language. So we'll answer the questions to the extent I answering, Malene Brondberg, or one of the native Norwegian speakers will translate in the local language. So we're really trying to address some of the language needs we have heard.

Going to the next slide, I want to recap the process of PARADIGME at the end of the Phase IIb trial, which we concluded, as you know, over the summer of this year. In the first year of this year -- the first half of this year, the recruitment into the PARADIGME clinical study really dragged and dropped significantly. Obviously, the COVID was a big part of it. But also in spite of many of the protocol changes and the operational changes we have made during 2020 and 2021 to improve the patient recruitment, which really had a very positive impact, we dropped from about 50 patients that were recruited in 2021 to only 3 in the first half of this year. So a very significant drop, 50 over the whole year of 2021 and only 3 over the first half of this year.

Obviously, we went through significant discussions and we had ongoing discussions with the participating hospitals, and really lead to the conclusion that this -- the poor recruitment rate in the first half of this year was unlikely to improve. So as a Board, we decided to call an independent data evaluation committee and kind of performed a second interim analysis.

So the independent data evaluation has really showed that 1 in 3 patient responded, so 30% of the patients responded, obviously significantly lower than we've seen in the LYMRIT study, and an average duration of response was about 6 months. While some of our competing technologies like the bispecific antibodies that are really emerging in the same therapeutic area has shown effectiveness of over 80%. So both in terms of the

number of patients, 30%. And in terms of the average duration of response below what we've seen than some of our competition.

Based on these facts, the Board decided that these results do not support further development of Betalutin in third line third-line follicular lymphoma, particularly also given the fact that the competitive environment is really -- was and is really changing very rapidly. On the one hand, the FDA is increasing the regulatory requirement for submission, which would now demand that we at least have enrolled a Phase III clinical study before we can file for submission. And secondly, the emergence of some competitive technologies, such as the bispecific monoclonal antibodies I spoke about earlier, but also CAR-T. That really led to the conclusion, a very unfortunate conclusion, to discontinue PARADIGME.

So I mean, obviously, we still have -- we're still excited about CD37. We saw very strong data in LYMRIT, but we really decided that given the investments required to get this compound to go forward to a major value inflection point, it's very unlikely that is possible in the current financial market, which as I'm sure you have noticed has dropped significantly since the beginning of the year.

So based on that, we decided to do a comprehensive review of the strategic position of the company. We retained Carnegie to help us and to explore viable alternative opportunities for the company, both internally and externally. So in summary, the results were not as we hoped for, let's be very transparent about that, on the one hand. On the other hand, the competition was moving really fast, particularly bispecifics and monoclonal antibodies and CAR-T. And thirdly, the FDA has increasingly put heavier demand before we could submit our clinical [indiscernible]. And given the fact that the equity markets, the stock markets are not in favor of raising a significant amount of money at this stage and [indiscernible].

So moving to the next slide. I want to talk a little bit about this comprehensive strategic review where we exploit all the options. And broadly speaking, we really compare 2 major strategic opportunities for the company. On the one hand, to go it alone, so basically focus on our early-stage R&D portfolio, and really the compounds we currently have in R&D were too early to be viable for financing in a public market environment today. So the go-it-alone strategy, the Board decided it was not a viable strategy. On the other hand, we look at a number of broad M&A opportunities, which is the alternative of the go it alone strategy. And we did it as we discussed last time in concentric circles.

Initially, focusing on or regional oncology companies, subsequently focusing as a broader circle around it, if you want to call it that way. Nordic oncology companies that even more broadly, other health care companies outside Norway, also in the rest of Europe and overseas. Again, the focus was twofold. On the one hand, finding a good strategic fit in terms of M&A target, something that really fits together. Again, using the [concierge service] I discussed. On the other hand, the potential to maximize shareholder value -- the value for our shareholders.

We also look at some transactions outside health care that was mentioned by many of our investors, if we did, yes we did. And in that case, we particularly will be focused on the listing on the Oslo Stock Exchange and some of the cash. Some people also mentioned that our net operating loss would be an asset. I just want to be clear, the net operating loss would only be an asset if they will be acquired by a company pursuing exactly the same field as we are. So no other oncology company could use it, but if it would be acquired by some non-health care company that asset would not be usable. That's the way the tax people review net operating losses.

In short, we discussed with over 25 potential companies, both in the Nordic and outside Nordic, that included big pharma, smaller biotechs, medical device companies, companies outside health care, both private and public. So I really feel we casted very, very wide net.

In terms of the companies where we became the furthest, we also, in particular, had a number of discussions with biotech companies in the oncology field, with assets in Phase II and later. Again, that is very much where the majority of the value is. But in short, the transaction of the proposal from APIM will be generated, by far, the most value for our shareholders.

So in conclusion, we consider the merger with APIM that we propose the most attractive option for Nordic Nanovector shareholders. Also, over the past 2 weeks, we received many e-mails from shareholders, and I must tell you, I have not heard a single proposal that I think or that the Board thinks is a viable alternative for the APIM merger. So we have been open, we're listening to any proposal, but I have not heard a single viable alternative scenario post the APIM proposal.

Now going on to the next page. Many of you asked questions about how we came to the valuation of APIM, and particularly the value split between APIM and Nordic Nanovector. Basically 75% of the value of the merged company going to APIM and about 25% to Nordic. So really what we have done and we pursue is a -- have to use an international independent firm specializing in biotechnology valuations. And many of these investors use these kind of organizations at a very regular basis and to [indiscernible] to make a good valuation of an early-stage company, including private company.

And we really took 4 different valuation methodologies into account, which is basically the industry data and historical information kind of review that. Secondly, in what stage of development is the lead assets and the other assets, how the company is structured. And then finally, based on the relevant financial information, the future commercial potential of the project, the targeted clinical indication and the overall risk of a compound like this using essentially a net present value, discount, cash flow approach to come to a valuation of the company.

And again, this valuation resulted in the 25-75 split, whereby the 25% for Nordic Nanovector is really related to our current value at the Oslo Stock Exchange, the 2 weeks prior to the announcement of the transaction -- of the proposed transactions.

So going on to the next slide. We really feel that the combined entity has the potential to create very significant shareholder value, in particular, by focusing on 3 broad areas: Advancing APIM's pipeline of oncology programs, and again, Kostas is going to talk more about that in the next 15 minutes, with multiple shots and goals in clinical -- multiple clinical studies for their key assets, in particular, ATX-101. Also evaluating the most optimal way to generate value from our portfolio of novel preclinical and early-stage compounds using the CD37 targeting immunotherapy programs. And then finally, some of the other APIM novel therapeutic approaches where again Kostas is going to talk in more detail about it.

With respect to the shareholders of APIM, the largest shareholder representing over 70% of the share of APIM agreed to a 12-month lockup in the company. So that's simply give you some additional security. More on the soft side, we already had a couple of joint meetings between APIM and Nordic Nanovector, and I can tell you it was a really great chemistry between the 2 teams. And we have started to work on a joint R&D pipeline, whereby we have multiple shots and goal that we look very, very positive.

So having said all that, I think that the Nordic Nanovector definitely came -- definitely came to the conclusion that we feel this is by far the most attractive opportunity for Nordic Nanovector. Again, we have not heard a single viable alternative from any of our shareholders. And I really like to hand over now to Kostas to tell a little bit more about the APIM pipeline. Thank you.

Presenter Speech

Konstantinos Alevizopoulos (Executives)

Thank you, Jan. Thank you, everybody. So in the next slides, I will try to give you some more information about APIM Therapeutics and to why we think that this technology developed by our company is really exciting and also why we believe that the fit with Nordic Nanovector is so important. And this is what exactly we want to do in the next period of time.

So if we go into the next slide, this slide summarizes practically what we are and what the technology, the key technology points that APIM brings on the table are differentiating factors practically. So I think the first point is the most important point. We are a company that brings a novel therapeutic approach, a new therapeutic intervention point. For those of you who participated in the previous webcast, I've explained a bit more about this intervention point. It really relates to targeting cancer escape mechanisms. And these are, of course, important in oncology.

So having this intervention, having discovered this intervention point, our company was the first to target this mechanism of action with our drug, which is called ATX-101. As you know, and since we are first to target [Indiscernible] peptide, also called -- it's a first-in-class drug. The beauty of this intervention point is that it's also applicable practically in every different tumor types. So it's not specific to a given mutation, to a given genetic alteration of any tumor type, it's really applicable in practically every tumor.

Now we have used our drug in really relevant animal preclinical models typically and originally shown that it has activity on its own. But also, it has a strong potentiating effect of other anticancer therapies, and we have

conducted extensive experimentation showing that more than 25 different drugs in different drug classes chemotherapeutic agents, radiotherapy or also targeted therapies are potentiated by our drug. So if you put those 4 bullet points together, it becomes obvious that APIM offers as a technology-driven company, numerous development opportunities. We can develop multiple, for example, combinations in multiple cancer indications. That's why we consider our product pipeline in a product due to this potential that it brings.

Having said that, which I would also like to point out, that this mechanism that we are targeting and relates to stress mechanism in cancer cells is also relevant for other diseases and especially inflammatory diseases. So we are talking about a novel mechanism, which is central in cancer, but also central in other diseases. So this gives you an idea about the overall potential that this technology is bringing.

Now the last bullet point is directed towards to our drug as a drug entity that one day will be delivered in patients at the commercial setting. It's practically chemically synthesized, highly scalable peptide, which is extremely stable and the tube has actually stability of more than 5 years. So really an entity which is easily made and can be easily used and administered in patients. So overall, I think these key technology points differentiate us from other companies as a unique company with really a lot of potential for further development.

In the next slide, what I've done is I presented the -- in a snapshot, the ongoing clinical development of our company. We have 2 Phase II studies underway, and this is an important message. It's an advanced development, mid-stage development clinical program. Of course, to arrive at this stage, we have concluded a first clinical study in patients with advanced solid tumors. We've administered our drug as monotherapy. The goal of this study was to establish the safety primarily of our component. Any new mechanism actually has to prove itself in a sense that it's really exciting to have a new mechanism, but you have to rule out that there is no safety issue for your novel drug, and this is exactly the concept of our Phase I study.

So the study concluded on an excellent safety profile of our drug and signs of clinical activity. And these data, together with the exciting work conducted in the clinical models and the preclinical proof of concept, led us to activate these 2 studies. And I mentioned in the previous slide that we are -- our drug is able to potentiate the action of other drugs and deliver the maximum therapeutic effect. That is the reason why our first study, a sponsored study in ovarian cancer, is a combination study. So this is a proof-of-concept study. And you can see in the slide that we are combining with 2 other partners. So please go back to the previous slide.

We are combining with 2 partners, doxorubicin/carboplatin in a segment of the disease called platinum-sensitive disease. And preliminary data, actually, the colored part is the ongoing part, but we can really say at this point that there is no safety concern, and we've met already the primary endpoint of the safety part of the study. And this is exciting for another reason. I told you before that a new drug has to prove itself that it's safe if you target a novel mechanism. And if your mechanism of action is primarily in combination with your other drugs, you have to prove that you are safe as used alone and also used in combination. So we have seen a fantastic safety profile up to now.

So we are really optimistic that this practically technology can be used to deliver multiple combination treatments in the future to patients. So that's a very exciting part.

Now we are entering a Phase II efficacy part, and you can see here also on this slide, the side of the patient population that we will be treating in this proof-of-concept study. On the bottom side of the slide, you see a second study that we are supporting. The official sponsor is the Columbia University in New York. That's why it's called an investigator-initiated study. I think it's important to note why this study has started.

Scientists at Columbia University, which are leaders in the field of sarcoma globally have actually evaluated data that came out of our concluded Phase I study in sarcoma patients that we recruited in this study. So in those patients, we saw really a prolonged disease stabilization that these experts at Columbia University thought was clinically meaningful. So they reached out to us and thought that it would be exciting for them to test our compound. And as you can imagine, we were glad to support such study with one of the leading global center. I mean, one of the most prominent sarcoma centers in the U.S.

So therefore, we started the study as ATX-101 monotherapy in sarcoma patients. And saw actually activity in the first patients, but what is more interesting to note is that these scientists at Columbia University have conducted also experiments in preclinical models using our compound. And what we've been able to show is they have

been able to reproduce practically all the data in sarcoma, of course, that we have also generated in our own labs. So that's an independent validation of our preclinical data by a world-class medical center.

And another second point of interest is that while doing those experiments, Columbia discovered without a surprise to us that if you combine our drug with other drugs, it has even a better therapeutic effect. And obviously, combination therapy, again, once again, becomes relevant for sarcoma, as I will analyze in the following slides.

So if we could move to the next slide. So I've talked about these 2 ongoing clinical studies. I've talked about the numerous possibilities that APIM has. This slide shows 2 studies that we think are worth performing. So that's why the study title is Planned Studies, and these studies address both indications with extremely high unmet medical need. These indications are glioblastoma, and the second indication is ovarian cancer, again, but a different -- more aggressive subpopulation called platinum-resistant disease. So why we want to target that indication -- those indications? Primarily because we have very good published preclinical data supporting use of our drug, together with different combinations in those indications.

So based on this preclinical data, and also input that we have received from key opinion leaders, we are highly motivated in starting such studies as a further step to validate our technology and provide, of course, the necessary efficacy data that is needed in order to advance to subsequent stages of development.

So if you go to the next slide, so this slide practically summarizes -- it gives a snapshot of our clinical development pipeline as we see it. I talked about the finished Phase I study, and the study report that was concluded and available earlier this year. We're now seeking to publish submitted those data. And then you see the 2 ongoing studies, the ovarian cancer and the sarcoma study. You see that these studies within the next period of time, and we have already achieved the safety endpoint on time. These studies will deliver progressively data, efficacy data, in increasing numbers of patients over time, aiming to provide, of course, the final proof of concept that we need in this indication.

On sarcoma, I told you that we were pursuing a monotherapy clinical study. Actually, we have to revisit this approach that we have right now, thinking that if the combinatorial approach is working so nicely in preclinical models and the investigators are willing to actually prioritize that in patients, actually, makes sense to combine our drug and follow a combinatorial therapy approach. And you can also see here that if we follow that approach, we will be able to initiate that in 2023 and deliver already efficacy readouts, clear efficacy readouts in the period to come.

Of course, we have the 2 planned studies that these studies that we would be willing to initiate, of course, already in 2023. And these studies, this unmet medical needs, actually come with rapid output in terms of final very relevant data practically on the ability of these patients to remain progression-free, and of course, survive in those indications. So overall, a pipeline that it has to offer over the next period of time, several inflection points, and we believe it's an exciting mix of studies that are aiming to validate, as I said, our technology going forward.

In the next slide, we summarize why do we want to do that. And I think we want to do that because having an innovative technology, we really want to deliver solution to patients. And you can see on the left-hand side of this slide the need in patients. In ovarian cancer, this need, depending on the population that you are targeting, is high or very high. You see that patients actually live less than 2 years in the first population, even almost a year, only 1 year in the most advanced population. And you see the same numbers below for sarcoma, a year, about a year in survival. And the glioblastoma even deadlier. So you can imagine that the medical need is so high that it drives treatment, it drives actually introduction -- fast introduction of therapies such as ours.

Now in the middle column, you see what the positioning is and the patients that we want to target within those indications, practically in ovarian cancer or glioblastoma, the majority of the patients with this indication. And in the sarcoma 90% or 100%, and in sarcoma 40% of the patients, so significant numbers of patients. And we -- our aspiration is really going forward to provide a new therapeutic option in combination at the second line or first line setting depending on the indication, first line in glioblastoma.

Having said that, and I told you about these unmet medical need and our positioning, obviously, this translates into a significant market potential. You see on the upper part the total market size. So a quite significant market size for these 2 ovarian cancer sarcoma indication, a bit smaller for glioblastoma, but still significant market potential.

On the bottom, it's actually interesting to know, I don't have time to go through this, but that's part of our technology offering, and what we bring on the table in this transaction is potential market values for indication that APIM has already validated preclinically. We have done quite a lot of work in those indications, and we have data supporting development in those indications. And these indications are also big markets. This is the reason why I've told you in the very first slide that the potential for development for APIM Therapeutics with different combinations and different indications is really so high.

So going to the next slide, actually I believe that the combined company, and of course, in APIM, especially at least for what concerns the ongoing part of the studies, is it offers a global program because these studies are running in different territories. And our idea is, of course, to globalize our program and make regulatory authorities aware of what we are doing. So we are working with them, the FDA and other authorities to make our program global. So it's a global program in attractive solid tumor indications. And what we have taken the -- and I really need to point that out. We have taken the approach that our technology, our pipeline, needs to offer a diversified risk profile.

If you put all your money into a high-risk indication, of course, there's a high risk that you will fail. So we've built our program after consulting with regulatory authorities and key opinion leaders, trying to diversify risk, mixing studies that have different risk profiles. And that due to avoid, of course, costly failures. That is why we have this mix of studies that we are running and studies that we would like to be performing. So I talked about these major 2 ongoing Phase II studies, which are important studies, advanced studies. They are now set to deliver significant data, and this is exactly the value that APIM brings on the table, and I've talked about plant studies supported by preclinical data.

So what I haven't said is that due to the unmet medical need, which is extremely high, we have also the potential for accelerated approvals in orphan drug disease status. And this is something that needs to be taken into account while evaluating our portfolio, really. And I told you about the markets.

Now we are excited to be discussing with Nordic Nanovector and evaluate the pipeline of candidates, that's for sure, in order to define a combined pipeline. But for what concerns really our aspiration going forward in the combined company, and me, as the CEO of the combined company, is really to be able to deliver this multiple value inflection point really, and this is really our aspiration.

Before turning back to Jan for concluding remarks, what I wanted to really tell you is we -- as you may have read about it and heard by Jan, we have spent the last 3 days talking to -- and I'm sitting here with Malene next to me and the team of Nordic Nanovector in other parts of this office. We have spent 3 days discussing with the Nordic Nanovector team, and I can tell you that I see great chemistry between the 2 companies. I see great synergies between the 2 companies. Nordic Nanovector has a very significant oncology development experience and know-how. This is not to be neglected. Matching this with APIM assets gives actually an outcome -- a company, a combined company that has a lot of potential. And I see that from the first days of interaction that we sat together, and each company presented technology to the other company. I see great synergies. So I'm really satisfied with all discussions.

Obviously, it's still early. We need to discuss more. There will be more discussions. We will also organize presentations and other -- going forward. We're hoping to organize also an R&D Day and discuss all these programs in more detail. But as this first discussion took place the last 3 days, I mean, that was a fantastic synergies and good chemistry between the companies. And this is important really to note. So I'm really happy to be in this position, and looking forward to next steps with working together with Nordic Nanovector, and I hope you can endorse this strategy.

So with that, I want to turn back to Jan to sort of put forward an overview, and thank you very much.

Presenter Speech

Jan Egberts (Executives)

Thank you very much. Yes, I think you can hear the excitement in Kostas' voice. Also the positive meetings he has had and then both teams had with each other. And frankly what I think is a super attractive pipeline of the 2 combined companies with multiple short term goals in the not-too-distant future. So I think we're all excited. I hope you are too.

But switching gear a little bit, talk a little bit about the upcoming Extraordinary General Meeting. So the shareholders who want to attend this meeting, they really must register no later than next Tuesday, which November 29 at 4:00 p.m. You can attend either in person or you can vote by proxy, so written. The deadline for the proxies and the advanced vote is really also that November 29, next Tuesday that I mentioned. Until the deadline, you can change your vote, you can withdraw your vote.

But anyway, I really -- and with me and all my colleagues and the Board really encourage you to participate, vote in advance or come to the meeting. To get very technical, how you get -- how you go in your electronic registration, that is through nordicnanovector.com, where the link is and then you -- as [Indiscernible] indicate, you do need a pin code to get into it.

You can also, for personal attendance, work through our -- the bank that conducts or supports the Extraordinary General Meeting, Nordea Bank, and you can use the e-mail address nis@nordea.com. In this case, you don't have to use a pin or a reference number. So anyway, there's more information -- more detailed information if this went a little too fast on our website, where you can find more about it.

So anyway, in short, I think we're all very excited about the proposal. We have spoken with many of you. Frankly, we have not heard any alternative viable approach or scenario or merger candidates. So we hope you all propose to support us during the upcoming Extraordinary General Meeting.

Having said that, I'd like to hand over now to the moderator for some Q&A. Again, we'll answer the questions in English in case I'm doing it, and then we'll translate it in Norwegian, and I think Malene is going to help with one of the other moderators. Thank you very much.

Answer

Unknown Executive (Executives)

Thank you, Jan. We'll just turn to questions and try and take them in order. So the first question, we have a series of questions, which really relates to Nordic Nanovector's early-stage pipeline, which I think can best be summarized by asking whether you can provide any further updates around the early-stage Nordic Nanovector pipeline at this stage in terms of the current status of key products such as Humalutin, potential combinations for Betalutin or any of the other early-stage products in the pipeline.

Answer

Konstantinos Alevizopoulos (Executives)

Malene, do you want to take that question as CEO.

Answer

Malene Brondberg (Executives)

Yes. Maybe you want to start, then I can follow up.

Answer

Jan Egberts (Executives)

No. I mean, short of it looks very positive. It's very early stage. So it's still not in the clinic. So it will be very difficult to financing in a public market environment, we as a publicly traded company. Really, in particular, since the stock market has changed so much for the wars over the last couple of months, financing a preclinical company, a company that have compounds that are not being pursued, that are not being evaluated in a clinical setting is very difficult. So yes, we have a number of compounds. They look encouraging, but it's very, very early stage.

Answer

Malene Brondberg (Executives)

Yes, then I can maybe also just add that if you could -- if you look at the slide with the process that we've been through, you could also see that we have talked to big pharma and other biotech companies and so on. And they

have, of course, also looked at the pipeline, which is also an expression about our view on that. It is a very early stage pipeline. It's not that there's not interesting projects, it's just very early days, and I think that should also be taken into account that others have looked at it as, again, it was plus 25 companies that have been in this process.

I think for the individual projects, I don't think we should comment on each one of them. As you know, what we have said, and I know that's another question coming in as well, we have the ASH presentation coming up in December. That is, of course, very, very interesting. But again, it is very, very early days for that day program. And you can even -- Jostein has also participated in an interview today, which I think has maybe just gone out on med watch. And there, you can actually also see what Jostein is saying on the pipeline, and how he also view this opportunity with APIM.

And I think that's -- that, of course, as he is our CSO, that definitely needs to be taken into account, and he is also one of the co-founders of Nordic Nanovector, and he is fully supportive of this transaction. And of course, he knows better than anyone what we got in the pipeline, but also how far it is from just getting us to the states of where we were with PARADIGME.

Question and Answer Operator Message

Operator (Operator)

Thank you, Malene. [indiscernible].

Answer

Jan Egberts (Executives)

The other comment I'd like to make is, as Kostas mentioned, we're currently evaluating our joint pipeline, and we are in the process of -- we are planning to organize after the merger an R&D Day where we'll go in more detail.

Malene, do you want to translate to Norwegian because...

Answer

Malene Brondberg (Executives)

No, I think we would do that in the end of the call, maybe.

Answer

Unknown Executive (Executives)

So the next question asks, could you please comment on who the advisers were on either side of the transaction for each company? And then there's a specific question for Kostas, which is a note that he is an adviser to Ventac, and a question as to whether or not that organization has been assisting APIM in regards to the transaction.

Answer

Konstantinos Alevizopoulos (Executives)

Should I?

Answer

Jan Egberts (Executives)

Go ahead.

Answer

Konstantinos Alevizopoulos (Executives)

No, for what concerns the part of APIM, obviously, when we say independent valuation by an international party that conducts valuation, we also recognize ourselves that this cannot be an entity for which there is a relationship...

Answer

Jan Egberts (Executives)

As a legal side -- excuse me, Selmer is our legal adviser and Carnegie is our bank. Then we'd have...

Answer

Malene Brondberg (Executives)

And then you can see from our press releases, what we've also said is that KPMG has helped us with the fairness opinion.

Answer

Konstantinos Alevizopoulos (Executives)

Of course, I can say that our legal adviser was short in this transaction, so which is a well-known, of course, legal law firm. I mean, this has been already communicated, I think.

Answer

Jan Egberts (Executives)

Yes. But the point that Malene made and I forgot, thanks for adding that, KPMG did also the valuation of the combined entity and gave this as a borge to ensure it's a fair valuation. So that's an important data point for our shareholders.

Answer

Unknown Executive (Executives)

The next question is essentially around the timing of the merger, and asks whether you can comment on the timing, particularly bearing in mind that there are value triggers ahead for both APIM and Nordic Nano in the relatively near term. And this question specifically refers to the posters of ASH, which Malene already mentioned, and potential results from the CD37 CAR-T program.

Answer

Jan Egberts (Executives)

Yes. I mean, as I mentioned, Kostas will be the CEO of the combined entity. We'll obviously have the EGM next week, next Thursday. After that, assuming that will get approved, which I do; assume, we would close the transaction relatively quickly, probably in a matter of a week. And then the combined company will be run under the guidance and direction of Kostas. So I assume that that's the question that was asked. Closing should be approval during the EGM, the Extraordinary General Meeting of Shareholders, and closing probably about a week later, give or take. With that, we'll leave you for [indiscernible].

Answer

Unknown Executive (Executives)

I think this question was also trying to get at the timing of the merger in relation to the fact that there are some upcoming data points for both companies.

Answer

Jan Egberts (Executives)

Yes. I mean, the 2 separate companies will continue to do the work they have been doing. So I really don't expect any changes there. People keep working on what they have been working on. So there's no change there.

Answer

Konstantinos Alevizopoulos (Executives)

I can comment also on that to say that on APIM side, obviously, we had a program and we have an ongoing program. And as an organization, our goal for the next period was also to expand because we, as you see, we have obtained very interesting data, and our goal was to expand our organization and to be able to conduct multiple studies. So actually, this timing -- the timing of the merger here suits us extremely well because the combined company has know-how and the combined resources that actually will facilitate the work to be done on these programs and the milestones that are planned.

So for us, actually it was a fantastic opportunity, the timing of the merger. That's why we pursued that 100% because it really fitted the plans that we have to grow as an organization and get more additional know-how in the oncology space for 2023. So it really came at the right moment for us.

Answer

Malene Brondberg (Executives)

If I could just follow up on that with the ASH posters, also comment that. Of course, the ASH posters have already been -- already out there. Of course, it's important, but it shouldn't be too much heavy weight on that. It's, of course, important, but they are already published. You can always find -- already find them on there.

Answer

Unknown Executive (Executives)

Next, we have a number of questions around financials, but really relating to the cash position of the combined company. The question is phrased different ways, but essentially asks how much cash APIM will bring to the combined company and what the cash position will be at the point of combination.

Answer

Konstantinos Alevizopoulos (Executives)

So APIM actually, at this point, brings approximately the cash situation of today is approximately NOK 75 million. That's the cash position, including warrants by shareholders that would be converted. So that's the cash position. And as we've talked previously, I mean, I think Nordic Nanovector disclosed their own numbers. I think that the core message of these numbers is that the combined company will have sufficient funds to enter 2024. I mean, that's the key take home message. Of course, we need to do, first, some consolidation work and finalize the transaction, but at this point of time, this is what we can say about the cash position, and of course, how long this cash position will last. I don't know if you want to add anything.

Answer

Malene Brondberg (Executives)

No, I think we said we had 95 end of -- roughly end of the year, but from that amount you need to deduct 25, which is a liability going into next year, because the winding down of PARADIGME continues in the first quarter. And that, of course, cost. So if you deduct that, we will roughly have 70, and then, of course, we have some transaction costs, which I also said last time, which will be north of NOK 10 million.

Answer

Unknown Executive (Executives)

I think is a subsidiary question, which I think effectively you may have already answered, but essentially asks, in light of the cash position, is funding secured for APIM's ongoing Phase II studies?

Answer

Konstantinos Alevizopoulos (Executives)

As we said, the ongoing studies, of course, I think what I just mentioned about the combined company having sufficient funds to enter to 2024 stance, we are in drug development. The studies are -- and also opening more studies requires additional funds. So certainly, going forward, we would need to raise additional funds. But at

this point of time, yes, I mean, we are funded for next year, and we would need to raise additional funds to continue supporting the studies and doing more work.

Answer

Malene Brondberg (Executives)

I think if I can just add to that, because, of course, we've spoken a lot about that also, ask Kostas just to comment on the CMC, because that's probably where we -- there is a big difference in Nordic Nanovector compared to the APIM business.

Answer

Konstantinos Alevizopoulos (Executives)

Yes. No, I mean, it is important to note that, as I said in one of the very first slide, our drug product is actually, -- of course, it comes with highly sophisticated science, but itself as a drug product, it's pretty much easily manufactured and used. So we do not have, fortunately, the limit for us and for the combined company, limitations in terms of shipment, stability of the product. So that's obviously the CMC part.

Certainly, you have to invest in further advancing your product towards commercialization. I mean, from a physical product perspective, of course, and we need to do that. But this part of the development part program comes with a very significant -- with very minor really, really risk. And just to give you an idea, actually, our drug product included in vials, dosing patient doesn't have any added ingredient, it's just our drug product. So it's pretty easy to do.

And one other point that maybe I want to make is that the plan of the studies, and you may have noted the numbers, noted on the side of the arrows, on the number of patients per study. So we also have for these studies that we are planning a very reasonable number of patients. And this translates into, of course, a number of patients that are recruited in a reasonable number of centers, and this takes the overall cost. But also the risk in recruitment, the delays, et cetera, reduces the risk. And I think this is an important factor to consider.

So from a -- and it's not my -- I would say I shouldn't comment on Nordic Nanovector operations, of course. But if you just compare in terms of the ease of using our drug, and actually, I think it would be very -- it would be actually quite simple to be able to conduct those studies from a compound perspective and the risk from that point of view is actually very low.

Answer

Malene Brondberg (Executives)

And then I can compare the CMC number, just to give some insight into that. If you look at -- we spend roughly NOK 440 million on a yearly basis in that level, and plus 60% of that has gone into the CMC. So that's...

Answer

Konstantinos Alevizopoulos (Executives)

For us, that's a big difference. With these numbers, we would make commercial stocks practically and create multi-kilogram NOK. So I mean, that's definitely we will not have this type of cost or complexity.

Answer

Jan Egberts (Executives)

Yes. So for the people who don't know, CMC means Chemistry, Manufacturing and Control. It's basically the entire process to make the drug.

Answer

Konstantinos Alevizopoulos (Executives)

Exactly.

Answer

Unknown Executive (Executives)

The next question asks, Kostas, could you comment on the clinical efficacy signals that you've seen so far from ATX-101 from the early clinical studies? And then the subsidiary question, sorry, is how is the drug intended to be used in clinical practice given its very short half-life?

Answer

Konstantinos Alevizopoulos (Executives)

Okay. Two questions. So the first question is, I've talked about the Phase 1 that we have concluded. The Phase 1 was performed by administering our drug in patients practically with no therapeutic options. Unfortunately, as you know, in oncology, advanced solid tumor patients, no therapeutic options, heavily pretreated that have already failed multiple prior treatments. The primary endpoint of our study Phase I, as any Phase I study is practically safety. You have too much heterogeneity to be able to consider efficacy results. Obviously, you monitor the responses of patients.

So we've dosed our drug as monotherapy. Remember that what I said that the optimal therapeutic effect, the optimal therapeutic effect of our drug is in combination. So monotherapy clearly has an effect, but clearly, the optimal therapeutic effect is combination. Having said that, we have seen significant disease stabilization in a lot of different patients. And in agreement with preclinical data, this were seen in practically all types of tumor types.

Can we conclude that ATX-101 will have fantastic efficacy going forward? From a clinical perspective, it's early. We cannot say that, but we have strong indications that there is clinical activity that merits further exploration. That's point #1. Point #2 is, remember what I told you, we had sarcoma patients in the study. And the data in those patients triggered the interaction with Columbia, and I hope you can agree with me that the leading center actually that has been, let's say, the target of any pharma company to run collaborations with because they are at the forefront of sarcoma research.

If these researchers consider that the data is worth conducting an investigational study, that they run practically at a very low cost, I think this provides really validation on the value of the Phase I data that we have. So we believe that, of course, it's early in development. Phase II now it's the development that will deliver the actual results. But I think the data is there to suggest promising activity.

Now in relation to the second question, whether the drug, I think it was -- the half-life was one thing. The other thing was how do you administer, if I remember correctly. But that's a weekly intravenous infusion. But when we dose it in combination, we actually use it together with partners. So if 1 drug is dosed on day 1, then our drug is dosed in day 2. And then when the next time the patient gets the second dose of chemotherapy, they also take the second dose of our drug. So it's really tailored to the combination therapy.

Now for what concerns half-life, there are 2 ways to dealing with it, to addressing this question. First of all, what I just mentioned on the preclinical data -- and what I mentioned on the Phase I data was conducted with this compound. So it gives you an idea that whatever the life of the compound is, it's sufficient to deliver activity. So that's, of course, an indirect point, but a point that needs to be made.

Now for what considers the half-life, I don't want to be too technical, but that's a technical question. Typically, a half-life of a compound is important. But in our case, our drug gets into the tissue extremely fast. So where you measure half-life is actually something which doesn't really mean much for this type of compound because the compound in 1 minute is already in tissues. I think the relevant question is, okay, it has a short half-life in the blood? It disappears. How long does it last in vivo? And we have data preclinically to suggest that the effect lasts for several days.

So if you put all these things together, I think there's good evidence from preclinical and early clinical data that the compound is active, and we are now looking forward to dosing it in combination, which we expect will deliver the best effect.

Answer

Unknown Executive (Executives)

A question about the operations of the combined company, which asks, can you tell us what the total number of employees for the merged company will be? And will you have -- or is there a plan to have offices in both locations?

Answer

Konstantinos Alevizopoulos (Executives)

Should I take that?

Answer

Malene Brondberg (Executives)

Yes.

Answer

Konstantinos Alevizopoulos (Executives)

So I think the combined company, Nordic Nanovector, I'm sitting here in the facilities of Nordic Nanovector, and people are housed here. So in my view, the labs are here. We will be here. I think the combined company will be based in Oslo at the Nordic Nanovector facilities, which are here, and the people are here. So that's an easy decision to actually be made.

For what concerns the head count, we are still -- and I have to say that we have been discussing and discussing clinical programs. We have been discussing integration. Certainly, the number, the exact number of -- I was actually making the organizational chart this day. We do have a number of personnel. I think will be around 12 to 15 people, approximately the combined company. We're still discussing actually. And this will include positions to be hired, also some positions to be hired, for example, supporting manufacturing and functions that need to -- are needed to support further development and the network of consultants.

So we will exploit some of the consultants that Nordic Nanovector was using, and we'll also use some of our consultants, I would say, 12 to 15 people with the new hires plus a few 6 or 7 consultants that are working and supporting the company. That's, at this point of time, the predicted size of the company. But as I said, we just had the third meeting. We have been overwhelmed with the transaction. We really need to sit down and consolidate all this, and this is exactly what we will be doing following acceptance, hopefully, of this merger.

Answer

Unknown Executive (Executives)

Malene, we've come to the end of pretty much most of the questions in English. I don't know whether we can hand over now and whether there are any subsidiary questions in Norwegian that you would like to address.

Answer

Malene Brondberg (Executives)

I don't know. Do you see any of them? We, of course, try to address them in Norwegians. The one that we've seen here, I think it's more of the same. I would say that we can -- initially, we watch them here on the screen.

In general, I would just say if some of you that haven't got an answer, then, of course, get back in touch and then we will definitely either call you or we will send them on e-mail. And again, we have nearly 12,000 shareholders. So it is a lot, plus there is still a lot of documents that needs to be prepared in connection with all of this that needs to be ready for next week. So we are basically working 24/7 to get this to go. And I think maybe we should -- I don't know, should we turn over to the Norwegian questions now?

With that, I think I will turn back to English, and then Jan, I will ask you for the concluding remark.

Answer

Jan Egberts (Executives)

Okay. Thank you very much. Now I hope you are all equally excited as we are about this proposed merger. Again, I think that's a great chemistry with team. It's very indicated also everybody is sitting together in the room in Oslo. So in short, I hope you will support us with this transaction and vote in favor at the upcoming EGM, either in proxy or in person. If you have any follow-on questions, we have all been able to find us, so I'm sure you'll continue to, and we'll try to answer them as expeditiously as possible.

Thanks so much, everybody, and have a great day. Bye-bye.

22.11.10. APIM Therapeutics AS, Nordic Nanovector ASA- M&A Call

Presenter Speech

Jan Egberts (Executives)

Good morning, ladies and gentlemen. Welcome to the Nordic Nanovector and APIM joint webcast where we will discuss the merger between our 2 companies. My name is Jan Egberts. I'm the Chairman of the Board of Nordic Nanovector. Together with me here are Malene Brondberg, our Interim CEO and CFO; as well as Kostas Alevizopoulos, I hope I pronounced his name correctly, the CEO and CFO of APIM Therapeutics.

I will first take you a little bit through the headline of the transaction, and then Malene will take you through some of the implications on the Nordic Nanovector side. Thereafter, Kostas will tell you a little bit about APIM Therapeutics and give you a bit of an overview on the company.

So first of all, I want to give you a couple of comments. I realize that many of you had a desire for more information over the past couple of months during the aftermath of the PARADIGME situation and the strategic review that we conducted together with the help of Carnegie. Unfortunately, due to the very sensitive nature, particularly stock-sensitive nature of our discussion and due to the guidelines of the Oslo BÃ¸rs, we were unable to provide you more information than we have done.

And really, we were very much governed by what could be said because, number one, we have to adhere to all the guidelines of the stock exchange. But secondly, we also want to make sure we give you 100% correct information. So in a bit a bit of an apologies, we haven't been communicating as we probably would have liked to, but that's just the reality of being a public company in a very stock-sensitive situation. At the end of the presentation, there will be an opportunity to ask some questions to the 3 of us: Malene, Kostas and myself.

Now I'd like to go to the next slide. I really urge you to very carefully review this page. We are going to make some -- this is a disclaimer about some of the forward-looking statements we're going to make, which is very important that you review this page very carefully.

On the next page, after a very disappointing announcement we had to make on July 5 of this year regarding the fact that the Board had to decide to discontinue the Phase II PARADIGME clinical study, we -- as you know, the Board decided to explore alternative strategic opportunities for Nordic Nanovector. A lot of very hard work has taken place, particularly between our leadership team, which particularly included Malene and Fredrik Haavind, our Chief Legal Counsel; the Board and our strategic advisers, Carnegie and Samer.

But I think we're -- at the end of all the hard work, we're very pleased to announce the merger between Nordic and APIM Therapeutics. Let me give you a bit of a highlight of the transaction. As I mentioned, we started the strategic review in August, and we have completed it now. And we have agreed with APIM Therapeutics to merge in an all-stock deal. I think the objective is to create a larger clinical-stage oncology-focused company, and that's really what we're attempting to do here.

Our combined company has a very broad oncology portfolio. I'll take you a bit through the highlights, particularly from the APIM side because you might not be as familiar. And again, Kostas will provide you more detail later in the presentation. But APIM's key asset is ATX-101, which is a first-in-class peptide, representing a pipeline in a product opportunity. And again, Kostas will talk a little bit more about it.

Currently, the ATX-101 is in a Phase I -- combined Phase Ib/IIa clinical study in ovarian cancer and in a Phase II study in sarcoma, 2 very difficult-to-treat types of cancer. Other near-term clinical opportunities from APIM include there in oncology. And there are some additional indications or contraindications in solid tumors and hematological malignancies.

In addition, we still have our Betalutin and other clinical-stage CD37-targeting programs, including the announcement we made last week regarding a more humanized version of our lead compound. So I think in short, the combined company has a very competent and experienced management team and also a very strong group of international key opinion leaders in the area of oncology. Also very important for our investors is to know that the combined company has funding through or into 2024. It's a very important data point.

On the next slide, I want to take you through a little bit what has happened over the last couple of months and give you a bit of a flavor on the work that's taken place. Again, like I mentioned earlier, this work was

particularly executed by Malene and Fredrik Haavind, our Chief Legal Counsel, with the support of the Board and our legal advisers.

Immediately after the announcement that Nordic Nanovector made very significant cost reduction in order to extend our runway, very quickly, our headcount was reduced from about 70 around -- in the middle of December to 8 FTEs today. And that's essentially Malene -- 2 people in the leadership team and then the rest are people in R&D, which is hopefully a key asset in our organization. More than 100 contracts had to be terminated, particular contracts related to the PARADIGME clinical study with external partners.

So a lot of very significant contracts. And they cannot be completely terminated. Many -- when you terminate a clinical study, you need to do follow-on work. So we need to recognize that, and we need to reserve cost for that. And we need to reach agreement with those partners how we're going to terminate those contracts.

Very quickly, the Board was reduced from 6 members to 3 members, and the leadership team was reduced from 6 members to 2 members. We closed the Danish office, and we significantly downsized the Swiss office.

In parallel, we initiated a broad strategic review of Nordic Nanovector, where we really compared 2 broad options. One is, can we develop a viable gold-alone strategy by leveraging our existing portfolio -- the existing Nordic Nanovector portfolio. And we compare this with the help of Carnegie external viable M&A opportunities.

With respect to looking at the M&A opportunities, we essentially used an approach of concentric circles. The primary focus was a Norwegian-based oncology companies. So basically, companies very with the activity that we are pursuing and in the same geography. And our secondary focus was more on Nordic oncology companies. And thereafter, there were a couple of other companies that were more [incendiary] space.

But again, our primary focus was to find a company that was very close to what we're doing from a strategic point of view. The team had discussions with over 25 companies in the Nordic and international arena, also in the U.S. and in the Far East. So a very broad portfolio of companies we have spoken with, more than 25. And again, the primary focus of the team in this part of the evaluation was a strategic fit. Again, we are in oncology. We were most interested in other oncology company; and secondly and very importantly, optimizing shareholder value.

With respect to the shareholder value, the situation is hopefully that every day, you can read our market cap on the web because we're a public company. So it's very straightforward what the market thinks about us. And as the Americans always joke, the market never lies.

And finally, we performed very extensive due diligence on both ourself or database available for particular -- for parties that were interesting merger and on the selected M&A targets. In order to run this entire process, we had weekly meetings between the management team and 3 Board members; Joanna Horobin, Karin Meyer and myself and our advisers to support the process and monitor progress. Then finally, we've got extensive legal support from Selmer, and we conducted the fairness opinion of the transaction -- or had executed a fairness opinion of the transaction by KPMG.

Let me give you a bit of the details of the transaction. Again, it is a merger of Nordic Nanovector with APIM Therapeutics. APIM is a privately held, clinical-stage oncology company based in Norway, as I mentioned before. It is an all-stock transaction, which means that Nordic Nanovector will issue new shares to APIM Therapeutics' shareholders. So they will acquire shares in Nordic Nanovector, and Nordic Nanovector will be the surviving entity.

Upon completion of the transaction, the former shareholders of APIM will own approximately 3/4 of the new company -- excuse me, Nordic Nanovector current shareholders are expected to own about 25%, 24% to be exact. Pursuant to the transaction, previously issued warrants in APIM will be exercised, which will raise an additional NOK 55 million. In addition, APIM Therapeutics together representing over 100% of the shareholders have agreed with this merger agreement, which is very important. So we know for sure that that's all taken care of on their side. Also, the major APIM shareholders, representing over 70% of their stock, have agreed to 12 months lockup.

In terms of the leadership team and the transaction time line, the management and Board of new company, as you know, I'm currently Chairman of Nordic Nanovector, and I will continue to be Chairman of the combined company. Kostas Alevizopoulos PhD, who is currently the CEO of APIM, will be the CEO of the new combined

company, and we'd like to welcome him here today. And again, he's going to talk a little bit about APIM in a couple of minutes.

The R&D teams from our side, Nordic Nanovector, and APIM will be combined. And obviously, Jostein will continue in his role. Further details will be announced in due course. Also, the exact composition of the R&D team will be communicated at a later stage.

So just to run you through the chronology. August 18, we announced a strategic review. On November 9, we announced the proposed transaction, so basically last night. Before this, we had dialogue and conducted due diligence on a lot of different parties in the period between the announcement and last night. And here today, we are giving you the presentation.

It's important, we're going to ask the Nordic Nanovector shareholder approval for this transaction. And we expect the EGM, the Extraordinary General Manager (sic) [Extraordinary General Meeting] to be held around December 1. And then we expect the closing of the transaction to take place later in the fourth quarter.

So now I'd like to hand over to Malene to talk a little bit about the update for Nordic Nanovector side.

Presenter Speech

Malene Brondberg (Executives)

Many thanks. Jan, if we could have the next slide, please. Thank you. So I'm just going to give you a brief update on what it is that we've done since we spoke at Q2. As Jan said, now the restructuring is complete, and we have now 8 full-time employees in the company. We have now also terminated all large contracts. And here, we're talking about the Icon contract, as we said on the last call. And we also terminated all our large CMC contracts.

And every time you make changes like these in a company, this always have a time effect and lack, and that's why it's very important that we got that done straight ahead. Because, of course, despite that we terminated the trial in July, it takes time before that all of this takes effect.

If you look at our cash position as a standalone, we expect end of the year to be roughly NOK 95 million. Further commitments related to the closure of the PARADIGME will happen during the first quarter next year, and that is expected to be around NOK 25 million.

As a result of all of this, we have an uncommitted net cash at a level of roughly NOK 70 million. And from that, that excludes any costs associated with the announced merger transaction.

So with that, I would like to hand it over to Kostas, and I'm pleased to see Kostas.

Presenter Speech

Konstantinos Alevizopoulos (Executives)

Thank you, Malene. Thank you, Jan, for the introduction. So welcome, everybody, in this meeting. And I'll be -- I'm excited to be able to present APIM Therapeutics for the first time to you.

Before I provide information about the company, since you haven't met me previously or have heard about me, let me say a few things about myself. So I'm a scientist by training. I've done with doctoral and post-doctoral studies in Switzerland and in the U.S. in molecular oncology. But more than 20 years ago, I decided to leave the academia to focus on biotech because I was always interested in practically turning ideas into interesting new technologies that could help patients.

So as I said, this is what I've done. And over the last more than 20 years, I've been involved in several biotech companies, initially focusing on research as Head of Preclinical Research, Head of Research before I, over the years, turned into Chief Executive Manager roles -- Chief Executive Officer roles. My expertise that have built up over the years is exactly development of interesting new assets primarily in oncology, but also other indications such as inflammatory diseases into -- from ideas into clinical programs. And this is the experience that I've been enhancing on over the last years.

This is -- this experience brought me to APIM Therapeutics, where I was recruited as a Chief Executive Officer since the beginning of its corporate life. And we have been able to turn interesting research by NTU to this

technology and assets that we are developing right now. And we've been able to bring this technology to the clinical-stage level, generating in the meantime very interesting data that I will present in a few minutes. So I'm really excited to be part of this new venture, and I'm looking forward to working with Nordic Nanovector and also working with you in making this joint company a success.

So if we go to the next slide, I can present also some additional information about our company. As I said, the company was created in 2010 as a spin-off from NTU in Trondheim, where our company headquarters are found today. This was based on work by Prof. Marit Otterlei, who's a professor at NTU. Currently, we are at the Phase II clinical stage developing our drug candidate, ATX-101, in oncology. And I will spend more time discussing about our therapeutic intervention point, which has a broad applicability in a lot of different tumor types.

We are a small, highly motivated and engaged team in APIM. We have benefited from support by a network of consultants, by a lot of advisers. And as I said, we've been successful in bringing this asset from an early idea to Phase II clinical stage, being supported in the meantime by a strong Norwegian investor base. You see the logos at the bottom of the slide. I'm sure you are familiar with those names. And these investors will be supporting us also in the next period of time.

Up to this transaction, the company has raised NOK 210 million in equity grants and tax rebates, and these have been used exclusively to finance R&D operations within the company that I will briefly present in the next slide.

Before I go to the next slide, actually, a few things about us. I've presented myself from the management team. You see on the left-hand side other members of the management team. Jens-Peter Marschner. He's our current Chief Medical Officer. He brings also significant experience in the development of oncology and commercialization of oncology assets, the environment of big pharma. So Jens-Peter, or JP as we call him, will remain and become the Chief Medical Officer of the combined company.

Marit Otterlei is the -- currently the Chief Scientific Officer of APIM, but really she is the inventor and the heart of APIM Therapeutics for all these years, she remains a professor at the Department of Cancer Research and Molecular Medicine. In the combined company, Marit will take a scientific advisory role, and she will maintain a relationship with the company, supporting the clinical development and preclinical development of ATX-101.

And Hans Olav MinsÃ¥s is actually a part-time Chief Financial Officer working from us as -- supporting us. And in the -- he will continue supporting the company going forward, but his role will be modified in the combined company.

On the right-hand side, you see our Board of Directors. So overall, an experienced Board of Directors. I'm sure you're familiar with some of those names. They are -- Board of Director members are also representing major investors in the company. We do have a couple of other very experienced individuals: Martin Welschof, who's the CEO of BioInvent and other oncology company. GÃ¶khan Batur, who's actually an adviser and member of our Board. And he has been really a key factor as well in making this transaction with Nordic Nanovector happen.

So in the next slide, this is a snapshot of our clinical pipeline in ATX-101 development plan. First of all, I have to say that we have conducted first-in-human Phase I study with ATX-101, which has -- is now finished. This study has shown -- has proven that our compound has a very favorable safety profile and provided indication of clinical activity. And this is really the study that has led to the development program that we are running right now with the colors.

On top, you see the 2 ongoing studies that we have in ovarian cancer, Phase Ib study, the first part of the Phase Ib/IIa study in ovarian cancer and a Phase II study in sarcoma. The first study is a combination study with standard of care, doxorubicin and carboplatin. And you see on the right-hand side, obviously, these names do not say much to you, but what I wanted to highlight is that while executing those studies, we are interacting with distinguished key opinion leaders: Prof. Meniawy, who's the primary investigator of our ovarian cancer study. He's a world-known expert in ovarian cancer, the Head of Australia and New Zealand Society; and Prof. Gary Schwartz who is a Columbia University professor. Actually the study is being run at Columbia University, New York. And he's one of the biggest sarcoma experts in the world.

So we benefit from very important and prestigious key opinion leaders in managing those studies. And so these studies are running. We are at the parts that you see on the slide, as I said, with the color. And up to now, we have been receiving promising results. First of all, no safety issues with our compound, which is very important,

especially in combination studies. And initially, we have seen quite a lot of -- we have seen clinical activity in patients. Obviously, the studies are ongoing, and we will be reporting significant data as we go forward over the time line of those studies, as you see depicted on the slide.

More importantly, it is the goal of our company to initiate additional studies in late 2023 in indications with very high unmet medical need. And these studies are another ovarian cancer study in a different population, platinum-resistant ovarian cancer as well as an indication, which is -- has a tremendous medical need, glioblastoma. At the same time, as we're running our development program, we will, of course, invest and advance our product development of our ATX-101, preparing for larger Phase III studies and also for commercialization. And this is part of our development program going forward.

In the next slide, please. I will try to present just some high-level details on the mechanism of action. It's a really highly scientific mechanism of action. I think the title really gives you an idea of what we are trying to do. We are trying to address cancer escape mechanism, which everybody recognizes that are really important in dealing with this deadly disease.

So our target is a protein called PCNA. It's practically an organizer protein found in all cells that performs its actions by interacting with other different proteins. And the processes that this target is participating are shown on the bottom left-hand side. What is important to know about these processes that these are extremely important processes for normal and cancer cells to be able to survive and proliferate.

What is more important is the implication of the target in cancer. Based on this work conducted by Prof. Marit Otterlei at NTU, it will show that this specific target plays a role in the response of cancer cells to anticancer therapy. And when a cancer cells is treated by anticancer therapy, it tries to survive. And by trying to survive, it activates stress defense mechanism, and our target is at the center of those stress defense mechanism.

So as you can imagine, if the idea here for an anticancer therapy, if the stress defense mechanism is relevant for cancer cells to survive, then it will block this mechanism, then we will be able to push these cancer cells to death and deliver anticancer activity. So this is exactly the therapeutic approach that we are developing: blocking the stress response in cancer cell.

I think the 3 major observations or key take-home messages also to make from this mechanism of action, which is novel as we are the first to target. The first thing is that this mechanism is active in practically all cancer types. So this gives us an idea about the development opportunities in different cancer indications.

The second most important point is that, of course, we are hitting cancer cells with different anticancer therapies, and we're blocking the stress defense mechanism. So we are making these anticancer therapies more active. And up to now, we have seen in the preclinical experiments that we increase the efficacy of more than 25 different anticancer drugs. Also the technology can deliver activity on its own in selected tumor types.

And the third most important observation is that this stress mechanism is actually not only relevant in cancer, but also relevant in inflammatory disease because there's also a stress response there. So this gives you an idea about potential development opportunities for also non-oncology indications.

In the next slide, this summarizes really the oncology background. I told you that the mechanism is active in many cancer cells, that we potentiate the actions of a lot of combinations. So we consider our technology as a pipeline in a product because we can develop a lot of combinations, which are key based on the mechanism of action for a lot of different indications. And we have been exactly doing so. In the last years, we invested a lot of time and effort to validate this approach, initially in, in vitro experiments, so a cellular experiment but also in animal experimentation. And by doing so, we've generated the scientific data that have been published Prof. Marit Otterlei and coworkers in a lot of scientific journals, validating the approach and our technology over the years.

And of course, by doing so, we're able to generate data that support the mechanism of action, the targeting of the stress response and the ability of our drug to really target the escape and resistance mechanism so -- in cancer cells. So this is an approach that we are pursuing right now, and this is at the core of our development program.

If we go to the next slide, please. So why have we selected those specific indications that we are targeting right now? We have selected them for various reasons. Of course, one reason is that we had extremely promising

preclinical data supporting development in these indications. At the same time, these indications are indications with really high medical need.

You see on the left part of this slide the medical need broken down per indication. For example, ovarian cancer, I've talked about briefly 2 different subpopulation: platinum-sensitive and platinum-resistant population. You see there the numbers. These patients progress in a few months, and they live overall up to 1 to 2 years. So there's a great medical need.

Our goal is to position our technology and ATX combination standard of care in the second line, and this address practically 90% of the total ovarian cancer population. In sarcoma, the medical need is even higher. You see that the interval of progression free is only -- it's less than 5 months, a survival of about a year. So really a big medical need. In that specific population, again, we want to position our drug at the second line and in soft tissue sarcoma, which represents practically 40% of all patients.

And lastly, glioblastoma, an even higher medical need there. Patients live short -- for a short period of time. And we are targeting all patients diagnosed with our disease, potentially hoping to place ATX-101 at the top line standard of care of the first line. So overall indications with various degrees, of course, of medical need and a high medical need definitely. And it's our goal as a company to develop for the benefit of patients new treatments in that.

Now on the right-hand side, you see the market potential as, of course, quite typical in oncology dealing with a high number of patients. You also see that there's a significant market size both at the level of ovarian cancer and sarcoma and glioblastoma. I -- some of those indications I would like to mention also have orphan status, which allows us potentially to benefit from accelerated approvals and also protection against competition.

And on the bottom hand of that slide, you also see other indications for which APIM has already generated preclinical data and could be potential indications to develop our drug in the future. Again, significant market potential also inflammatory diseases, as I mentioned, overall, bringing -- creating a significant market potential.

So I think the take-home message from these slides of APIM that I want you to stay with is that this is really a totally new mechanism of action. We are first to target that action. It has really a broad potential in a lot of different cancer indications. We are already beginning to see promising data in the clinic. So we hope we can deliver more interesting data in the future and really create value to the -- to APIM and now the combined entity.

So with this, I would like to turn back to Jan and to -- for the remaining couple of slides in the presentation.

Presenter Speech

Jan Egberts (Executives)

Okay. Thank you very much. Very exciting. Very interesting. Obviously, we still have our key asset, our CD37-targeted immunotherapy pipeline. We'll continue to work with them, and we continue to see how we can -- the best way to pursue this towards the market.

You have probably seen our announcement from last week regarding the humanized monoclonal antibody, which we are very excited about, which obviously is in an earlier stage as we had to abandon the PARADIGME clinical study for Betalutin. So anyway, I just want you to be assured that the key assets we have -- the Nordic Nanovector key assets we had are not going to get shelved. We'll continue to work with them, and we continue to be excited about their model.

Okay. The final slide, we're quite excited about the merger. It really will create a clinical-stage oncology -- a Norwegian clinical-stage oncology with a very broad pipeline in late -- in the clinic, and therefore, very significant upside potential both for solid tumors and for hematological tumors.

In summary, our combined pipeline will include ATX-101, as you heard earlier, is a first-in-class peptide, really super exciting data. Then there's some additional near-term clinical opportunities for ATX-101. Again, very much focused on solid -- both solid and hematological tumor.

Then we still have our CD37-targeting immunotherapy program, which we continue to pursue. Currently, unfortunately, back in the preclinic. And then there are a number of additional opportunities in a wide range of

cancer indications. It's one of the -- first thing of the Board is going to be to prioritize what our key short-term goal.

Very important for investors, we do anticipate a very rich news flow over the next 12 to 18 months with a number of ongoing and planned clinical studies. A strong and experienced management team with a strong group of key opinion leaders -- international key opinion leaders. Significant organizational synergies, we're both in oncology, both Norwegian and I think also culturally a very well-aligned team. And we feel very confident this will enable us to create a very lean, efficient and experienced organization. As mentioned before, the combined company is projected to be funded into 2024. So in short, a strong foundation to build a leading oncology-focused company.

In summary, I hope you all are equally excited as I am an equally optimistic about the restart of our company after the unfortunate events with Betalutin. And I hope you all support us with this transaction at the upcoming EGM early December.

Now I'd like to open the floor for questions and hand over to the moderator.

Answer

Unknown Attendee (Attendees)

Thanks, Jan. Can I start with the first question? The first question is, what has gone into the valuation of the 2 companies resulting in this kind of distribution of ownership? Nano has spent billions whereas APIM has raised NOK 200 million in its lifetime as one asset and is about to start another Phase II.

Answer

Jan Egberts (Executives)

Yes. Now our devaluation of Nordic Nanovector, you can obviously read everything in the newspaper. We got significantly negatively impacted by the result of the Betalutin clinical study -- the PARADIGME clinical study. So that's a very straightforward. And I mean APIM had a private valuation. So there were a number of investors who put money in that. And so essentially, it's a combination of our publicly traded valuation, and there was a premium on that and APIM's valuation from your last route.

Just to come back to the other part of the question. The stock market, like I said earlier, as the Americans say, the stock market is always right, which is a bit of a joke and I understand. But the reality is the stock market has valued us the way it valued us today, which is a combination of the cash we have, the value of our Betalutin on our CD37 programs and some other assets we have. That's basically how the market looks at us today.

Answer

Unknown Attendee (Attendees)

Next question, could you please elaborate on any external validation or interest in ATX-101, for example, in terms of future partner-funded studies?

Answer

Jan Egberts (Executives)

Kostas, do you want to take that? You're muted.

Answer

Konstantinos Alevizopoulos (Executives)

So -- yes. So to -- so the question was to comment on potential -- could you repeat the question, please, the external validation of ATX...

Answer

Unknown Attendee (Attendees)

I think it was what interest has there been in ATX-101, external interest and whether that would help in terms of creating partner studies in the future.

Answer

Konstantinos Alevizopoulos (Executives)

Yes. So APIM Therapeutics, as you -- as I presented, is currently running 2 major oncology studies in indications with high unmet medical need. We have recently finished our Phase I study. This study was the first clinical study that actually delivered and -- the safety data, which were important to derisk a mechanism, which is totally new.

I think we are now in the process -- or we were in the process of actually presenting or starting to present those data to international investors and pharmaceutical companies. This mechanism has traditionally generated a lot of interest with pharma because it is exactly a mechanism which is totally new.

Having said that, the total new mechanism of action always generates some skepticism in the sense that pharma would like to see additional data. This is the exact data we are generating right now. So I think the fair answer to the question is that this mechanism and our technology has been presented, and this is an ongoing process. The current data is very supportive, and we hope that we will be able to actually interact further in the next period of time with the investors and pharma companies and really target by partnering approach that will deliver more value to the company. I think that's pretty much a summary of the existing status of APIM Therapeutics.

Answer

Unknown Attendee (Attendees)

Thank you, Kostas. There's a couple of questions about the pipeline for the new company. What priority will existing Nano assets get in the new setting? [indiscernible] partnership with [Rhinomed] has still not been concluded. Where are we with this?

Answer

Jan Egberts (Executives)

Yes. Let me take that question. One of the first charters of the Board is to really do a comprehensive review of the joint pipeline and prioritize what are the key assets. So that we haven't come together as a new Board. And the announcement -- we mentioned the Board member is going to be Malene and myself will be from Nordic Nanovector; Erlend Skagseth and GÃ¶khan and one additional Board member from the APIM Therapeutics side. But again, one of our first charter is going to be to do a comprehensive pipeline review and prioritize [indiscernible] that we make sure we put our resources behind the most exciting assets.

Answer

Unknown Attendee (Attendees)

That's good. And there is another question about what the future pipeline would look like. The next question...

Answer

Jan Egberts (Executives)

You can take note of the review, what I mentioned.

Answer

Unknown Attendee (Attendees)

Yes. Exactly. Next question is, what are the costs associated with the merger transaction?

Answer

Jan Egberts (Executives)

Sorry, could you repeat that?

Answer

Unknown Attendee (Attendees)

Yes. What are the costs associated with the merger transaction?

Answer

Jan Egberts (Executives)

Malene?

Answer

Malene Brondberg (Executives)

Yes. It's a little bit too early to say right now because we still have a lot of things ongoing. There is still a lot of work that needs to be done, both on the [indiscernible] on the legal side and also on the number side because we convert with a public company merging with a nonpublic company, and there are certain standards for when it comes to accounting that needs to be addressed. But we will most likely see a -- we will go into something like NOK 10 million-plus.

Answer

Unknown Attendee (Attendees)

Okay. And then there's a question about what clinical and commercial synergies can we expect to see from this merger?

Answer

Jan Egberts (Executives)

No. I would particularly expect to see a number of benefits on the R&D side. Obviously, we're both in oncology -- we both are in hematological malignancies. I think there's a strong management team. So that's the benefit of leveraging that across both -- the assets of both companies. And I think we have a strong Board. So I see a number of different areas where there will be strong synergies.

Answer

Unknown Attendee (Attendees)

Okay. And then there's a question about you, Jan, that said, "Why should Jan become the new Chairman of the new Board?"

Answer

Jan Egberts (Executives)

Yes. That's up to the shareholders. And a few more responsibility to hand it over to the -- the merged company gets a good start. Unfortunately, the outcome of PARADIGME is something that nobody can do anything about. It's -- as we have mentioned before, in oncology, a lot of compound fail in clinical research, particularly at later-stage clinical research. We have mentioned it before. But ultimately, it's up to the shareholders.

Answer

Unknown Attendee (Attendees)

Okay. And I think the final question I can see is, how do you plan to regain investors' trust after keeping everyone in the dark and the negative results of the PARADIGME study?

Answer

Jan Egberts (Executives)

Yes. As I mentioned in my opening comments, unfortunately, as a public company -- or fortunately, we're getting governed by Oslo BÃ¸rs regulations and guidelines. And they are very strict about what and how you can disclose certain information. So hypothesis you might have and/or indications you might have, you need to make sure that you're communicating 100% correct, that you communicate exactly the same information in a timely fashion to all the shareholders.

We work very closely together with our advisers, particularly our lawyers, what and when and how we should communicate. So unfortunately, I will admit there was not much communication, but we really were having -- being handicapped by the fact that we're a public company, and we are very much governed in how and what we can communicate.

Answer

Unknown Attendee (Attendees)

Thanks, Jan. I think that covers all of the key topics of the questions that were posted today.

Answer

Jan Egberts (Executives)

Okay. Thanks. Thank you very much, everybody, for your attention, and hope you will support us.

Answer

Konstantinos Alevizopoulos (Executives)

Thank you very much.

22.08.31. Nordic Nanovector ASA, Q2 2022 Earnings Call, Aug 31, 2022

Presenter Speech

Jan Egberts (Executives)

Good morning, ladies and gentlemen. My name is Jan Egberts. I'm the Chairman of the Board of Directors of Nordic Nanovector. Welcome to our second quarterly release and first half of 2022 results. Together with me here are Malene Brondberg, our CFO and Interim CEO; and Lars Nieba, our Chief Technology Officer.

On the first slide, I need to share with you our safe harbor statement, basically about forward-looking statements. I urge you to pay attention to this.

First of all, a quick update. Unfortunately, as all you have heard, is we had to discontinue the PARADIGME clinical study studying Betalutin. The reason, as have been shared before, is the difficulties in enrolling sufficient patients into that study, which made the Board consider where we are and do an interim analysis.

Now the interim analysis was executed by an independent review board, which basically, yes, came to the conclusion and the Board came to the conclusion that the regulatory feasibility of getting this product approved was such that it made no sense to continue the clinical study. Obviously, a very unfortunate and unexpected outcome.

Based on the, yes, the efficacy data which I spoke about and also the fact that given some of the recent developments in the marketplace, in particular, as related to bispecific monoclonal antibodies, we did not feel that this was a result that will yield a regulatory approval.

Based on that feedback which have been communicated to the market, the Board decided to restructuring and do that support. And to initiate that, we have requested support from Carnegie, and we're working together very closely now to explore various strategic options for the company moving forward. I'm sure some of you will have some questions. So at the end of the meeting, we'll allow you to ask some questions to go a little bit more detail about this top line slide.

So just to go a little bit more detail about the PARADIGME situation and the discontinuation of the study, obviously, we have communicated a number of times the recruitment. Initially, the recruitment was not particularly good. Then Lars came on board, recruitment significantly increased. And then unfortunately, corona hit, which really created a drop off in the recruitment. Particularly over the past couple of months of May and June, the recruitment was very slow. And we started to kind of weigh, on one side, the amount of cash we had available; on the other hand, the recruitment rate. And if you look at the 2, we as a Board felt that we needed to take a step back and analyze where are we.

So the COVID impact is across many, many clinical studies, particularly in the oncology field. And the primary reason for that is that patients with cancer, the oncology patients, oftenly are very reluctant, and the doctor is very reluctant to take them to the hospital because the hospital is being seen as a very dangerous place for those people that could get infected by corona. So many of those patients stayed home and obviously didn't go into the clinical study.

The other area I already touched on before is the fact that the bispecific antibody really emerged very rapidly on the clinical arena. So like I said before, we initiated an independent review on the efficacy data of the PARADIGME. And that review concluded that the efficacy data will not yield Betalutin competitive profile in third-line follicular lymphoma, particularly not a profile that would allow us expedited approval. So that's a very important thing.

So a couple of comments about the independent review. The independent review was done by an outside physician and a statistician. What a lot of people think is that we actually have all the data available basically that we can flip of our computer and look at it. That's not the way it goes. The direction from the FDA are very clear. These data go into a confidential file where only selected individuals, in particular, external individuals can look at the results. The primary reason is that people don't want you to look every week how you're doing in your clinical study. And the reason for that is you need to maintain the integrity of the clinical study.

So to that extent is, number one, we as a Board or management did not have access to the individual patient or the patient results and the patient data, only an external review one. Secondly, FDA is very reluctant to have

multiple interim reviews. So as you know, we had one in 2020, and it was a very special decision by the Board to do an additional one.

Currently, we're winding down the study as expeditiously as possible. Basically, there are some -- the company has some responsibilities in terms of following up the existing patients. So there are some ongoing costs associated with that, and Malene is going to talk about it in more detail later on. And some limited analysis will be done to meet the reporting requirements. So eventually, there will be a report out there kind of summarizing the top line results of the clinical study.

However, what I think is very important to know is obviously, the Phase I clinical study, the LYMRIT study, was very positive. We're still trying to understand what happened there. So there's clearly still utility of this compound in other -- in additional clinical studies. That's one of the things we're looking at it. Obviously, it might be the mouse variation, the Betalutin; or it might be the more humanized variation, which is the Humalutin. But the clear efficacy or potential of the compound, we still believe in, although it didn't work out in this clinical study.

So having said that, I now would like to hand over to Malene, our CFO and Interim CEO.

Presenter Speech

Malene Brondberg (Executives)

Thank you very much, and also good morning from me. Yes, so as Jan said, it is a very serious and also a very unfortunate situation we are in here, which unfortunately, of course, meant that we had to start to make people redundant. The data right now is that 25 staff members have been made redundant, which is approximately 70% of our staff. We have also slimmed down the leadership team and that's significantly, so that was slimmed down by approximately 60%.

We have started -- and this process, of course, started already the day after we announced this, that we closed PARADIGME. And we are now going through at least 300-plus contracts. Some of the bigger contracts like with our CROs, like -- and a CRO. I know there's been a lot of speculation. It's -- you can actually look it up on ClinicalTrials, it's been there all along, it's ICON. And we are, of course, having negotiations now with them because they need -- we need to wind it down in a compliant way and a follow-up on the patients that we have in the trial. So those discussions are ongoing. The discussion is ongoing, but of course, also our big suppliers on the CMC side.

So here, you could just see the Q2, which came in on the spending -- or the costs were NOK 103 million compared to NOK 104 million last year, so basically in line. You could see here what the -- the cash outgoing in Q2 2022 was lower than the Q2 year '21, and that's, of course, good. We have in there also we have to pay what is called a change order for the CRO. That is not in that number which, of course, also needs to be deducted.

We are right now, and as you can imagine, the team is working 24/7 to close the contracts as soon as possible. We expect the close of the contracts to be -- or the cost to be in the level of NOK 170 million to NOK 200 million. You can say that is an awful lot of money. Yes, it is. But unfortunately, we are in an industry that is a very, and of course, that is good for the patients, which is why we're here, a very regulated industry, which means that there is a lot of regulations that we have to comply with. This indicates a cash position of roughly NOK 90 million to NOK 110 million.

So as Jan also just said, we have engaged Carnegie to help us with the focusing on realizing the shareholder value. As you know, I'm a shareholder myself, so of course, we will do everything we can to get the best out of this situation. We have some key assets. We have a -- we still have a good pipeline with the CD37 headed up as -- of the guy, Jostein Dahle, and his brilliant team. We also have, as Jan just said, Betalutin/Humalutin. We have a Oslo listing and then we have some cash.

So what we have in terms of staff, we have the R&D team. We have a very few people now on the admin. And then we have a very limited team left as well on the leadership team. And that team is now, of course, trying to push forward in the best possible way. The strategic review is expected to run into Q2 -- sorry, Q4 2022. Thank you.

With that, Jan, I will hand it back to you.

Presenter Speech

Jan Egberts (Executives)

Thank you. This is the final slide, and then we want to see if there are any questions. So like I said before, the decision to discontinue PARADIGME, yes, that really follow the independent external review, very unfortunate outcome. But I think it was very important to make this decision so we can reposition the company in time.

This really prompted the restructuring of the company. Malene and her team and Lars have taken already significant staff to reduce staff and terminate the various agreements, over 300 agreements, as Malene mentioned. So that's not a trivial task. And particularly as an organization, it has been significantly slimmed down. A lot of work is being put in the shoulders of a relatively small number of people. And currently, we're reviewing very strategic options with Carnegie to realize shareholder value, and we'll communicate back as results come out of that.

So having said that, I want to open for -- the floor for some questions.

Presenter Speech

Malene Brondberg (Executives)

And here, we want to invite Lars, our CTO.

Answer

Malene Brondberg (Executives)

So we start with the audience. Yes?

Answer

Unknown Shareholder (Shareholders)

[Foreign Language] Sorry, speak English or Norwegian?

Answer

Jan Egberts (Executives)

If you can, English, otherwise, we can do simultaneous...

Answer

Unknown Shareholder (Shareholders)

My name is [Ewan Rogers], I'm a shareholder. I think you need to explain a bit more about the Carnegie mandate and the timing. Malene said into Q4, do you have a firm date? Or is this just some endless ongoing work?

Answer

Jan Egberts (Executives)

The mandate is to look for strategic options for the company in the broader sense. So that could be looking at other companies where we could potentially merge into and other things that are available.

In terms of timing, as expeditiously as possible. I cannot predict the future. We're working very hard at it, but I cannot give you a firm time line.

Answer

Unknown Shareholder (Shareholders)

This is just words, Jan.

Answer

Jan Egberts (Executives)

Sorry?

Answer

Unknown Shareholder (Shareholders)

This is just words. You have to be more firm about this.

Answer

Jan Egberts (Executives)

No, I cannot be more firm.

Answer

Unknown Shareholder (Shareholders)

Could you, in baby language, explain to me, what can Carnegie provide which the Board and the management can't provide?

Answer

Jan Egberts (Executives)

Well, Carnegie has a lot of access to companies that we have, but that's -- they're very experienced in that. Obviously, like you know, the team has been slimmed down significantly, and Carnegie is helping us with this process, very customary, number one.

Number two, in case we do have a transaction that makes sense from a strategic point of view, we need advice if the valuation is correct, both our valuation and the valuation of another company.

Answer

Unknown Shareholder (Shareholders)

In the press release on the 21st of June, you said that you should give some feedback regarding FDA. What's that?

Answer

Jan Egberts (Executives)

So there were communications back and forth with the FDA. And basically, based on those evaluations, do you want to provide the more specifics?

Answer

Lars Nieba (Executives)

Yes, sure. Thank you. Yes, based on the results we got on the 21st of June, we were in contact with the FDA. We got several written feedback from them. Based on that feedback, we went together with the Board to conclude what the FDA has written, which is confidential. And the Board concluded that a pathway forward for accelerated approval is not the path forward. So we could go forward...

Answer

Jan Egberts (Executives)

It's not viable, yes.

Answer

Lars Nieba (Executives)

It's not viable. We could go forward, but we would have to do then a Phase III trial in third-line follicular lymphoma, which the Board said is not a competitive or a viable option from a financial point of view.

Answer

Unknown Attendee (Attendees)

I'm [Helsper]. Just a quick question on tax losses carryforward. It's not on your list. So I was wondering if there is a value in the cost that you accumulated over the years.

Answer

Malene Brondberg (Executives)

Yes, of course. There is a carryforward. And it is, of course, also on our list. But that said, it has to be a very specific situation. We, of course, also looked at that from a legal point of view, how does that work. And it's not straightforward, but of course, it is there as well.

Answer

Jan Egberts (Executives)

It needs to be the same industry and there needs to be a lot of overlap. We're -- the reason we didn't mention it is we're not tax accountant, but we have retained advice from tax consultants, but the very specific requirements in order to use it. But it's clearly one of the key assets we're looking at.

Okay. So now -- oh, sorry.

Answer

Unknown Attendee (Attendees)

First of all, congrats to Malene on the new position. Do you consider the combination treatment with Betalutin and rituximab to be a valuable asset for the company?

Answer

Lars Nieba (Executives)

Yes, very good question. Yes, sure. As you know, our Archer-1 trial was a trial which showed pretty good results. And part of the interaction which we had with the health authorities, in particular, of course, the FDA, was to go -- to think about how can we move forward in a combination therapy in second-line follicular lymphoma. And one of the possible combination partners is, of course, rituximab. So we have a synopsis for that, but we move ahead. And as pointed out by Jan, we do see the potential to move ahead with either Betalutin or Humalutin. And if so, we would do it in a combination trial.

Answer

Jan Egberts (Executives)

But just to be clear, that would require a new study.

Answer

Lars Nieba (Executives)

A partner, yes.

Answer

Jan Egberts (Executives)

Yes, it would require a new study...

Answer

Lars Nieba (Executives)

It would be Phase II, Phase III.

Answer

Jan Egberts (Executives)

Very significant expenses, so it's not...

Answer

Unknown Attendee (Attendees)

Well, thank you for the answer. Some quarters ago, you were asked why you didn't recruit more patients into the Archer study, and then [one couldn't] all the answer because you have got the answer you needed already. Could you be a bit more specific about what types of answers you got from those 7 patients, which as far as I can see now have obtained a median duration of response of 3 years?

Answer

Jan Egberts (Executives)

Before you answer that, I want to make some comments. In the pharmaceutical industry, when we look at a new drug or treatment, we have different phases. And the objective of each phase is different. A Phase I study is a very early exploratory small study for relatively modest cost, typically 10 to 15, anywhere depending on the indication, from 8 to 20 patients. And really, you're trying to test what kind of results they'd yield.

In the Phase II, which this study essentially was a Phase IIa or IIb, you're really starting to look for efficacy, does the compound work and some safety data. And then the Phase III, which sometimes you have to do, particularly in chronic treatments, you look for safety data. And the results vary very significantly.

So typically, about 60% of the compounds don't make it past Phase I. Then between Phase I and Phase II, there's another drop of, depending on the therapeutic indication, of about 50% to 60% of the compound. So the fact that Betalutin didn't work out is very customary -- not customary, is very unfortunate, but it's still very much in line with what the industry is. It's about 50%.

And then the Phase III studies, which you tend to do in more chronic diseases, there, the drop-off is often less. And if there's a drop-off, it tends to be more because of safety issues than of efficacy issues. And safety issues are typically less relevant in oncology because these patients are already really sick. So that's kind of to put the perspective what the, yes, the role of the different phases in the clinical results are or the clinical studies are.

So now I'd like to give over to Lars to answer your question.

Answer

Lars Nieba (Executives)

So yes, kind of what Jan pointed out, we had 8 patients in the Archer-1 study, and we show some good indications for efficacy. And that is why we went forward with that 8-patient number to the health authorities to discuss with them what is the best way forward. And as mentioned, we have a synopsis, and that synopsis was discussed with the FDA to say how fast can we move ahead into a Phase II/III study. And that is why we said, yes, we do have enough data to move ahead into the next phase, as pointed out by Jan.

Answer

Jan Egberts (Executives)

Yes. So the thing you need to keep in mind, each phase, obviously, as a Board, you have to weigh the expenses against the potential results. So if you make a very large Phase I study and knowing that a lot of compounds fail,

in essence, you "waste a lot of study." And you always need a Phase II or a Phase III for approval. So it doesn't make sense to make it to a large Phase I clinical study.

Answer

Unknown Attendee (Attendees)

Well, could you still be more specific about what type of answers you got from those 7 patients? I just referred to [Renoldi].

Answer

Lars Nieba (Executives)

As mentioned, we have seen good efficacy. I need to -- honestly, I don't have it now directly at hand. To my knowledge, we have still 5 patients in response out of the -- sorry, it was 7 patients, not 8. So out of the 7 patients, so median duration of response, honestly, I haven't done my analysis yet. But the complete response rate was pretty good. So that is why we moved ahead, and that was the most important part for us.

Answer

Unknown Attendee (Attendees)

The last quarter, you said that you had shared clinical data with a potential partner. Are you still in dialogue with that potential partner?

Answer

Jan Egberts (Executives)

What are you referring to? I'm not aware. I'm not aware of that statement, to be honest, so I cannot comment on that. And I'm not sure who made that statement.

Answer

Unknown Attendee (Attendees)

But it's in your report.

Answer

Jan Egberts (Executives)

I'm not aware of that.

Answer

Malene Brondberg (Executives)

I think...

Answer

Unknown Attendee (Attendees)

Or maybe Skullerud said it on the presentation, but I'm sure he did. I'm sure either it was in the report or Skullerud said it on the last presentation.

Answer

Jan Egberts (Executives)

I'm not aware of that statement, so I cannot comment on that. I was in that presentation, but I don't recall it.

Answer

Malene Brondberg (Executives)

I think what Erik might have alluded to is that there is a constant, of course, outreach both from the company and also coming in. Of course, that's just nature of the business.

Answer

Unknown Attendee (Attendees)

Yes, that you had said many times. But the last quarter, he said that you also had shared data with a potential partner.

Answer

Malene Brondberg (Executives)

I can't recall that. But yes, there are discussions all the time, of course. If that's...

Answer

Unknown Attendee (Attendees)

I suppose that you're not sharing data with everybody all the time.

Answer

Malene Brondberg (Executives)

No, I don't think...

Answer

Unknown Attendee (Attendees)

I guess that's in the nondisclosure environment?

Answer

Malene Brondberg (Executives)

No, no, no, we can't, so we are not -- no, we are not -- we haven't -- there's, of course, discussions with companies, but no, we're not sharing the data.

Answer

Jan Egberts (Executives)

I mean also remember, very important, we don't have any additional clinical data until 2 months ago beyond the interim analysis from 2020. Again, I start to repeat myself, my apologies, but it's not like on a day-to-day basis, we know how the clinical study is going. There are very distinct moments. When you start the study, you don't know anything. You're completely black in the fog until you do an interim analysis.

When an outside review board looks at the data, then you don't know anything for the whole period until the Board decided to do the second analysis. But it's not like every day you open your laptop like you look at your revenue, as an example, as a company. That's not the way it works. It's all confidential. In a confidential database, nobody from management or the Board has access to that. That is a requirement of the FDA, the Food and Drug Administration.

Answer

Unknown Attendee (Attendees)

Okay. Since you mentioned it, I find it a bit hard to believe because I see some inconsistency between your statement right now and Lars Nieba some quarters ago because I gave him the question, if somebody in the

company had access to the clinical data in the PARADIGME study, and Lars Nieba said, just a few people had access to that study.

Answer

Jan Egberts (Executives)

Yes, let's clarify that because I don't want a misconception to exist.

Answer

Lars Nieba (Executives)

So as Jan pointed out and also how the interim analysis went forward, yes, there was an independent, also the review board where we had a statistical analysis plan called SAP. And that one was then evaluated by the independent review board and the results from that board. We as a leadership team and the Board, only a few people, not the whole leadership team, very few selected people got access to make a decision...

Answer

Jan Egberts (Executives)

To the results.

Answer

Lars Nieba (Executives)

To the results...

Answer

Jan Egberts (Executives)

Not the raw data.

Answer

Lars Nieba (Executives)

Not the raw data.

Answer

Jan Egberts (Executives)

To be very clear, not the raw data. So you have to remember, there are literally 10,000 individual scans of all the patients being made. And those get reviewed by an outside physician, and he basically says, is there still cancer or has the cancer gone away, in remission. We don't have access to that data. That's an outside independent physician. Then basically, they do the analysis.

And they haven't -- before you start a clinical study, you have a so-called SAP, statistical analysis plan. So before you start it, you need to agree that with the FDA, and that's what you execute. An external statistician executes it and then writes the report, which summarizes the data. So it doesn't say Mrs. A has cancer and Mrs. B does not have cancer, et cetera. It says X percent of patients have this, Y percent of patients have that.

Answer

Unknown Shareholder (Shareholders)

I have to come back to the Carnegie study. It seems to me to be very open-ended. There must be some deadline. What is the -- what are you actually -- I asked the mandate and you said -- gave me 3 or 4 points. There must be some more written statement in this agreement. We can't accept some open-ended study from the Board. That is...

Answer

Jan Egberts (Executives)

It's not an open-ended study. It is...

Answer

Unknown Shareholder (Shareholders)

Then give me a date.

Answer

Jan Egberts (Executives)

I'm not giving you a date.

Answer

Unknown Shareholder (Shareholders)

What is the agreement with Carnegie then?

Answer

Jan Egberts (Executives)

Carnegie is helping us evaluate strategic options for the company.

Answer

Unknown Shareholder (Shareholders)

That's words. Give me some more.

Answer

Jan Egberts (Executives)

It's all I can give you.

Answer

Unknown Shareholder (Shareholders)

This is not typical, Jan. This is ridiculous.

Answer

Jan Egberts (Executives)

Okay, are there any questions in the audience? Or otherwise, we go to the online. How do we conduct those questions? Are you reading them?

Answer

Unknown Executive (Executives)

So Jan, I can read questions from the online submissions. If you can hear me okay?

Answer

Jan Egberts (Executives)

Yes, we can hear you fine, thanks.

Answer

Unknown Executive (Executives)

Okay, thank you. So we'll start with a few questions on PARADIGME. The first question is that asks the difference in signs of efficacy between LYMRIT and PARADIGME seems to be quite significant. Finding subsets in PARADIGME with differing efficacy seems like the imperative task to crystallize shareholder value. Can you shed any light on your logic to either pursue or not the further analysis of subsets in terms of data response?

Answer

Jan Egberts (Executives)

Sorry, I couldn't hear it very well. Would you mind repeating the question?

Answer

Unknown Executive (Executives)

Yes, the question essentially is finding subsets in the PARADIGME data sets with differing efficacy seems like an important task to crystallize value. Can you shed any light on that?

Answer

Jan Egberts (Executives)

Yes, I can shed light. So we have looked obviously at that if there are subgroups. And the issue is if you make subgroups, they become very small. The total sample is already not very large. If you start creating subgroups, those are even smaller, and you really start to lose statistical power. So the opportunity to have statistical significance significantly reduces.

Answer

Lars Nieba (Executives)

Yes, absolutely, Jan. So the other part of the first question is, when I got it right, is what is the difference between Part A and Part B because we have seen difference in efficacy in between Part A and Part B. And yes, that's true, and we looked into that one and we do have a significantly different patient population.

So after the phase -- after the Part A, we also discussed, of course, with the health authorities on new protocol. And our patient population in the Part B or the patient population which was far heavier treated, to quote one of our investigators, they said, "Look, your patients in Part A were at a cliff, whereas in Part B, they're falling off the cliff." And we tried to get some back. And at least in 1/3 of the patient population, we got some back, but that was not enough for us. So whereas in the Part A, we show 70% overall attractive response rate, but they were still far healthier. But we still believe in our onetime injection, that is why we also discussed potential ways forward.

Answer

Jan Egberts (Executives)

Yes. But the key hypothesis we have that because of corona, a lot of patients who really could have benefited from Betalutin stayed at home. So physicians tried to keep them at home as much as possible. And then only at the last, last, last moment, they took them to the hospital and then included in the clinical study. So to Lars' point, we got the patients with the significantly worse prognosis in the latter part of this or in the PARADIGME clinical study. And that's just an unfortunate outcome of the corona situation.

Answer

Unknown Executive (Executives)

Thank you. So the next question just asks for some further detail in terms of the fact that you've said that approximately 1/3 of patients responded in the trial. Can you say anything further about the split between complete responses and partial responses in the context of the overall response rate?

Answer

Lars Nieba (Executives)

Honestly, I don't have it at hand, but we will answer that question then on online.

Answer

Jan Egberts (Executives)

Yes. And obviously, we will publish the results probably in the first half of next year. The resulted need to get analyzed and synthesized. That will get published in the first half of next year. That's a requirement of the FDA, so I just want you to be aware of that.

Answer

Unknown Executive (Executives)

Thank you. A further question which I think, Lars, you probably pretty much answered, but this question asks, do you have any further theories on why the interim results deviated so much from what has been presented earlier in the trial?

Answer

Jan Egberts (Executives)

Yes, so there are 2 things you need to keep in mind. First of all, Phase II clinical studies always result lower -- always have yield lower results than Phase I. And the reason for that is a Phase I study is a very small, very controlled study in a relatively small patient population. So you always expect a little drop-off in the Phase II, and we did see that particularly in the interim analysis, but nothing to be concerned about.

But then secondly, because of the corona, like I mentioned earlier, the hypothesis, and that's not scientifically proven, but the hypothesis is that patients stayed home longer, the physicians kept them at home as long as possible, and only at the last, last moment when the patient and the physician were essentially with their back against the wall, they decided to include them in the clinical study.

Answer

Unknown Executive (Executives)

Thank you. And then there are a couple of questions regarding a potential path forward for Betalutin, which again you've alluded to in comments, but essentially asking, given the failure of PARADIGME, how confident are you with regards to a potential path forward for Betalutin?

Answer

Lars Nieba (Executives)

Yes. As mentioned, we are still believing in Betalutin/Humalutin as a onetime treatment. I think what we have shown in all of our studies in PARADIGME Part A, PARADIGME Part B, DLBCL and Archer is that Betalutin really works. We have shown that. Now the point is what we have seen is that a lot of new compounds were coming up, and the objective response rates you have to reach in today's world are pretty high. So you're more reaching 60%, 70% or more.

And what we are looking forward now is what is the right combination partner which we can use in combination with Betalutin to move ahead. And as said, we do have a synopsis. However, I think we need to find a partner because our financial muscles are not where we would like to have them, of course, for such a study. And going into another Phase II, Phase III is quite costly. So yes, that is one part of our asset, as Malene pointed out, it's an -- it's still a very important asset of the company.

Answer

Jan Egberts (Executives)

Yes. And in particular, with respect to these new compounds that Lars was alluding to, initially, we had an approach with an expedited approval, which wouldn't require us to do a Phase III clinical study prior to approval or prior to market launch. Now the threshold has risen because some of these new compounds, in particular, these bispecific monoclonal antibodies.

So you would look at a new clinical study, very similar to what we have done here, number one. Number two, the pathway which we had in the past, which was an expedited approval, is not viable anymore. We probably would have to do a Phase III clinical study prior to approval, which is not necessarily a promise in a very large indication, but a smaller indication like a third line where we work initially, which is, by definition, a smaller indication that is less viable.

Answer

Unknown Executive (Executives)

Thank you. We then have a number of questions regarding the costs of closing the PARADIGME trial, firstly asking, can you give any further breakdown of where those costs are going? And in particular, what proportion of those costs are planned to go to ICON?

Answer

Malene Brondberg (Executives)

Yes. As I said, we're showing a combined number today. And as I also said, we are in the middle of the negotiations. So to stand here to say what we expect will probably not be right. I'm sure everyone can appreciate that. If you are extending your house and then you're trying to negotiate a price, you probably won't tell the builder what you expect in terms of the price. You, of course, have something in your mind, and we are going to do everything we can to get the best deal.

And as I also said, this is a heavy regulated industry. So there are standards and compliance that we need to follow. And of course, we have a follow-up plan. When you close -- if we take a step back, when we took the decision to discontinue PARADIGME, you have a 14- or 15-days window to basically to come up with the plan for how you want to follow up with the patients. And then that goes back into your CRO, which here is ICON.

And then that sort of is information to all the countries. And then they sort of have to look and agree and they -- or come up with if they have any objections to it at least. So -- and after we have that, that's why it takes a while to get to these negotiations because not until we have that, we know what we need to ask from ICON and what they need us to help with.

So our biggest, and I've said that all along, our biggest cost in general is CMC and, of course, the clinical. But I'm not going to, for that reason, to say today what is what. But I -- as I said, I'm a shareholder myself. I've taken this on because I will try to make the best deal for everyone.

Answer

Jan Egberts (Executives)

Just to put a little bit more meat on the bone, as the Americans say, when you discontinue a clinical study, you still have to follow up the patient. That's an ethical medical requirement. So you cannot just say, sorry, patient, the study didn't work, you're on your own. That is not the way it works. You have to continue to follow up the patient, so there are costs associated with it.

As a matter of fact, Lars was alluding, there's still some of the LYMRIT patients, we're still following up. So yes, and that has some costs, and those costs are unpredictable because they're typically elderly patients. So you don't know how long they're going to live. I mean let's take the disease out in general, I mean they're at an old age. But there is a medical ethical requirement, you follow up to patients and you need -- and the company needs to incur the cost. That is what you have agreed when you start a clinical study.

Answer

Unknown Executive (Executives)

Thank you, Jan. And just one follow-up question in that regard, which is for how long do you think you may have to carry the costs for winding down PARADIGME?

Answer

Jan Egberts (Executives)

Essentially unpredictable.

Answer

Malene Brondberg (Executives)

Yes. Yes, it depends on the -- as you can appreciate, as I said, we have more than 300 contracts we've been through. Some of them, the smaller ones, of course, easy to get out of. But of course, the bigger ones is that's where we have to be on our toes to get the best deals for us. Of course, we know the suppliers, of course, want the best deal for them. So it's going to be down to the negotiation, of course.

Sorry, we [can't edit]. At this stage, we will, of course, at a later stage, be able to say exactly where we are. But today, we can't say more, unfortunately. We wish -- we worked day and night to try to get this going as fast as possible. So we worked throughout the whole July to get this to go together, but of course, unfortunately, also had to make people redundant.

Answer

Jan Egberts (Executives)

Yes. Trust me, I've been associated with a lot of different companies, I have not seen many people work as hard as Malene is currently doing trying to minimize costs. So I want everybody to be assured that it's all hands on deck, people are working super, super hard, nights, weekends, et cetera.

Answer

Unknown Executive (Executives)

Thank you. The next question is also about costs and asks, can you say anything more about which employees are still left in the company, including in the senior management team, and whether or not there will be any further cost reductions and potentially reductions in pay?

Answer

Jan Egberts (Executives)

So to comment on that, I don't think we can specific who is left, who has gone. Obviously, we have a new CEO. From a philosophical point of view, I'm not a believer if you ask to work our people super hard to ask them to take a pay cut. It's an unfortunate outcome of the industry we're in. So I'm more a believer like you take certain positions out and don't ask everybody to take a pay cut. These people work super hard. It's not their fault that the compound didn't work out. It's just an unfortunate outcome of the industry we're in.

Answer

Malene Brondberg (Executives)

I think I said when I presented that and who's left, we, of course, have Jostein Dahle and his team, which is an excellent team. And then we've got a few left on the management side to make sure that, of course, we still need to report. We are still in Oslo Børs. There is still a lot of work. It's very expensive actually to be on Oslo Børs. So all of that still needs to happen despite that we are closing down PARADIGME. But of course, we have -- I think we could say now we have cut into the bone, of course, here in an interim capacity as well. So of course, we can't rule out, of course, it depends on what happens next, which is where Carnegie comes in and helping us.

And it is, just to come back to the Carnegie question again, it is also is a very extensive big process when it comes to document that needs to be put into place. And it's not just straightforward. It's not just lining of targets and then trying to agree, and that's why it's also difficult to put exact timing on it because it's a little bit like, sorry for the analogy, it's a little bit like dating. You have to make it happen. And that's why -- and we want, of course, to try to get the best deal. And that's why we trimmed it down as much as we can in terms of the cost. So that is aligned with what we need to do. I understand it's difficult just to get them. We can't say it's this day when we -- but we are working as fast as we can.

Answer

Unknown Shareholder (Shareholders)

Give me a figure. What's the budget?

Answer

Malene Brondberg (Executives)

For?

Answer

Unknown Shareholder (Shareholders)

For Carnegie?

Answer

Malene Brondberg (Executives)

It's a deal between us and Carnegie. We can't go into that. We won't go into that on any of our suppliers. So -- and that's the same here.

Answer

Jan Egberts (Executives)

It's success-related, you can tie that. Any more questions from the webcast?

Answer

Unknown Executive (Executives)

Thank you. A couple more questions, Jan. Just one further question on costs, which asks, given the costs associated with closing PARADIGME, can you give any estimate for how long the cash runway will be with the NOK 90 million to NOK 110 million that you estimate you'll have?

Answer

Malene Brondberg (Executives)

We can't right now because again, first, we need to close those big important contracts or get those negotiated and get them in. That's step one. Then step two, of course, is that we need to, in general, also figure out what we do with the pipeline. As I said, we have Jostein's team working really hard, doing a great job. But of course -- and we have a lot of -- in general, as Lars also said, Betalutin/Humalutin, we got a lot of assets. And what we do there going forward is still under review.

Answer

Unknown Executive (Executives)

Thank you. So just a couple of questions on the pipeline. The first asking, are you still working as usual with Alpha37? And are you still in partnership with Orano Med on that compound?

Answer

Lars Nieba (Executives)

Yes, we are still working on Alpha37. And we are, of course, still working with Orano Med as our partner, and we are making progress there as well.

Answer

Malene Brondberg (Executives)

As I said, our CSO, Jostein Dahle, is still in place and working full speed ahead doing a great job.

Answer

Unknown Executive (Executives)

Thank you. And then just lastly on the pipeline, a question asking, in case you're considering combining Humalutin with rituxan in combination, can you remind us how much clinical data you have on Humalutin at this point in time?

Answer

Lars Nieba (Executives)

Sure, it's pretty easy. We only have preclinical data. We would need to go, of course, first in a Phase I study with Humalutin, but it would be a very short Phase I study to identify the right dose.

Answer

Jan Egberts (Executives)

So very similar to what we did in Betalutin, Phase I and then IIa, IIb, and then most likely also a Phase III clinical study prior to approval.

Answer

Unknown Executive (Executives)

Thank you, Jan. And then one last question, which simply asks, what value do you see in an Oslo Stock Exchange listing?

Answer

Jan Egberts (Executives)

No, I mean there is significant value. I mean there are a lot of companies that are trying to go public. And there's a lot of paperwork associated with going public, an S-1, as they call it in America, and a couple of other documents. So it's very significant. Exact monetary value are kind of put on it, but it is very significant.

Answer

Malene Brondberg (Executives)

And it takes roughly 6 months to go public. And of course, as you kind of want to understand, in this market, it's difficult. So that's of course a...

Answer

Jan Egberts (Executives)

And success is not guaranteed.

Answer

Malene Brondberg (Executives)

No.

Answer

Unknown Executive (Executives)

Thank you. That's all the questions that we have posted online at the moment.

Answer

Jan Egberts (Executives)

Okay. Thank you very much, everybody. Again, sorry that we -- you had to share the situation, but it is what it is. And we're trying to find a plan moving forward. We're working on that, it's not trying. We're working on a plan moving forward.

Answer

Malene Brondberg (Executives)

Yes.

22.07.06. Nordic Nanovector ASA- Special Call

Presenter Speech

Jan Egberts (Executives)

Good morning, ladies and gentlemen. My name is Jan Egberts, I'm the Chairman of Nordic Nanovector. Together with me here are Erik Skullerud, our CEO; Malene Brondberg, our CFO.

Unfortunately, it's a very sad day for all of us today. Openly, we had to announce last night the discontinuation of the PARADIGME clinical study for Betalutin. So obviously, in particular, a sad day but not just exclusively for the shareholders who put a lot of money in the company, but also for the employees who worked very hard and also have invested a lot of their personal money in our company.

And finally, and probably even more importantly, the patients who had expected a very positive new treatment for this very deadly disease. So unfortunately, we had to discontinue the clinical study. We're going to share some data with you. Unfortunately, we cannot share everything at this stage. And the reason for that is that the guidelines by the FDA, the Food and Drug Administration, which is the U.S. regulatory authority. They don't allow you to release all the data at this stage in order to maintain, as we call the integrity of the clinical study. So unfortunately, we cannot share everything that we probably would have wanted to, just given the fact that we are still in discussions with the FDA.

So having said that, I'm going to hand over in a minute to Erik and Malene. And at the end, there will be an opportunity to ask some questions. So please, Erik, go ahead.

Presenter Speech

Erik Skullerud (Executives)

Thank you very much, Jan. And also from my side, good morning, ladies and gentlemen. Thank you for joining us. I'd like to echo what Jan also just said. This is one of those situations where as a manager, as an employee in a company, as the one who is reporting the data to you today, it's one of the toughest things that you have to do.

Obviously, you put a lot of effort. You put a lot of emotion. You put a lot of time into to what you believe is going to be a great asset for patients. And when the data then reads out the way they have done this time, it is equally hard to really find the right words to characterize it. I think from a personal point of view, I would say I'm gutted. I really am because this is something that I really had a great belief in. So it's really sad when you see data -- to see the data the way we have seen them.

That being said, I want to take you through a little bit of a story over the last few weeks. And what may have seemed like a very long time to you has also seemed like a very long time to us, but for different reasons. When we did our Q1 report back on the 13th of May, we told you that we continued to have issues around enrollment in the study. It was still not going the way we expected, and we were sad to report that we only had a couple of patients that had entered the study. That today has changed somewhat.

But before we jump into the detail, I just want to remind you again that some of the statements that we're making today is going to look forward as well. Some of what may become plans. So please look at this and familiarize yourself with this before investing further.

As I mentioned, the inclusion enrollment back in Q1 we reported was fairly flat. And as you can see on this slide, only one new patient has been enrolled since we reported that last time. We then, at the beginning of June, sent out a press release and announced that we would go into a comprehensive review that today I can tell you has taken place, and we'll give you some details in a second but that also included, importantly, an independent expert panel that would review the data.

Why independent and why an expert panel? And I've said this to some of you in communication previously. It is of the utmost importance that the integrity of the PARADIGME study is maintained. It is of the utmost important for us that we follow the ethical guidelines, the rules and the regulations for conducting these type of studies.

And that means that we don't, we, Nordic Nanovector don't have access to the data as such. In order to continue that integrity and maintain that integrity, we therefore, appointed an independent expert panel to review the data.

This consisted of 2 people. One person, a world-renowned biostatistician and one person a world-renowned hematologist, really top-of-the-line opinion leader with no association to the study whatsoever.

And this is important because we wanted really a third-party review. I hope for your understanding that we cannot go out with the name of these people, but they are really experts in their respective fields. So we believe that we can definitely ensure that this is something that we can truly validate as the right review.

We also did a survey among our investigators partly on paper. We sent out an electronic questionnaire to every single site. Approximately 25% of them responded. We spoke to several opinion leaders, investigators, face-to-face. I personally spoke to about 15 of them while at the EHA back in the beginning of June and we will share some insight with you as well.

We have started interactions with FDA. But as you saw in the press release, this is an ongoing communication and we expect this to take some time. So over the next weeks and possibly in a couple of months, we'll have further interactions with the FDA in order to get further guidance from them.

And this is important not only for the data that we have but also, and arguably more important, and you've seen this in the press release, also based on the strategy that we want to move forward. On top of that, we're reviewing our cost base, and we'll get back to that in a second. And you have also seen in the press release that we have announced a restructure of the company as a consequence of this.

But I want to touch on a couple of these things.

First of all, the survey among the investigators completed. We did a survey, very similar survey last year, last summer, as the one we have done this year, and they have pretty much shown the same. They mentioned 3 different areas why they had challenges in recruiting patients. Number one, and a standout is on the inclusion and the exclusion criteria in the study. It has been a hard study to include from the get-go. That's not news to us. It's confirmation, but it's still one of the key root causes for why we have had the challenges that we have had.

Two, page -- study sites are generally tired partly because of Corona, but more importantly, because of capacity, the change in investigators, change in study nurses, change in study coordinators and a heavy workload due to COVID and Corona in genera. And three, COVID and Corona itself has certainly had an impact both on patients, patients recruitment, patients' ability and need to go to the hospital and as such, the possibility to include them.

We further then discussed also with leading KOLs at EHA and also during the last couple of months, in order to better understand what is the investigator point of view, and we did this face-to-face in order to get really deep insights. Again, a lot of what I just mentioned has been confirmed. But I think over and above that, there's a couple of things that this has taught us that I'll get back to on the following slide.

But again, they're also confirming that COVID has had an impact. Competitive studies has had an impact and the share inclusion exclusion, and therefore, finding the patients is important. The interaction with the FDA, as I mentioned, we have started that.

But again, referring to what we also sent out in the press release, there are 2 things that we want to understand better. I will remind you that this is a study in a very specific group of patients. A patient group that even today has a significant high unmet medical need. And we need to get clarity in our conversations with the FDA, what do they foresee in the data versus that patient group? And get full clarity on that.

The other part of this is the fact remains the asset as such has shown both in Part A but also in Archer promising data that we want to explore further. Now we fully acknowledge that we cannot do this by ourselves hence, why we need to also seek partners in this. So there is a business development part of what we're talking about here as well. But the guidance from the FDA will help us further these strategies as we move out in time.

So back to the discontinuation of PARADIGME. And I think bottom line for us, the rationale for why are we discontinuing the study is the data and the quality of the data. When this was presented to us for the first time, I can imagine -- you can imagine how our reaction was, it was basically we saw this and we went, this is strange. One out of 3 patients is responding to the treatment in approximately 6 months of duration of response.

And this is significantly different than what we saw in LYMRIT Part A. Hence, you may therefore understand why we mentioned the signs of efficacy in the press release that we sent out just a couple of weeks ago. There is

efficacy there, but by the standards that we feel we need in order to make Betalutin in third line FL a success, this is not what we were looking for.

On top of this, also, you have seen over the last few weeks an announcement of the first bispecific go into the market. This was not necessarily a -- was not necessarily news to us. We knew this was coming. What we have found out in our communication with opinion leaders and investigators is that both Roche, but also a couple of the other companies that are working on bispecific from a clinical development point of view, have so-called early access programs, and that basically means that each and every physician can apply for getting the drug for free and, therefore, giving it to patients accordingly. So that's something that has definitely impacted also the rate of patients that we could have included in PARADIGME.

And you have -- will also have seen press releases from some of the CAR-T players out there, that they are pushing more wide use of CAR-T, but I think it's fair to say, and I'm saying this on the basis of what I heard at EHA. The excitement in the scientific community for bispecifics is significantly higher than that for CAR-T. So these are 2 areas that from a competitive point of view, have further heated up as we have gone through just the last few weeks of activity.

So in this context and looking at this and the development program, the PARADIGME study, and what we have seen of data, our estimation and our suggestion is, therefore, that this is not a viable proposition moving forward in third line. We feel that the competitiveness of the profile that we now see is significantly lower than what we expected. And therefore, the Board together with us in management has spent the last few hours in heavy discussions around this, and it's, as I said, to begin with, it's a really tough thing to communicate, but the decision is to discontinue PARADIGME.

So where to from here. First of all, we have already started, but I hope you can appreciate this is also a fairly fluid situation. We have already started to review our cost base, our infrastructure and the cost of closing down PARADIGME. This will take us some time.

At the bottom here, you can see we're aiming to give all of you an update when we do our Q2 report towards the end of August. But at this stage, it's too early to say exactly how is this going to affect run rate, et cetera. What we can say is that run rate's and cash burn is going to go down significantly but we need a little bit of time for actually making that happen.

The restructuring of the company will start immediately. And the purpose again here is to reduce cost to a minimum and only focus on the essential pipeline activities moving forward with one exception, and that is, again, as per the press release, our communication with the FDA on the way forward for Betalutin.

The Board will review and optimize development strategy for the pipeline. We have an additional 4 assets, as you know, from the R&D Day, et cetera, that we are also working on. And we're really now looking into how can we best prioritize that, number one. How can we move that forward in an optimized fashion. And again, we'll come back with more information on that shortly, more towards the end of August for the Q2 presentation.

I mentioned earlier the business development strategy that we're also furthering. This is not to say that this is something that we're starting. You are all aware of what we have also reported in previous calls. The difference this time is obviously that also a potential partner now have access to what does this -- do these data look like and also further details in that sense, which may make us more interesting from a partnership point of view.

And finally, we will confirm all of these numbers. But to the best of our understanding today, the cash position towards the end of Q2 is approximately NOK 280 million. So for those of you that over the last few weeks, have been speculating online around, yes, now they're going bankrupt, let me say right here, no, we're not. There is not -- there is enough cash in the bank to take us forward.

But obviously, all of this is depending on that. We do the right things that you can see on this slide in the weeks and months to come in order to ensure that we transform the company accordingly. And that will be partly a restructuring and partly evolving the development strategy.

So I'm not telling you something here that you don't know. These are the other 4 assets that we have in the pipeline at different stages, I'm not going to give an update on where we are specifically today about this. That is for the upcoming again Q2 call.

But you are aware of Humalutin, the follow-on to Betalutin, if you want. Alpha37 is progressing together with our partner, Orano Med. We have several humanized antibodies in the pipeline, and we're looking at this as we are in the areas of NHL, but also in autoimmune disease. And finally, our CAR-T program that we are working on together with the University of Pennsylvania that we're expecting further information on in the second half of this year.

So in summary, PARADIGME is being discontinued. We will continue to partly speak to the FDA around Betalutin, but also exploring further partnerships for Betalutin as we move forward. The strategic focus, as I mentioned, is switching to the pipeline. We are restructuring the company based on partly cost but also the pipeline. And what is that -- what that will look like from an early stage strategy point of view, we'll come back to when we get back to you in August. And that is really the next time that we intend to communicate more fully.

Finally, I want to put a couple of smaller points here. I have personally felt the frustration from all of you with all the e-mails that I have seen over the last few weeks around why aren't you guys talking to us? Why aren't you communicating? I hope you understand. And when you get into a situation that we have been in, where also we, as admitted in Q1, didn't feel we fully understood. That is a very frustrating situation to be in therefore, to spend a lot of time on communication, yes, we try to the best of our ability to respond, but we also have a business to run, and that's what we've been trying to do.

As I hope you will have seen in the presentation, we have really tried to turn every stone in understanding why had -- why has -- what has been going on? Why has that really happened. And although the results at the end of this journey is truly sad and unfortunate. I hope for your appreciation as well that people at this end have been working extremely hard.

And a final note, there's about 70 people in the company that today is not feeling very well. They have spent hours, they've spent days, weeks on working extremely hard for where we are. And I hope you can appreciate that our focus now is with them. Taking care of those families, their livelihoods and ensuring that we also do what's best for our employees.

So I believe with that, I think we stop, we'll open it for Q&A, but I really appreciate your patience as we go through in the next couple of weeks and what we have to go through as a company. As I said, I feel gutted, and you hear that in my emotion as well. But we're going to do what's best for you shareholders. We're going to do what's best for our patients, and we're going to do what's best for our employees in the weeks to come.

Thank you very much. And with that, I'm open for questions, guys.

Question and Answer Operator Message

Operator (Operator)

Thank you, Erik. Hopefully, everybody can hear me okay. Just to remind people listening to the webcast, if you'd like to ask a question, please type that into the chat room and we'll take as many questions as we can today.

Let's start with some questions around Betalutin. So the first question essentially asks when did the Board learn that only 1 of 3 patients responded to Betalutin, and could this have been communicated to shareholders earlier.

Answer

Erik Skullerud (Executives)

I think the short answer to that is we don't believe that this could have been communicated any earlier. The Board acted as quickly as they saw the data, number one. You also saw in the press release that for us, the integrity of the study was at the utmost important. So communication with the FDA around the data has been crucial.

And therefore, you have also seen the time line the way it has been. I believe we could not have done this any earlier. In fact, when I look at my experience from other situations such as this, we have, if anything, been quicker than what I've seen in the past with regards to communication of the data as such.

Answer

Jan Egberts (Executives)

Yes. Jan, can I approach here? One additional comment. People have to remember that neither management nor the Board has access to the clinical data. So the clinical data basically go into a repository, a database that nobody has access to. And the reason for that is that that's the requirement by the Food and Drug Administration in order to maintain the integrity of the study. So it's not like you check every day how you're doing. That is impossible, very -- when we wrote the clinical protocol for the study, we had an interim analysis, which was sometime in 2020. And that was it. And then at some stage, you get nervous on how things are going, and that's why we decided to do an additional exercise where we also needed to maintain the integrity of the clinical data.

So like I said, again, it is not a situation where you just turn a button and say, how is it going today with the clinical study. But the whole -- the entire period from the moment we got the results is a matter of days or frankly, weeks, but no more than that.

Answer

Erik Skullerud (Executives)

Thank you, Jan.

Question and Answer Operator Message

Operator (Operator)

The next question asks, how much has the company spent on planning for the Phase III study for Betalutin and what happens to that study now in the future?

Answer

Erik Skullerud (Executives)

So the most of the -- most of the investment in the planning for Phase III is really internal head counts that have been working on this. It's very little that has been done externally with potential vendors. We have not gotten to that stage yet. As you will have heard in previous updates, we have spoken to the FDA.

We have discussed both with the FDA, also with clinical experts on what this is going to look like from a potential Phase III confirmatory study. The fact that we're stopping PARADIGME also suggests that the whole Phase III program will be up in the air. It will definitely not be as a single entity. It will be with a partner if that was to happen. We need further guidance from the FDA around is that even sensible to do. And that's something that we still will need to investigate. But that being said, as far as we are concerned now, the whole Phase III confirmatory study is on hold until we have further guidance from the FDA.

Question and Answer Operator Message

Operator (Operator)

Thank you. And on the subject of partnerships, the next question asks what are you hoping to achieve when you refer to the exploration of potential partnerships going forward with Betalutin? And are you planning to license out Betalutin for treatment in combination? And in what potential indications could that be MZL, DLBCL or second line possibly?

Answer

Erik Skullerud (Executives)

With all options are on the table.

Question and Answer Operator Message

Operator (Operator)

Okay. Thank you. There are a number of questions asking about the current data in reference to the interim analysis, essentially a question asking whether the management and the Board had access to the data at the time of the interim look and asking how you might explain differences between the data that has been observed today versus the interim analysis.

Answer

Erik Skullerud (Executives)

So a couple of points on that. First, interim analysis was part of the statistical plan, and it was intended to look at what was the dose that we were going to take forward. So this was not an analysis to look at efficacy in the way that we have done it now with the independent expert review. That's very important to keep in mind.

Secondly, the numbers at that stage were very small. Third, in looking at where we are today, the data has continued to deteriorate. And as such, a -- the efficacy that we're looking at today is not what we would have hoped for a long even also looking back at the interim data.

Question and Answer Operator Message

Operator (Operator)

Thank you, Erik. There are a couple of questions asking whether or not you believe there's been any impact on the study from COVID or COVID vaccines and whether or not changes in inclusion or exclusion criteria could explain some of the differences in data that have been observed.

Answer

Erik Skullerud (Executives)

So I think the latter one first. With regards to the change in inclusion and exclusion criteria, it is too early to say if that has had an impact. With regards to COVID itself, I would refer back to what you heard from Professor Leo Gordon back at the R&D Day. He mentioned a couple of thoughts there, which was related to COVID and efficacy of generally oncology drugs. Rituximab was highlighted in his presentation.

So we don't know the answer to, has COVID actually impacted the study as such. But if one were to speculate, one could say that maybe that is a contributing factor. Maybe the patient group is a contributing factor, but we just don't know at this stage what has contributed to the data that we see.

Question and Answer Operator Message

Operator (Operator)

Thank you. There are a number of questions asking what will happen to the Archer study at this stage, whether it's still live and what the future could be in that setting?

Answer

Erik Skullerud (Executives)

So the Archer study is somewhat still alive. And the last patient is going out of our chair, I believe, towards the end of the third quarter. But beyond that, Archer as such is finished. Again, I would refer to what we wrote in the press release. The -- our intention or our view for the future is there is still an opportunity for Betalutin in potentially other settings of the patient populations looking at both the Part A data and what we have seen also in Archer that may be a way of looking at where do we go from here. It's really too early to say. But to the person who asked the question, Archer is still there, but it is very close to finalization.

Question and Answer Operator Message

Operator (Operator)

Thank you, Erik. And then a specific question asking, do you believe that the current data suggests that a single dose regimen of Betalutin is unlikely to achieve a compelling antitumor effect?

Answer

Erik Skullerud (Executives)

I don't want to speculate as such. But I think all the data that we have seen also previously, looking at everything we've seen to date, suggests that 1 dose is sufficient.

Question and Answer Operator Message

Operator (Operator)

Thank you. And then a number of questions, and I think, to some extent, you covered this in your comments, Erik, but essentially a number of questions asking on when we can expect any updates to the pipeline, and in particular, asking specifically about progress for Alpha37 and what we might expect from that going forward?

Answer

Erik Skullerud (Executives)

Yes. No, I would refer to what I said earlier on the 31st of August. As I said, our focus right now is on the restructuring of the company. We're working on the pipeline as well, but we'll give an update on the 31st of August.

Question and Answer Operator Message

Operator (Operator)

Thank you. And then a few financial questions. The first is which says you've mentioned plans for restructuring the company to reduce costs. Can you give us any indication on how much you're expecting to reduce expenses and what the subsequent cash runway would be?

Answer

Malene Brondberg (Executives)

Yes. It's Malene here. This is too early to say that as you probably would -- you can imagine that we have a lot of vendors that we, of course, need to have discussions with to figure out where we are in that sense. And also, of course, we -- it also will impact, of course, the employees, management and everything. So it's really too early to say. But we will -- when we get to August and we report Q2, we are able to say -- we should be able to say more at that stage. As you can see also from the release that we have in June, approximately NOK 280 million in the bank. And as you could see, with -- we came from NOK 352 million. So we have already -- and as I also said at the last call in Q1, we are constantly looking at the cost and have been doing that.

So of course, we do know where we're going, but of course, we do need to go through a lot of difficult discussions, first of all, before we are ready to say anything. And I think also everyone can appreciate that going into these discussions would be better to start the discussions with the people we are going to discuss with than to discuss it here today.

Answer

Erik Skullerud (Executives)

And I think just to add to what Malene just said, you, dear investors are the first we are announcing this too. We -- our employees will have seen this morning as well, just like you did. Our vendors as well will have seen this morning. So you are really the first to know. So I hope for your understanding in the sense that what Malene just said, we're really starting a lot of this work as we speak. But you can also see from the run rate in Q2 that we have already put some breaks on the spend, that will continue and numbers that will be presented on the 31st of August will also be different to what you have seen today.

Question and Answer Operator Message

Operator (Operator)

And I think that probably means that specific further questions with regards to cash burn expenses, et cetera, we'll have to await that further update.

Answer

Erik Skullerud (Executives)

Yes.

Question and Answer Operator Message

Operator (Operator)

Malene, I don't know whether I can hand over to you at this stage for any questions in Norwegian.

Answer

Malene Brondberg (Executives)

Yes, I don't think -- right, I think we have covered most of them because they are along the same lines. We will, of course, continue to take questions at the IR inbox. So we are here. But as you can imagine, today is going to be a very busy day because we do also have all our employees.

And as Erik just said, you were the first one. So we haven't even spoken to them yet. So please, if you could just bear with us. We will come back on those. And what options -- I can see one of the questions here is what options will there be for the company going forward. As Erik said, they're all cards are -- all options are on the table, and it is really too early to say.

Answer

Erik Skullerud (Executives)

So I think with that, let me, first of all, say thank you to all of our investors for the support you have given us, you are giving us over the years. I also like to say a big thank you to investigators that have worked with us during the course of PARADIGME to date and to the patients that have been involved and have had the hope that this was going to be something that could come to fruition for them one day as well but also to our own employees that have been working tirelessly on both execution of PARADIGME, the other programs that we are working on and also looking forward to working with now the development of the pipeline and also a big thank you to all of you for listening today.

So with that, I think we will sign off. Again, wishing all of you a nice summer, and thank you very much for your support. Bye-bye.

Answer

Jan Egberts (Executives)

Bye-bye.

22.05.13. Nordic Nanovector ASA, Q1 2022 Earnings Call, May 13, 2022

Presenter Speech

Erik Skullerud (Executives)

Good morning, everyone, and welcome, a warm welcome from this side to all of you for today's Q1 2022 webcast of the highlights and financials for Nordic Nanovector. My name is Erik Skullerud, I'm the CEO. Together with me today, I have our CFO, Malene Brondberg; and our Chief Operating Officer, Sandra Jonsson.

Over the next few minutes, we'll take you through the highlights, the way we see them, and what we have seen going on in the first quarter.

Before we jump into that, forward-looking statements. I know you are all aware of this, but obviously we will be using some forward-looking statements here. That is for the purpose of trying to give you a feeling for how we think about the future. But obviously, events outside of our control can influence this. So please make yourself familiar with this before investing.

Most of you will have seen our press release from this morning. We are today reporting 108 patients enrolled in PARADIGME. I will come back to more detail around this as I go through the presentation. But needless to say, this is a number that also we are not satisfied with. And I want to underline that.

We hope that things would look up after the COVID pandemic. It seems to be on the downturn in most countries, but it has been lingering on for longer than what we also anticipated. But I'll get back to more detail about that in a second.

The second important point on this slide is to be aware of our cash position and how we still look at our run rate, but also more importantly when we expect the results. The way we look at the situation at the moment is that we can still reach results by the end of the second half of this year. So we're not changing that guidance. But again, I want to underline, it's not that many more months that we have to have with these kind of rates that we now see before we have to reconsider that.

But that being said, we do also see drivers currently that is giving us confidence that we should be able to change the situation. And again, I'll come back to that in a second.

We haven't only had enrollment in PARADIGME as a priority this last quarter, we have also been able to do a couple of other things. Most of you will remember that we raised finances at the beginning of the year at NOK 250 million. And again, I want to thank those of you that participated in this for the support. We know this is important to you that you spend your money right. And believe me when I say it is important to us that we also spend your money right. So we're doing everything we can to, on one hand, do as much as we can on the results side, but on the other hand, be very mindful of the finances that you so kindly help us with. So really appreciate that. Thank you.

With regards to the results, as I mentioned, our guidance today is based on 108 patients that have been enrolled in the study. The study itself is going on in about 80 centers at the moment around the world. We see several centers that are extremely active, but we are also seeing centers that are less active. And again, I'll come back to this in a second because I think this is one of the things that you should anticipate with studies like this, that there is some fatigue in the marketplace when you get towards the end of the study. But again, we are also getting positive signals from many of these centers. There's a lot going on.

I mentioned the guidance around when we should expect results, et cetera, and I did touch upon the help that you, as our investors, have been giving us in the early part of the year. As you can see, there's also parts -- other parts of the pipeline that are making progress. Alpha37, we had interactions with the FDA, not virtually or face-to-face this time, this was questions that was asked around how do we best produce this, how do we use an assay to best produce potential clinical material. They agreed with our approach. So that has given us a stick in the ground, if you want, on how we move that program forward.

This is obviously a collaboration with Orano Med, and work is ongoing with this accordingly. Most of the work today is being done by Orano Med, but we also have a responsibility more on the clinical or on the development side.

We have also published 2 different papers with Humalutin. This for us is important in the sense of further proving the value of CD37. One of these publications is with a PARP inhibitor, a combination. The other one is related to more of a diagnostic approach that you can pretty much predict response to the treatment. And this is again, when it comes to further development, something that seems to be increasingly important when it comes to targeted therapies. You want to know that when you give the product, you can have a response right away, also important when you speak to payers.

And finally, we, as you will all be aware, we had our AGM back in the end of April. At that meeting, we welcomed Thomas Ramdahl as our new Board of Directors member. Thomas has a grand experience, amongst other things, from Algeta. We welcome him to our Board and very much look forward to working with him.

We also want to say thank you to Per and Rainer for their participation, their support and their guidance over the years, 2 very valuable Board members for us.

I know that some of you have asked questions around health cap, payer situation and so on. I think it's only fair to say Per has spent a lot of years on the Board with us, done a great job. As he said it himself, he has a lot of other challenges as well. And the way the -- where the company is now is probably beyond what his strength is. Clinical development and more towards commercialization is not where he has done most of his work. Hence, also why we now have Thomas on board so that we can really utilize the capabilities that he's bringing to the table.

I want to say a little bit more about PARADIGME because, as I said, also for us and for me as CEO, I'm a shareholder as well and obviously I want this study to be successful and successful as quickly as possible. So when we see what's going on in the market today, it gives us pause for reflection. And if anything, it gives at least me and the team even more reason for working harder in ensuring that this becomes a success as quickly as possible.

On the right-hand side here, you can see some of what we hear from centers out there with regards to why is this going on. So although we have 2 patients that are included -- enrolled during the course of the first quarter, what we're also hearing from centers is there is COVID fatigue out there. There are areas where the health care system, as such, still is struggling. This is not the sole explanation for what is going on.

On the other hand, we are also competing for patients. There are competitive studies that is taking some of the patients that we could have taken. And if I look at more in general terms, what is the feedback specifically on the study itself, it is, and you will have heard this before, it's the inclusion and the exclusion criteria. It is a hard study to recruit to.

Again, this is not an excuse. You have seen double-digit quarterly enrollment rates before, we should be able to do that again. Why am I saying that? Now that the world is opening up, we have access to centers all over Europe, all over the world, with the exception of the U.S. In the U.S., we can still not go into centers.

So the fact and the lack of face-to-face meetings, face-to-face motivation, face-to-face discussion for us is one of the key drivers over the last couple of years, but more specifically, the last 6 to 9 months due to the Omicron variant, et cetera. Lockdowns, et cetera, is one of the key reasons for why we have not had access to centers, and hence, also had not had a chance to have as impactful interactions as we could have had.

You see over on the left-hand side here, some of the things that we believe are the key drivers and therefore some of the key differences in why you should believe us this time. Because I am sure that most of you will also say, well, Erik, tell us, you told us back in Q4 that I should believe you for the following reasons. You haven't delivered. So why should you believe us now?

And to me, it comes back to these 3 things. Number one, the access face-to-face to centers is opening up and it basically is open now. That should improve things. The second, we know that peer-to-peer interaction amongst investigators is one of the key drivers for why you are successful and why you are not. We're taking the opportunity at the upcoming EHA Congress to take all of our investigators -- basically to get them all together in one room, share best practice, use that as a communication platform for why this is so important, why do they -- why should they look at further patients in the study and how do they best do that. And they learn from the people that have done the best job because we have a lot of centers that have done several patients, while some others have only done 1 or 2. So that is important for us.

And finally, the medic-to-medic interactions. We haven't done a good enough job of that. We could have done better, and we're changing it. So we have already started, But over the next few weeks and months, we're increasing the number of engagements between our medics and our investigator medics. And those are the 3 main reasons why this time around, things should hopefully be different.

Also last time I spoke to you, I mentioned this funnel that you see in the middle here. And I said something along the lines of, I have very seldom seen so many patients in that funnel. And I meant that, and I still mean that.

Now so why is the explanations? Why don't you see more than 2 coming out of the funnel? And for me, there's a couple of key drivers, and this is feedback from the centers. These patients that were on top of the funnel, but is not coming out of the funnel falls into a couple of categories. Some of them have gotten corona, have been delayed. The center, therefore, did not initiate and has still not initiated. That is, to me, a reason that was valid back then. It is not so much a valid reason today.

The second one is more important and that is patients that are, for whatever reason, not fitting the inclusion or the exclusion criteria. It could, for example, be blood platelets that are too high or too low. You have to wait, and they just don't come into the right range for the study. Hence, the patient cannot participate.

And the third bucket is around patients that, for whatever reason, either will not want to be part of a study. They do not want a radio-immunotherapy even though they acknowledge that the results, at least the results that you can see so far, are very promising but they just don't want to be part of a study like this. And we have to accept that as well.

And these are the 3 categories, the 3 main reasons for why people in the funnel does not drop out at the bottom and become an enrolled patient. We have even gotten to the point of one patient that went all the way through the funnel, was about to be dosed, but for enrollment reasons, inclusion reasons, did not fall into the study. The patient is still under consideration. But this is again one of these where we hope we can see the patient go through, but at the last minute they don't come in for whatever reason.

Now again, this for you may be why are you telling us all of this? For me, it's important that you understand the kind of picture that we are looking at and why these things are happening. This is normal in a clinical study. It is irritating, it is frustrating, I admit that. And I am, as I said, as frustrated as you. But it is the nature of doing clinical studies.

So away from the inclusion/exclusion in the study and a little bit of what else are we working on. We have had and we are having interactions with the FDA. This is part of business as usual for us. They have focused of recent more around the confirmatory Phase III program. We have gotten guidance from the FDA that helps us do further work on the confirmatory Phase III program.

You will remember that last time we spoke about the importance of starting early with the confirmatory Phase III. I think it's -- needless to say, but I'll say it anyway, the PI3K story and the ODAC meeting surrounding the PI3K inhibitors have proven to us why this interaction is so important. You need to start this early. You need to get it right. You need to have this interaction with regulators so that when you submit your BLA, you also have your confirmatory Phase III study running.

Some, not all, but some of the PI3K inhibitor companies have not done that and this is one of the reasons why they have gotten into trouble. There are other reasons as well, but this is one of the reasons. So that's why we're starting this early.

Secondly, our regulatory strategy is very clear. Once we get to the submission of the file, we know what we want to achieve, we know how we want to get there and we have a plan for how we want to get there.

I also want to highlight some of the work that we're doing on the supply chain. And I mentioned to you during Q4 that we're doing a lot of work, both in confirming, that we're doing the right things for the supply chain, but we are also focusing in on cost of goods. We have progressed this work even further now.

And the result of what is ongoing will have 2 consequences for us and also for U.S. investors. Number one, the cost of goods. We will be able to reduce cost of goods significantly and that will be obviously important for our profitability when we commercialize.

The second point is around environmental impact and how we move product around. And also that -- in that sense, we're making progress. And our carbon footprint, if you want, will be significantly lower also as a consequence of the initiatives that we're putting into place.

So we're very happy with how this is progressing. I've said it on a couple of occasions, this is like hand in glove. It is important that we ensure, on one hand, the clinical development, but on the other hand complete readiness also from a CFC point of view.

So in that sense, and this is more than -- of a schematic, but this is the reason why we're doing all of that. We want to make sure that this picture is as narrow as possible so that when we have the top line results at the end of the year, the next thing that we will do is to pull together a report that will be shared with the FDA at the so-called pre-approval meeting and everything else will actually follow from that.

In general terms, they will tell us, here is the file -- or we will tell them here is to file that we are suggesting that we will put forward to you. They will say, okay, this is what we did. Wonderful, you move ahead or can you do the following analysis accordingly. And from there, this will then happen towards what will become the BLA submission. And over on the right-hand side at the bottom here, you also look at the different alternatives from a regulatory review point of view.

Then shifting gears to somewhat of what's happening on the competitive side. And again, a lot of different things have happened since the last time we spoke together. First thing around PI3K. I think we all have key learnings from that. For us, the most important learning from what's going on with PI3K is the connection between, on one hand, studies that they did to get accelerated approval. And currently, what the FDA has reported back as what they say as the toxicity that they see in confirmatory studies as well. And the connection between these 2 impacts overall survival. And this is the reason for the ODAC meeting and this is the reason for why PI3K inhibitors have been asked now to do comparative studies early on in order to get approval.

But I think it's also fair to say that they're also saying about PI3K inhibitors if you show a better safety profile, a single-arm study may even be sufficient for you. So they have not closed the door completely on PI3K inhibitors. Why am I saying this? Because this is important for us, partly because the door is still open for us also to utilize PARADIGME as the basis for our regulatory file, and that's important to get that confirmation.

Secondly, obviously, the proof will be in the data. We have to show good data, otherwise, accelerated approval is also for us going to be a question mark. But more importantly, that has to do with the toxicity. We know that for Betalutin the toxicity is very mild. Arguably, you could say it's better than most of the other alternatives out there. This suggests to us and gives us confidence that when we do our confirmatory study, we will be able to show the overall survival that you need in order to convert your accelerated approval to a permanent approval. And that is, for us, confidence.

The second part that has changed since we spoke last time is with regards to CAR-T cell therapies. You saw those of you that are close to this, that Novartis came out with a press release just a couple of days ago with regards to the ELARA study and the approval for third-line therapies.

I think there's a couple of things to notice in that press release. Number one, they're talking about the toxicity also there, the cytokine release syndrome. The neurotoxicity of the product is occurring in cytokine release syndrome, it's approximately 50% of patients. Neurotoxicity, somewhere between 20% and 30% of patients. This is still a fairly toxic regimen.

And for those of you that are interested, I would refer you to a review that was done back in September 2021 in the oncology journal in the U.S. because that is, in my point -- from my point of view, third-party confirmation of what we've been saying all along with regards to CAR-Ts. The results are impressive, no doubt.

However, there's toxicity that you have to take into consideration. There is a cost of treatment that you have to take into consideration. And most importantly, there is a cost for the health care system when you use a CAR-T that you have to take into consideration. These patients that get a CAR-T will have to be in a hospital for weeks. They have to move away from their homes for weeks. For these 3 reasons, the cost, toxicity and the cost of the health care system, a lot of patients are saying no to the treatment.

And even the top opinion leaders out there are saying this is a great treatment, but only for the few: the healthy, the fit, relatively in this case. It is not for the elderly and the frail. Where are we positioning Betalutin? In the

elderly and the frail. So this is why we feel, from a competitive point of view, we still have a big space for Betalutin.

Final point of this slide is related to bispecific antibodies. And yes, again, important class of drugs, good for patients and impressive results. Again, the toxicity here, and this is also what you see in reviews, is quite high. So when you look at reviews from opinion leaders, they're saying this is going to, first and foremost, be a competitor for CAR-T cell therapy.

Again, in younger, fitter patients, they're obviously not on the market yet. So we still need to see what kind of cost, et cetera, they will come with. But that is all we know at the moment with regards to bispecific.

So in looking at how we're positioning Betalutin, first in third-line, as I mentioned, for the population that we're targeting, the frail, the elderly, we have big confidence that there is still a high unmet medical need for the use of Betalutin eventually.

And secondly, the value proposition with one-injection efficacy and a very favorable toxicity profile is something we feel and are confident is good for these patients. We have to show the data, as I mentioned, and that is obviously why we're working so hard on PARADIGME.

And also when we look towards the future and we look into second-line, a potential combination with rituximab, that's a further opportunity for us. And as you can see here, we also have what we believe to be the future positioning when we have that study done and confirmed. So that's about it as far as Betalutin is concerned.

I also want to talk about for 2 minutes, the rest of the pipeline. We obviously have these 5 different candidates at different stages of development. And in the last quarter, we have news on 2 of them, arguably 3 of them: Alpha37, I mentioned, and I also mentioned Humalutin and I'll talk a little bit about our CAR-T and give you an update on CAR-T towards the end of the next slide here.

So as you can see, I mentioned the 2 publications that we've had on Humalutin. These 2 publications for us are important, as I mentioned, partly because of CD37 and the faith that we have in the target that we're working towards. But also starting to look towards the future on what this therapy could potentially offer patients with an additional diagnostic associated with this. And this is really the first time we published this data so we're obviously very excited about this.

Secondly, with regards to Alpha37. We're making progress there as well with our partner, Orano Med. I've mentioned this on a couple of occasions, we're expecting further updates on Alpha37 when we get into the second half, the third or the fourth quarter of this year. But the progress of Alpha37 is significant. We're moving forward at a nice and steady pace with the program.

And the last thing I want to mention is CAR-T. I'm excited about this drug. It's really early stage, I acknowledge that. But the program has now truly been kicked off. It was kicked off in January and we're making good progress also on that. We're expecting data to show you on the initial parts of this when we get towards the end of this calendar year.

So that's the update from a business point of view. I'll now let Malene take over and talk to you about the financials. Malene?

Presenter Speech

Malene Brondberg (Executives)

Thank you very much. Good morning, everyone. So just a quick update on the finances. And as you could see, we came in on a spend at roughly of NOK 100 million, which is more or less on par with the last year. Again, our biggest areas where we spend money in is the CMC and then the clinical.

If we go to the, as I said, the cash flow, we would -- I said last time that we have roughly NOK 150 million. We ended up at NOK 148 million. And the biggest -- or the explanation for the change compared to last year, as I also said last time, was a change order or a milestone payment with our biggest CRO that we had to pay.

For the next quarter, we expect roughly a spend of around NOK 100 million to NOK 110 million. And again, we continue to spend the money, especially on the CMC side, as we get more and more towards the close of the study.

So here is just a quick slide that shows what the cash position is, and we are right now at NOK 356 million. And as you could see also and as we also talked about last time, we had the private placement and then it was followed up by a repair issue, as Erik also just alluded to.

And we, of course, reiterate our guidance here that we have a cash run rate going into the first half of 2023 at least of 3 months. And we're, of course, doing everything we can to expand that as much as we can savings. And one of the savings that we have, as you probably noticed this morning, we haven't sent the PR out on Norwegian as we've done sometimes in the past. That is one of the savings we made because everyone is now only sending out in English and we've decided to do the same.

We hope that works for everyone. With that, Erik, it's back to you.

Presenter Speech

Erik Skullerud (Executives)

Thank you, Malene. So in summary, the situation we find ourselves with PARADIGME, we are obviously making progress but we're not making progress at the speed that we would have wished, and we're doing everything to change that.

As you've seen on the finances, we are still in a good position. We're looking at every single dollar to make sure that the run rate will be as long as we possibly can. You do know that the money that we spend is mainly on Betalutin. The latest numbers that we have looked at on the internal side is we spent more than 90%, close to 95%, of all of our funds on Betalutin. The rest is going to the rest of the portfolio.

But my CSO, Jostein, continues to remind me that, Erik, we can't forget about that, either. And hopefully, what you've seen in the presentation today is that we haven't forgotten about it. But we are also wary about spending the money that you kindly help us with on what we consider to be the most important priority and that is Betalutin, that is PARADIGME and is building the CMC capabilities.

I am very happy of the work that we're doing on the CMC side and that we're able to simplify that and therefore show over time less of a cost associated with the whole CMC strategy that is also going to improve our profitability when it comes to commercialization.

So finally, I just want to leave you with a continued thank you for the support and what you showed in giving us the money back in January as well for the fundraising. We are doing everything we can to get PARADIGME back on track. We will do a deep dive with all of our centers and get further information, further understanding and make sure that we pull the right levers for PARADIGME moving forward.

And it's already ongoing, but it's obviously also going to take us a little bit of time of really getting our heads around what exactly going on with that. But we have confidence in bringing you the result towards the end of the year. But as I said to begin with, we need to ensure that we change the trajectory of enrollment in order to do that.

And so with that, I want to thank you. I want to open up the floor for questions from the audience. So Jan, Frazer.

Answer

Frazer Hall (Attendees)

Thanks, Erik, and good morning, everybody. Should we allow you to take any questions from the room first, Erik, and then we can move on to questions via the webcast.

Answer

Erik Skullerud (Executives)

Okay. Do we have any questions from the room here? I don't think so. I think we'll go straight to the webcast, Frazer.

Answer

Frazer Hall (Attendees)

Okay. Thank you very much. [Operator Instructions] Just to start off, the first question is regarding the impact of COVID-19 and asks, can you elaborate any further about the impact on a country-by-country basis? And asks, in particular, have you started to recruit again in Norway and Scandinavia?

Answer

Erik Skullerud (Executives)

So let me use a couple of examples from Norway. This struck me as somewhat interesting as well. I know most of our shareholders are Norwegians, so I'm sure you will relate to the 2 articles that have appeared in Norwegian newspapers over the last few months.

Number one was an article that was probably just before Easter, which was related to the number of deaths due to COVID up until the 9th of January 2022. In Norway alone, that was about 1,370 deaths. Between the 9th of January and Easter, the same number of people in Norway died due to COVID. That's not to play around with numbers, but what I think it shows is that even though the noise in the media, the amount of time we spend on talking about COVID has dissipated, but it's still out there. So it's still something that is going on. That is not an excuse for us, but it's an important thing to keep in mind because it is a driver of what's happening in the health care system.

And the other article that struck me was the national hospital, or as we Norwegians will know it, Rikshospitalet, who has not been able to do critical surgery within heart, lung and even cancer over the last few months because most of their people have been taking care of COVID patients.

And that's striking again in the sense of what's going on in the health care system because the health care system is still, I would say, not on its knees. They're catching up, they're doing a great job. But it still has some impact, although the impact today in May is not the same as it was in Q1 and we have to acknowledge that.

But for Q1, this seems to have been the case from a COVID point of view.

What was the second part of the question, Frazer?

Answer

Frazer Hall (Attendees)

The second part was just specifically, have you started to see a return to or a pickup in recruitments in Norway and Scandinavia more broadly?

Answer

Erik Skullerud (Executives)

So the short answer is pickup in enrollment, no. Pickup in consideration, yes. I have spent the last couple of times, I think, I've spoken to you on, I guess, you would say complaining a little bit about us, Norwegians. We are generally competitive and I was kind of hoping that the Norwegians would do well around. We are seeing a pickup.

Sandra, our COO, spent time in Denmark the day before yesterday, Sandra, I'm looking at her and she's nodding, talking to Danish investigators. And yes, they are very committed and they do see potential patients. And I would underline potential because we don't know that they actually will go into the study. We also know that there are patients that are in there at the top of the funnel, both in Norway and in Sweden at the moment.

So yes, we are seeing a pickup in the Scandinavian countries. And maybe, just maybe, this is a leading indicator for what could be the case in the next few months. We do see a pickup in interest up here in Scandinavia.

Answer

Frazer Hall (Attendees)

Thank you, Erik. The next question asks whether or not you can give, and there are a couple of different questions on theme, more visibility around the funnel. Can you, for instance, tell us how many patients are in the funnel at the moment or who may have passed through the funnel and are under active consideration for enrollment at this stage?

Answer

Erik Skullerud (Executives)

So we've said before and I say the same again, this is not trying to keep information away from you. But looking at these numbers, they go up and they go down. I think I've used the analogy before of like sour milk and a little kitten. It's one week, you look at them and you go, hallelujah , this is impressive. Next week, you look at them, and this is pretty not so good and then they bounce back up again. So it's very hard to make any sense of the number.

So if I were to say 10 is in the funnel, what would you make of it? It doesn't really mean anything. That number is not the right one, by the way. But I'm using that in the sense that we're looking at these numbers because it's important for us to understand what is happening and we can make some sense of it.

But when it comes to how many is in the funnel, and on the basis of that, how many is coming out of it, I think it's fair to say that with 2 patients coming out, back to my Q4 statement, we had a lot of patients in and we did in the funnel. Two of them coming out, 1 going into late-stage screening, but then dropping out. I think that is proof enough that for us to talk in more detail about the numbers, it doesn't make that much sense. It's not that we don't want to, it's just that it doesn't really help much in this sense. And I hope for your understanding on that.

Answer

Frazer Hall (Attendees)

Thank you. There are a number of questions which ask whether or not you could bring more visibility to patient recruitment by reporting recruitment or enrollment numbers more frequently, for instance, possibly every month.

Answer

Erik Skullerud (Executives)

Yes. And I think -- so first of all, thank you for that question. And I know there are investors out there that also have sent these type of questions to us over the last few weeks, and apologies for not answering those questions. As you know, we have been under embargo for communication with you the 4 weeks leading up to this conversation.

That being said, I think our policy around doing this on a quarterly basis, we will continue to maintain it. I will say that and then I will say, I know that based on what we have guided this morning, you will have arguably even more questions on that.

So I think bottom line for me is we will continue to do it on a quarterly basis. But I will also say that we should also look at how can we better help you in understanding this. But I think bottom line for me is when you look at the number of patients that have gone in, I think the lowest we've ever had was towards the end of last year and into beginning of this, which was 0. The highest we've ever had has been 14, I believe, in 1 quarter.

So if or when we see significant change to how we are reporting, maybe that could be a trigger. But I still do believe that the best way for us to do this is to use the quarterly updates because I'm afraid that it would confuse people if we were to do this more often than that, number one. And number two, keep in mind, there's work associated with doing these updates. Quite a lot of work as well.

I want to make sure that we focus where our resources is best used, which is trying to get more patients in and rather maintaining a stringent system around how we report and do that quarterly.

Answer

Frazer Hall (Attendees)

Thank you, Erik. We have a couple of questions relating to the number of patients to be recruited for PARADIGME. Essentially asking, is it possible or do you have any hope that in negotiation with the FDA you could reduce the number of patients required for filing the BLA?

And further goes on to ask, are you in any active dialogue with FDA regarding this possibility at the moment?

Answer

Erik Skullerud (Executives)

So we are continuously in communication with the FDA. I think it's probably premature to say, are we going to be able to do this with less patients? The guidance from the FDA is pretty clear when it comes to accelerated approval specifically: you need a specific power statistically on your study. In other words, how many patients you need to show results in, in order to submit an accelerated approval for BLA. And that's where our numbers are coming from.

Now FDA is obviously using, on one hand, they are using science. On the other hand, they're using judgment. It's going to be up to them to tell us how many patients we would need. All we have today is that we have to fulfill the numbers that we have also shared with you in order for us to do an accelerated approval. Anything about that -- above that, to me, would be pure speculation from my side and I don't want to try to do that.

Answer

Frazer Hall (Attendees)

Thank you, Erik. The next question asks whether or not you see an increased interest from potential partners as you get closer to full recruitment of PARADIGME?

Answer

Erik Skullerud (Executives)

So I'm not sure if this is related to recruitment or if it's just purely related to the fact that the world is opening up post COVID. We are obviously attending business development conferences and we've had a couple of chances to do that in the last few weeks where the feedback is more.

Interest is definitely there and it sounds to us that it's a bit of a reinvigoration of interest. But if that is related to we're moving closer to finishing of enrollment, if it's just our business development person that is doing a really good job or if this is they finally get to talk face-to-face again over a cup of coffee, it's hard for me to say. But there are still several active, ongoing conversations with regards to potential partnerships.

Answer

Frazer Hall (Attendees)

Thank you, Erik. And just a further question regarding any interaction with FDA, asks whether or not you've had any discussions directly with FDA about the outcome of the decision from the AdCom regarding PI3K inhibitors and whether or not you consider that, that decision can favor a potential approval of Betalutin due to the need for new therapies in the space, or whether the FDA may actually impose more strict requirements with regard to the outcome of extended studies.

Answer

Erik Skullerud (Executives)

So the last conversation we had with the FDA was before, and in fact, just a few days before the ODAC meeting. So for obvious reasons, there was no comment from the FDA to us specifically around that.

So whatever -- I would refer to what I said during my presentation on the impact of what has happened at ODAC, but we have not had direct feedback from the FDA on implications for us based on what's happening with the FDA.

I will iterate what I said in the presentation. Our take on it is that PI3K is in the situation that they are due to the high toxicity of the drug. That's fundamental for why they have been asked to do these randomized studies early on and not just part of their follow-on confirmatory studies. And that seems to us that may give us an advantage in this sense due to the fact that our toxicity is significantly lower than that of the PI3 case.

Answer

Frazer Hall (Attendees)

Thank you. We now have a series of questions essentially regarding cash burn and the cost base of the company, which ask, given the current relatively low recruitment rates, are you looking at particular measures to extend the cash runway and conserve cash as far as possible? And there are subsidiary questions, which I'll follow on with.

Answer

Erik Skullerud (Executives)

Malene?

Answer

Malene Brondberg (Executives)

Yes. We are, of course. We are always doing that. That's not just an exercise that we do now. That's the obligation we have towards the shareholders, of course, to look at how we spend their money and we do that all the time every day.

And that's also why we came to the conclusion that one of the things that we could maybe leave out is the Norwegian PR. We have other things that are similar to this, which, of course, in the grand scheme, is not a big cost but it adds up. Everything adds up and every penny counts. So of course, that's what we will do, of course, or continue to do.

Again, the biggest spend here is, of course, on the CMC and also the clinical. And that's, of course, important that those areas have the money that they need. So that's why we need to do everything that we can to move the money into that area. We've done that all along, and my team is working full stop to get this right.

Answer

Erik Skullerud (Executives)

And Malene does a very good job of also reminding me of how we need to ensure that this is continuous, not just something we look at on a quarterly basis. We look at this virtually every single week on how much we spend and how it's moving forward.

Answer

Frazer Hall (Attendees)

And a follow-on related question to that is -- asks, essentially looking at the number of centers that have likely recruited patients over the last year or so, it seems that there are still a large number of centers, possibly 60 or so of the 85 active centers that may not have recruited patients in the last 12 months or so. Does that mean that you should be considering closing some of those centers that aren't recruiting to further conserve cash?

Answer

Erik Skullerud (Executives)

I think that's something that we continuously monitor and continuously look at. We have closed a significant number of sites in the last, I would say, about 12 months. We've gone from, I believe, more than 90 -- more than 95, maybe as many as close to 100 down to the 80 that we have today.

Out of those 80, to the question's point, there's about 60 of them that are truly active. That's where we spend our resource. The other 20 are centers that are still open, either as part of Part A or as part of PARADIGME. And we still need to monitor those sites, hence, why we can't close them down completely. But all the efforts with patient recruitment is really focused on these centers that are truly recruiting, number one, but also interested in recruiting because there is a lot of activity that goes on also apart from what you see in patients coming out as recruited, as I mentioned earlier, with regards to the funnel.

Answer

Malene Brondberg (Executives)

And I can just, Frazer, if I may, just to say that we, of course, me and my team as well, we have a weekly conversations, of course, with the clinical team as well about this. And this is one of the things, again, that, yes, we monitor all the time, which we have to do, of course.

Answer

Frazer Hall (Attendees)

Thank you. Just moving on, there's a question on Archer asking how many of the Archer study patients are still in remission and how many have passed the 3-year readout at this point. So can you give any updates or is there any update on Archer at this stage?

Answer

Erik Skullerud (Executives)

The update is very much the same as what we said last time. We still have, to our knowledge, there's going to be one patient, which have their last visit in October this year. The other patients -- we had 7 patients initially. One of them had a -- went into -- went -- well, did not respond very well to the treatment and that we have reported earlier. The other 6, to our knowledge, is still in remission.

But obviously, and you may also know this, this is also public information, we are stopping monitoring these patients partly because of the number, but also partly because we are -- we feel that we have proof of concept of the combination and the effectiveness of the combination.

But the last update that we have is the same as what we gave in the Q4 presentation, that those 6 are still in remission.

Answer

Frazer Hall (Attendees)

Thank you. Erik, I just wanted to hand it back to you to ask if there are any further questions in the room at this stage.

Answer

Erik Skullerud (Executives)

I don't think so. No, no further question here. So I believe that if that is -- if that's the last question, Frazer, from your side, then I think we bring the presentation to a close.

I want to thank those of you in the room, those of you online for your active participation, your support. The questions, we appreciate them. And wish you a wonderful day and also a happy 17th of May when you get there on Tuesday.

So thank you very much, and talk to you soon. Bye-bye.

22.03.01. Nordic Nanovector ASA, Q4 2021 Earnings Call, Mar 01, 2022

Presenter Speech

Erik Skullerud (Executives)

Great. Good morning, everyone, and welcome to the Q4 Results Presentation for Nordic Nanovector. My name is Erik Skullerud, I'm the CEO since 5 months back now. So this is my second quarterly presentation. Together with me today, I have 2 of my colleagues, Malene Brondberg, CFO, that you will already be familiar with, and I also have a new colleague that I want to introduce to you, Sandra Jonsson, who is our new COO. So the 3 of us will be entertaining you, hopefully, today and also having a good conversation, hopefully.

Last time that I was here was back in October, I believe, and little did we know then, of different events that have happened in Q4 and also into Q1. And honestly, a couple of weeks ago, I thought I was coming back to Norway at the back end of omicron, only to find out a week ago that obviously, the geopolitical landscape have changed, and we find ourselves in a new crisis. So I just want to take a moment to just think about and give a bit of good feelings down south towards our friends in Ukraine. I hope that this is a conflict that will not take too long. It doesn't look very good, but they should know our thoughts are with them.

Before we jump into the presentation itself, some forward-looking statements that you are all familiar with. Make sure you realize the aspirational nature of what we are about to say today, and that you familiarize yourself with those, before investing in the company. As mentioned today, 2 of us will be presenting, Sandra, feel free to reach out to her after the presentation and get to know her somewhat. But Malene will talk about the financials, I will talk about a business update first. So let's jump straight into it.

In Q4, we spent a lot of time focusing in on PARADIGME, which is our primary priority. Today, we are reporting 106 patients, and we'll talk about this number a little bit more in detail in a bit. As you well know, we changed our guidance early in January to suggest that we are now getting the results of PARADIGME in the second half of this year. We maintained this guidance today, although, and you will see that in a moment, omicron has hit us very hard. We did get questions on this already in December. We did say already back then that this was something that we were going to take our time to evaluate. We have done so, and you have seen the consequences, but we'll spend a little bit more time.

Secondly, we also did an emission, now just after Christmas, with the new time lines for PARADIGME. It became obvious to us that we needed to get in more and increased financing in order to reach the final readout of the study itself. We got about NOK 250 million, and let me already now say a big thank you to those of you that were part of investing at that time. As you will also know, we have an emission ongoing, and I know that there are certain question marks around this based on the geopolitical environment that we find ourselves in.

But that being said, please keep in mind, that when it comes to emissions like this and the specific Norwegian repair type of tactic associated with this, this is something that is weeks in the planning, before you actually go out and execute it. And on top of that, it is really important for us to think about all of our shareholders, not just the big ones. We also want this to be an opportunity for smaller shareholders.

As mentioned in Q4, we have also added 2 new people to our executive management team. Pierre Dodion that you were introduced to in the R&D Day back in November, and Sandra, who is joining us as of the 10th of January, was appointed back in December. In addition to that, we have a couple of other things that we have also announced and that you will be familiar with. Number one, we announced a collaboration with the Health Partnership around better understanding the potential barriers to entry for radio nuclear medicines in the global environment. This is important, when it gets to our launch, because that's going to underpin the success of the launch itself.

And finally, we announced a collaboration around CAR-T, together with the University of Pennsylvania, something that we are really excited about. This is one of the foremost research collaborative organizations in the world, when it comes to cancer medicine. They have developed a unique technology around CAR-T, and as such, is a collaborator that we're very proud to be associated with.

So back to PARADIGME, when it comes to PARADIGME itself, as mentioned back in November, we did already then see some early, early indications, that this was going to potentially be a challenge for us. We mentioned already at the R&D Day, that this was something we wanted to spend time on, better understand. We

spent the whole of December, and especially the Christmas and New Year's period, diving into this analysis. I think we must have spoken to somewhere in the area of 30 to 40 different centers myself, I've been on 20 to 25 of these calls, to better understand what was the impact on the ground, with regards to cancer treatment, hospital environment and how that could affect our study.

As such, we went out with new guidance in January, and this time, we put a lot of effort, and we wanted to be ahead of the wave. We wanted to be transparent and open to you, around the impact that this has had, on inclusion in PARADIGME. And hence, the guidance that we're giving today is the same that we gave back in the beginning of January, so we did not get any new patients from then until today.

Again, we saw this coming, and I will describe exactly how we saw that in a little bit, but that was important to us to already back then go out with it. The good news is, this situation is, as we can see now, starting to change.

So let's spend a little bit of time on that. On the left-hand side of this slide, you will see targeted initiatives that we are putting in place, either have been, are or will be doing, as we speak. We spent a lot of time and efforts, and I mentioned this also in my Q3 presentation, on really segmenting and better understanding the different centers out there. Where are they on this journey? Are they the kind of centers that will -- yes, we're really interested. We are screening and therefore, we are including patients. Are they on the journey of -- we are kind of staying on the fence. We think that this is a good study, but we haven't found the study -- a patient, excuse me, or are they -- we have other things to do. And for those of you that are involved in clinical studies, you know that all of these different types of centers exist in any study out there.

About 70% of our centers are actively engaging, actively trying to find patients, actively trying to work with us. The last 30 is for us, they need to be in there, because they help patients in the past, but they are not necessarily that active today. The main countries as far as inclusion is concerned, and this is a question that we have gone over and over again, and today, I'm happy to relieve some of those questions, are North America, U.K., Ireland and Spain. As a Norwegian, I'm a bit disappointed, to see that the Nordic countries is not on that list, I must be honest. Because when we look at the development of Betalutin, a lot of the early patients were included in Norway, in Denmark, in Sweden. And for whatever reason, and I'll get to that in a second, that is not happening today.

I think it's fair to say that with Dr. Kolstad, moving from Radiumhospitalet, one of our biggest supporters, moved jobs, so to speak. We still have a great working relationship with him. I'm going myself to meet with the Radiumhospitalet tomorrow, to meet the new principal investigator there. And our senior management staff is now going on a tour around the whole of Scandinavia in the next couple of weeks. So Sandra will be doing this, together with our MSLs. This is important to us. We're a Norwegian company, with a Norwegian base, and we should do better in Scandinavia, from an inclusion point of view.

That being said, and I mentioned the guidance that we gave back in January. On the right-hand side of this slide, you can see how we monitor the study. All of those different parts, those filters, if you want, in the funnel, are where we look at patients. So we know exactly how many patients are under consideration, how many have consented, how many are in early screening and how many are in late screening. Back in December, we saw that the lower part of the -- or the upper part of this funnel, started to thin out. There was less and less patients. And we saw that they were still in the funnel, some patients, that also got included up to the 6th of January, 7th of January.

The good news today, is when we look at this funnel, we have more patients in the upper echelon of this funnel, than what we've ever had. And I'm not just saying that to please you, but these are true numbers for us, where we can see that this is going in a very good direction. So we have a lot of patients under consideration, partly because of initiatives such as Trial B. You see on the left-hand side also, we have added one additional clinical scientist. This person is -- every time we get a patient under consideration, this patient is in direct contact with the center in question. And as such, we have a much better feeling for these patients now, than what we did 6 months ago.

So over and above the clinic itself, there are several pieces of the puzzle that we need to get right, before we can eventually submit the file. We've spoken about the clinics, and we've gone on about how many patients are enrolled and what we need to do. Over and above that, it is the regulatory interaction itself. We have 2 interactions that we will do in the next 4 to 6 months. One is coming up at the end now of Q1, which is with the FDA, around our future Phase III confirmatory study. This is around a discussion with them, on what is going to

happen and how is the study going to look like? Just as a reminder, and we'll get back to this a little bit later, the PI3K inhibitors that have been taken off the market, several of these products did not do this interaction well. We do not want to make the same mistake. And as such, those interactions are happening now.

The second point with regards to the FDA, is around production manufacturing supply chain. You heard from Lars back at the R&D Day, and there is a reason for why we keep on talking about this. Without that part of the puzzle, we will also not be able to submit a file. And as such, getting that right and doing it upfront, is really important. And I'm really proud of the work that is being done in that field, because we're making great strides, in order to be ready, and we're fully on track in making that happen.

So that's one part, or 2 parts. The third part, and we'll get back to that at the end of the presentation, is our strategy around partnerships. Again, a lot of work is happening, and I think some investors may think that this is a matter of just turning a switch. This is work that needs to happen and needs to happen over time, especially with big pharma, strategies around how you partner, is they will only go in, once they see the data. So I would anticipate, and I think we should all anticipate, that until we have the data, the big pharma will not knock on our door and say, we want to partner. That's not to say, that we're not talking to them, because we are. But it's not to say, that they're going to say, we're going to sign you up until we actually have top line results.

So back a little bit to the manufacturing side of things, because this is important. The first thing we need to do, and we have been working on in the last 3 years, is around the so-called PPQs. This is qualification around how our production process happens. A validation that we can do the same over and over and over again, and ensuring that, that product process can go from clinical substance, into commercialized substance.

The second thing that we need to do, is to take all of that information, categorize it and put it into the BLA, into the file itself, and ensure that, that file is solid, that, that file can be used with the FDA, and as mentioned, the first interaction that we have with the FDA, specifically on manufacturing, is going to happen in June this year. But so far, everything is on track. As far as I am concerned, and I have seen several companies do this, we're ahead of the curve on this one. The team is doing an incredible job. And then when we get to launch, obviously, it is to supply the market. But already now, we're also thinking significantly about cost of goods, profitability. How can we streamline this process, so that at the end of the day, the profitability of the company is insured.

So in that sense, we have in the last, I don't know how many quarterly reports, talked about what happens before we submit. Today, I want to talk a little bit more about what happens after we have the results. When we have the results, the first thing that will happen, is that a lot of people in a lot of places will start analyzing. Already now, a lot of analysis is happening, but in order to make this happen, number one, and to fulfill our obligations, both on patients that are early in the study, patients that have progressed through the study, and patients that are [old] towards the end of the study, all of that data points, tens of thousands of data points needs to be analyzed.

Now everything you see on this slide in gray, is stuff that we cannot predict from a time line point of view, because it has to do with the nature and the quality and how good or bad the results are. In other words, when we give our first, we hit the primary endpoint, that is when we can start predicting how long that process will be. So both from a data cleaning point of view, pulling the file together point of view, we need to see what the data is actually telling us. During the course of that time, we will request a so-called pre-BLA meeting with the FDA. And in that meeting, we'll have a conversation with them about the data package, the quality of the data package and how that is, according to what they expect from us. Again, our expectation and all the interactions we've had so far, is that we're doing the right thing, we have the right study in place, we've done the right statistics, and we're executing according to what they expect from us. So that will be a very key moment for us, where we have that interaction, and we can then start the filing.

As you know, due to the nature of our fast track, we can interact with the FDA on a continuous basis. And believe me, we're doing that as often as we possibly can. That is to ensure that we don't get any surprises during the course of this journey. Once we get to the submission and the submission is done, the time lines become much clearer, because when that happens, the FDA has 2 months to review the data and then they will tell us, either you get a priority review, which is 6 months or you get a normal review, which the vast majority of these submissions actually get, and that is 10 months. So the highest you will get with regards to the review time itself, is 12 months, and then we'll be ready to launch. So this is what this is going to look like, once we have gone through the motions of analysis, discussions and review with the FDA.

But we're not just thinking about that. We're also thinking about the commitment that we have as an organization, because of the approval route that we have taken with the FDA, the Phase III confirmatory study. And again, this is preliminary, what you see in front of you. It is second line rather than third line FL. It is a combination, rather than single agent. So those are areas where this differs from what you have seen in third line. The market opportunity over here, is also close to twice that of third line. So we're talking about significant upside, if or when we do this and go into second line. But that is the discussion that we will have now with the FDA, towards the end of the first quarter, to align around this design.

And just to remind you, in NHL, which is our focus, our primary focus, this is one of -- still one of the largest unmet needs within cancer. The fact that so many PI3K inhibitors are going out of the market, makes that unmet need even more significant, especially in the patient group that we are talking about, and I'll get back to that in a second. And again, just to remind you, the clinical data that we have so far is extremely promising, and you can see in the middle of the slide here, the 2 numbers that have been circled, this is the patient group that is the closest in the Part A, the data that has already been published, to what we are doing in PARADIGME. So this is kind of from a comparison point of view, and let me remind you, it's not exactly the same, but it's the closest that you get in the numbers that we -- or in the data, that we have presented so far.

But let's dive into the competitive environment. I'm going to show you 3 slides, because I get a lot of questions from investors on this. The first one is related to, and you've seen this before, but it's important to underline the patient population. On the horizontal side here, you see patients from left to right, those that are young, fit and is available for more aggressive treatment, also more toxic treatments. These are patients that constitute approximately 25% of the total population, in third line. In third line equally, the right-hand side, the unfits, the elderly and the frail patients, they constitute approximately 75% of the total patient population. These are the ones that we are after. And that's important to keep in mind.

Now when you think about going from third line into second line, the combination treatment the efficacy becomes much more important. Efficacy, you will have seen in the ARCHER study. That's our first combination trial with rituximab what we're looking to do also in the confirmatory Phase III. Efficacy becomes more important. But again, half of that population in second line is elderly, frail or they cannot have more aggressive therapy, for whatever reason. So that's the first thing that's important to keep in mind.

You see a couple of X's on this slide. That is the 3 different PI3K inhibitors that have been pulled off the market. Those are no longer competitors. So from a purely competitive intensity point of view, those are gone. As such, we believe we anticipate the competitive intensity in this marketplace to be significantly less, when we enter, than what it is today, because this slide also includes other treatments that would be launched ahead of when we get in there. So this picture over the last 3 to 4 to 5 weeks, have changed in our favor significantly.

The second piece of questions that I'm getting on the competitive intensity is then, not so much towards PI3K, although I'll touch upon copanlisib in a second, but it's related to the other 2 major groups of treatments. Number one, CAR-T, number 2 bispecific antibodies. With regards to CAR-T, the most significant threat perceived by other investors, is around efficacy. And with regards to efficacy, yes, efficacy is impressive by CAR-Ts. However, keep in mind the full profile of this group of treatments. Approximately half, if you look at FL only, of these patients get what you call the cytokine release syndrome. This is toxicity that is potentially deadly, if not treated and not treated well. And you need a highly specialized unit in order to treat it. This is not for frail patients. This is not for elderly patients. And also when you look at bispecific antibodies, that same number of cytokine release syndrome is approximately 35% to 38%. So it's less, but it's still significant toxicity.

Now let me qualify that, because obviously, bispecific antibodies, we do not have in the market yet. So we do not have so much clinical experience with it yet. We only can go by what is actually being shown in clinical studies so far, both Phase I and Phase II. And again, efficacy is impressive. But as such, we believe that those 2 product classes will be more for the fit population, more for the patients that can actually tolerate this. Those are younger patients and are patients that we will not be competing for anyway.

The final point I would like to make, is with regards to copanlisib; because copanlisib, we're getting a lot of questions on accelerated approval, how will copanlisib, if it gets a full approval, how will that affect our chances of getting accelerated approval. Now keep in mind how they have designed their studies. Their studies are done, both CHRONOS-3 and CHRONOS 4 are done in patients that are sensitive to rituximab therapy. That is one of the exclusion criteria, for the population that we are targeting. In other words, first of all, from a competitive

point of view, we don't believe that this is necessarily a big competitor. But more importantly, our ability to get accelerated approval, we do not believe that, that is going down, as a consequence of them getting a final approval, for that specific reason. We are targeting a different population than what they are.

So in that sense, let's talk a little bit about the positioning and what we will be bringing to market. And obviously, there are several dimensions to this, that we're keeping a little bit under wraps, because we don't want to show our future competitors exactly what we'll be doing. But from a top line point of view, in third line, we are targeting elderly and frail patients. We're targeting that with the value proposition of duration of response, a onetime-only injection and a manageable tolerability profile, something which is unique in this marketplace, something that we can compete on, and we can sustain a competitive advantage. That is what we believe for third line.

In second line, it becomes a combination proposition. What can we do, when we combine Betalutin with rituximab. And we have seen -- and you have seen in preclinical data that there is a synergistic effect. In other words, we enhance the efficacy of rituximab even further, and you get the over and above effect from Betalutin. We have shown it in early clinical studies, in the ARCHER study and that's the first comfort you should take in our ability to be successful, also in this setting. And finally, we're working now on looking at further patients what could happen, what does happen once you get off Betalutin, we're looking into our own studies, what happens to patients that get off betalutin and get rechallenged with rituximab. We're looking at that, and we're hoping in the next 6 to 9 months to have a first-line analysis of it, but we're trying to build this value proposition to strengthen this value proposition, in the phase of also going into second line. So we're thinking forward here as well.

The final part around Betalutin, and then I'll stop on Betalutin itself is around the HPP collaboration. This collaboration, as I mentioned, upfront, is intended to dampen barriers for entry. And for those of you that are truly interested in how you succeed in pharmaceutical marketing, this is the way to do it. Doing this upfront, and I'm not going to take any of the accountability for this. This was done way before my time. Other brains were thinking much better than mine on this. This is something that we are doing. In fact, we were one of the first to initiate this, but other big radiopharmaceutical companies have joined us on this journey. As such, companies that are launching pharmaceuticals in the radiopharmaceutical space now, they're breaking the way for us, if you want. They're utilizing this going into the market, and we will learn together with them, because this is a collaboration of sharing of data, we will understand exactly what it's going to be [taking] to be successful in this marketplace.

So that takes me to the last slide, which is related to Betalutin, and then we'll go into the rest of the pipeline for a couple of slides as well. But what I want to highlight with this, is what we also presented back in November, December in our R&D Day. We initially talked about Betalutin, the pipeline that we're trying to create of the product itself, but we also highlighted the 4 other assets that we have in the pipeline, 2 of which are now under collaboration, one with Oranomed, the Alpha37 also radioimmunotherapy, and our CAR-T product.

And just a couple of pieces of news around what's going on in the other part of the pipeline as well, because we are spending, as I mentioned, last time, 80% to 90% of our efforts of our energy on Betalutin. But we also do find time to do a couple of other things. So for Humalutin, we have submitted a paper preclinical, but this is together with a PARP inhibitor. And for those of you that are familiar with PARP inhibitors, you will know that these are big in breast cancer, in ovarian cancer and some of the more promising oncology therapies out there. So we submitted a paper together with olaparib, a combination treatment preclinical, to show the dual efficacy of the 2.

For Alpha37, we're also progressing very nicely with our partner, and right now, we're waiting for answers from the FDA, around production, early-stage production, early stage reduction GMP manufacturing for that specific molecule. Again, we are targeting an IND, together with Oranomed, and we're getting the next milestone for us internally towards the end of this month also there.

The final piece is related to humanized and to CAR-T. For humanized, we are in the midst of choosing the final candidate that will bring forward. This is -- as you know, this is a clean antibody. And here, we're looking at partly NHL again, or potentially immunological disease. We spent the last few weeks on talking to opinion leaders around Europe, on where is the best opportunity, how can we do this the best, and we're collating those results as we speak.

Finally, on CAR-T, the program has not been -- has now been started. So that is work in progress, and we're expecting further announcements from that towards the end of this calendar year.

So just a couple of words on CAR-T, and then I'll let -- and then I'll speak a bit about partnering as well. But on the CAR T collaboration, as I said in the beginning, we're obviously very excited about this. This is a collaboration that we believe for future reference, will be an extremely important one for us. We also believe that this will be the next-generation CAR-T because of the way that we do this with them and the technology behind it. If things go the way that we hope, if this thing -- if things go the way that we will -- we aspire, you'll see a different way of both mechanism and efficacy and safety, than what we've seen with previous generations of CAR-T therapies.

So that brings me to the last slide before I let Malene take over with the finances, and this is around our partnering strategy. A lot of questions are coming from investors around how we do partnering. As I mentioned in my last presentation to several of you, we have one person internally. In fact, we have several that are working basically night and day on the partnering itself. And the conversations that we're having, is falling into 3 different categories. One, is around commercialization for Betalutin. This is about North America, it's around Far East. It's really how do we make a success of Betalutin around the globe.

The second one is falling into considerations around, let's call it, mid-stage pipeline assets. So this is around Humalutin, it's around Alpha37, and to some extent, even our earlier-stage assets, where it's more around how do we bring this into humans and how do we bring this through the clinical development cycle. And the last one is the CAR-T example, where we're forming alliances, collaborations with other scientists, in order to start scraping the surface and really understanding what an asset could look like. So this is what we're spending time on. We have several conversations ongoing with different parties as we speak. But as I said, with regards to commercialization, I would not expect a big partner until we get to the top line results. For the other 2, there is definitely a possibility that we may get traction.

So I think with that, I'll let Malene take over and talk about the finances and then I'll come and summarize. Malene?

Presenter Speech

Malene Brondberg (Executives)

Will you hand that over to me?

Presenter Speech

Erik Skullerud (Executives)

I will do that.

Presenter Speech

Malene Brondberg (Executives)

Thank you. Okay. Good morning as well from me. Let's see how this works. Well. No? That was the other way? Fantastic. Here we go. Okay. So as you can see, we spent -- the cost was NOK 133 million in the Q4. And as you can see here, the net cash position from the operating activities ended up around the -- or NOK 89 million. What's more important is, of course, if you look at the spending that we are going into now here in Q1, because you could see at the end of the year, we had NOK 278 million.

And then you can ask, why did you go out and then take some money in at that point, because that's quite a lot of cash. And with the new cash that we have the NOK 250 million gross, which boils down to roughly after we paid, the help we had, roughly NOK 233 million. So add those 2 numbers up, you could say that it is a pretty good cash position, and it is a pretty good cash position. What you can't see and what you see, when you see our Q1 numbers, is that we had a pretty good outgoing -- pretty good, I would say. It's not good, of course, to have a

good outgoing. But we had a good -- had an outgoing -- will have in the Q1, which is roughly around NOK 160 million.

We had last year a NOK 130 million approximately, and the reason why we have this much more going out this year in Q1, is because we had a change order, which is part of the business, when you do work with the suppliers like ICON, which is our CRO. So when you reach a milestone, you have to pay out, and that's why -- so you can see that the cash position would change dramatically, when we come to the Q1. So just if anyone wonders why did we actually go out at that point, and of course, unfortunately, we have, as you know, to extend the time line. When you look -- and that's why we had to go when we went. Of course, it wasn't an ideal situation when it came to the market. But unfortunately, that's the nature of the business and the market.

So -- when it comes to the cost for the Q1, we will probably look around the NOK 120 million mark. But hopefully, that will give some explanations into why -- if we look at the good cash position, what's actually going to happen with that cash position. If we look at the repair issue, which we have ongoing, we've also got a lot of questions, why do you do this repair issue. Why didn't you just cancel it? Well, the repair issue, it wasn't something that we just started yesterday. It's a long process, and when we did the private placement and completed that, as you know, on the 19th of January, we actually, at that stage, started the prospectus -- update of the prospectus, and that takes more than a month to get that through.

It takes roughly 6 weeks to get that through with authorities here in Norway. And it is a quite costly process. So of course, we could have said, okay, now we're going to cancel the repair, because we are right now on the 14. But on the other hand, as Erik just said, we want to give everyone a chance. So if we had gone out and they -- there was still an opportunity to come in. And since we have already spent the cost and a lot of time out, so there's a lot of time going into this planning, and doing the [prospectus], that's why we continued, mostly because we want to give everyone the same opportunity. It is running until the 11th of March. And of course, with everything else, as also Erik said, going on in the world, let's see where we end with that.

With that, I think I'll hand it back to you.

Presenter Speech

Erik Skullerud (Executives)

If I would always be as efficient in presenting, as you, Malene. So I want to just leave you with this slide. I'm not going to spend a lot of time talking about it, because we've seen it before, and it's kind of in a nutshell. What is it that we want to leave you with? Our asset Betalutin, which we spent days and nights in supporting, promoting, making sure that we do the best job for bringing that to market, is our top priority, and it remains our top priority. But there is more to Nanovector than just Betalutin. There's also other assets that we're working on, and that we're trying to bring through into clinical development, and eventually into patients.

So although Betalutin on its own could be a pipeline for us, we're also looking at other attack points based on the science around CD37. And I didn't mention CD37 in my presentation, but I still am just as excited, even more excited today, than what I was when I joined the company, because I did not know that there was a CAR-T going in as I joined. And I think that adding to the wider pipeline, is a significant step forward for us.

As Malene has said, from a financing point of view, we have money well into 2023, and we have money beyond the readout of the top line results for PARADIGME, and we are obviously extremely excited about 2022. This is, for us, the year where push comes to shove. This is when we will see our little baby walk for the first time, and hopefully, those results, and we believe that those results will be really, really good ones.

So with that, let's end the presentation. I believe that we have some time for questions. So let's go for those. Anyone in the room first, before we open to online questions? There does not seem to be any questions in the room? Do we have any online questions?

Answer

Frazer Hall (Attendees)

Yes. Good morning. We have a number of questions online. We'll start with some questions if we may, around PARADIGME, and we have a number of overlapping questions regarding PARADIGME. The first one of those is, a question as to, why you do not report more often, how many patients are included in the study?

Answer

Erik Skullerud (Executives)

So let me just remind you of what we have done in the last quarter-ish. So we spoke to you on, if I'm not completely wrong on, what was it the 17th of November, which was Q3. We then reported a number. We had another R&D presentation, R&D Day on the 30th, where we reported a number. And we had a 6th of January, where we reported a number. And today, we're reporting a number. I don't see how we can do it more often than that, to be honest. So that to me is as often as we can get. That's number one.

Number 2, as I think you can see, this isn't something where we just turn a switch and numbers flow into the study. This is a rare disease. This is a rare disease and patients are not that easy to find. So on those phases, our estimation is that, quarterly reporting have been often enough. But that being said, we have made an exception through the course of the last quarter, with 4 interactions, and I hope that is sufficient.

Answer

Frazer Hall (Attendees)

Thank you. Next follow-up question on PARADIGME is, around -- can you offer any further explanation, as to why the recruitment rate seems to have stopped since early January, when you last reported?

Answer

Erik Skullerud (Executives)

It's a very good question. And as I mentioned, my own Christmas, New Year holiday was spent on pondering and researching that question. For anyone out there that have family, that are in hospital for whatever reason, and have been to a hospital of late, you will have seen the chaos that is in the hospitals. Whether that is in Norway, Sweden, U.S., Greece, Turkey, Australia, Italy, Spain, Germany, and I've spoken to hospitals in all of these countries in the last 6 weeks, it's the same thing that you see. And although we're going out of omicron in Norway and in Sweden, in Denmark, in Switzerland at this stage. In Germany, they're not yet. In Spain, they're not yet, although they're saying they may get out of it towards the end -- of Spain.

The point is, for the patients that are not severely lethally ill and have immune deficiency, which these patients have -- they're not coming to the hospital. They're not being enrolled in studies. I mentioned this in the R&D presentation that we had back in November, 60% less patients have been included in studies in the U.K. in 2021, than those that were in 2020. And that being said, what we have also seen with omicron specifically, is that the message that we heard from the experts, when Omicron hits back in November, and it was iterated throughout December and into January, was that this strain is not going to be as sensitive to the vaccines. So another driver for why patients do not come into hospitals.

And the final driver is just that hospitals, and this is, in my mind, the biggest driver for the chaos that we're seeing at the moment, patients that have been -- not going to hospitals for whatever reasons, are now coming back, but they are crash landing into intensive care and into severe care, which means that those beds that could be used for cancer treatment, are actually being taken by severely deadly ill patients. Hence, while you also see the chaos in the hospitals, it is no longer omicron specifically related, but this is the backlog that we have, by the way, expected for the last 2 years of patients coming into the system. And that to me, are the 3 key drivers for why you have not seen inclusion as such in the study. But as I said, over the last 2 to 3 weeks, we have seen a lot of patients starting to go into consideration. We have started to see them go into screening, and this to me is a leading indicator for that -- this is a situation that very likely and let's hope that there is no further strains that we'll get, but it's very likely we can see the light at the end of the tunnel.

Answer

Frazer Hall (Attendees)

Thank you. And the next couple of related questions. Firstly, when do you expect the enrollment rate for PARADIGME to pick up again? And following up on that, do you think the guidance of readout in 2022 is still achievable, when the recruitment rate has been so slow?

Answer

Erik Skullerud (Executives)

So let me tackle the second part first. Yes, we do. Again, assuming that we don't get another omicron or another strain that we even have more issues with, number one. But number 2, when are we expecting them to pick up again? I would say something in the area of the next 4 to 6 weeks, we should see this trend turn.

Answer

Frazer Hall (Attendees)

Thank you. And a further question on PARADIGME, is regarding whether or not you can give any more specific numbers around the number of patients under consideration or in enrollment at this stage, versus historically?

Answer

Erik Skullerud (Executives)

So I can say that, like I said in my presentation, the number that we see now, is higher than at least what I have ever seen from an enrollment and from a consideration and early-stage screening. I have not seen this number since I joined, and from what I've understood from others in the company as well, these are very high at the moment. I do not want to go out with specific numbers, and I'll tell you the reason why. Patients that are going into enrollment, and this -- the funnel is there for a reason, because the numbers that go in -- to the early stages of the funnel, they come down. Some patients come in and then they go back out again. They don't make it all the way to actual enrollment.

So in the part of Norway that I come from, directly translated, these numbers are -- and this is where the quote, it goes like, 'sour milk in a kitten.' It basically does, it swallows walls and then it comes back up again. This is how we would describe, what's happening in these numbers. Hence, for us to go out and say, the number early stage is 15, and I just made that up, by the way. This is not the real number. The next week, it would be 12%, and then it goes down to 2, and then it goes back up again. These numbers are changing on a continuous basis, hence, why we don't go out with them. We would confuse sorry, my language, the hell out of you, if we would do this. And so we'd much rather be in a safe place, where when we are saying, this is the number, you know that you can have confidence in it.

Answer

Frazer Hall (Attendees)

And just one further question around PARADIGME, which is how long does it take on average from the top enrollment stage to the bottom? I.e., how long does it take for a patient to go from screening to dose?

Answer

Erik Skullerud (Executives)

Very individual, but I think I mentioned this before, approximately 2 months from when we first see that patient until they are finally enrolled. But the delta and the difference between numbers here is significant.

Answer

Frazer Hall (Attendees)

Thank you. We now have a series of questions regarding the repair offering. The first of those is given the current share price is trading below NOK 14 and the cost of the repair offering, can you not save costs by canceling the offering at this stage?

Answer

Erik Skullerud (Executives)

I wish it's not the way the financial system works, unfortunately, and there is also a legal obligation, that when you go and do a private placement, you have to treat all shareholders equal. You can make a decision not to do so. We're of the belief, that we should treat all shareholders the same, big and small. And by the way, when I started, one of the first few questions that I got, and I believe even this was in one of the RADFORSK discussions. It could have been somewhere else, but I got several questions related to the same, why have you guys always prioritized the bigger investors, and not the small investors? It's a little bit of, damned if you do, and damned if you don't. This time around, we decided we want to treat all of you in the same way.

Geopolitical issues is something that we can't control. And I dare to say, that we find ourselves in the situation that we are, due to those specific issues. And as Malene alluded to in the beginning of her presentation, is this isn't something that you turn a switch and then it just goes, within 24 hours. There's a lot of time and commitment that is put into this. But bottom line is, we couldn't have saved the money, because that is something you have to pay upfront when you do this, and that is just the way the financial system works.

Answer

Frazer Hall (Attendees)

Thank you. And on to a rather broader question now, which is a question as to what is the level of interest for radioligand therapy and Betalutin specifically among both doctors, or doctors treating patients and patients themselves?

Answer

Erik Skullerud (Executives)

If anyone read, was it Fierce Pharma yesterday. There was an article related to Novartis' PSMA molecule, where they said -- and it's very much along what we have also said about Betalutin the whole time. The interest is definitely there. The headline of this specific article, was the following; Novartis' drug gets increasing confidence and commitment from oncologists, but supply issues and, something else, needs to be overcome. Basically, what they were saying was that out of X number of oncologists asks, the faith in the product is tremendous. But -- and this is what they're saying, Novartis have to make sure that they get it right with regards to supply chain, distribution and getting this product to us.

In other words, what we have picked up, by the way, together with them, around the whole HPP organization because they are, as you can understand, one of the other companies that are supporting this rollout. And over and above that, I would also underline from '19 -- when was it, 1919 -- or 2019, sorry, to 2021, you had 4 big radiopharmaceutical collaboration signed for the western world, significantly more, if you include also the Asia, Southeast Asia, China around radioimmunotherapy, and you see new companies popping up on a constant basis in this field. This is something that is definitely very interesting at the moment.

Answer

Frazer Hall (Attendees)

Thank you. We also have 2 or 3 questions around the Archer study, which essentially asks whether you can give any further updates around Archer and in particular, of the 7 patients enrolled in the study, can you give any specific updates on complete and partial responses, duration of response? How many patients are in remission, et cetera?

Answer

Erik Skullerud (Executives)

So I think the last update we gave was at the R&D Day, where we said out of the 7 patients, 6 had either complete or partial response, but none of them had gone into remissions. And that's the latest piece of information I have. I have not heard anything since then. Keep in mind that the patients in Archer are now all going towards 3 years of follow-up. So if this really holds through, this is a significant result that we're seeing in

this study, although small, and with all the caveats you should have for an early-stage study. But still, these results are impressive, no matter how you look at it.

Answer

Frazer Hall (Attendees)

Thank you. Just as a reminder, at this stage, if there are any further questions, please do submit them via the link on the company's website on the webcast link for today. The next question is a broad question, which asks why has Omicron hit you harder than the first COVID variant?

Answer

Erik Skullerud (Executives)

Very good question. I think there are a couple of reasons. First reason is probably, the first strain, there was a lot of uncertainty what was this even, and it took time for the community to really figure out how to manage it and how to respond to it. Once they got their act together, and we saw this for the second strain, if you want, the delta variant. As soon as experts came out and said, no worries, vaccine is there. This strain is also receptive to the vaccine. You saw that our recruitment numbers went through the roof. Omicron is a different story. The same experts came out and said, 'no, this time around, sorry. This is not as receptive, as sensitive to the vaccine.' And I think that lack of guidance, if you want, or that uncertainty is arguably 1 out of 2 main reasons for why omicron has hit us harder.

The second reason is the sheer backlog of patients that are coming in, as I mentioned earlier, crushing into intensive care -- into severe care and that are taking the seats, the beds for these patients. Those are the 2 reasons for why this has hit us more than the first strain.

Answer

Frazer Hall (Attendees)

Thank you. And then just lastly, we have 1 or 2 questions on the competitive positioning of Betalutin, which essentially asks, whether you can add anything further with regards to the competitive positioning, with respect to other classes of drugs either currently on the market or in development? And again, you made some specific comments on copanlisib, but there are 1 or 2 questions asking, whether there's any further information you can share around that particular drug, and how it sits competitively versus Betalutin?

Answer

Erik Skullerud (Executives)

So it will -- let me take the second one first. With regards to copanlisib, I think one is the patient group that we are targeting, which is different, and that's important to keep in mind. 2, for copanlisib and I would extrapolate this to any, also future launch of PI3K. The fact of that what we have seen, what we have seen in the last 4 to 5 weeks, with 3 products being withdrawn and one Umbralisib, that have withdrawn their application for MZL, there is no doubt that this is going to hurt the whole class, not just the products in question. So my assumption, is that this is going to be seen as a class effect. And I also believe, that irrespective of what happens with copanlisib, they are going to have a fair share of convincing to do, with the scientific community, around why these drugs should be used, to begin with. I don't know that, but that would be my assumption, based on what I've seen in the past. This is not something that doctors look kindly upon.

With regards to the other classes, I mentioned the efficacy versus tolerability part. What I did not mention, was the whole economic consideration. If you work with the CAR-T, the efficacy, even if you get it to work, you're using a drug that costs approximately in the U.S., before rebates, $450,000 just for the injection itself. If you upon that, take the number of days that you need to stay in the hospital, and if you assume that approximately half of these patients actually get the side effect of cytokine release syndrome, that is an enormous cost over and above.

And the last thing that I would like to highlight with CAR-T is, again, for those of you that are scientifically interested and are reading the New England Journal of Medicine, there were 2 articles just before Christmas

related to CAR-T, but in DLBCL, large cell lymphoma, where the cytokine release syndrome numbers were significantly higher. They were in the 70s and 80s percent. So if you add that into the equation, it almost seems that, that class of drug, although as effective as it is, you really need to know what you're doing, when you use them. And again, therefore, the whole underlining of what type of patients do you give this product to, becomes so much more important. And I think for the bispecific antibodies, you have seen Monotuzumab, sorry, results so far, there are other products out there that are also under development that we don't know these results for. It is promising from an efficacy point of view, but we only have clinical data. We don't have clinical experience in the real world yet, from these products. And we need to have that, before we can make further estimations.

And the last point I would add on bispecifics is, we also don't know the price. What are they going to cost? So again, that is something that is outstanding. That's something that we just have to wait for.

Answer

Frazer Hall (Attendees)

Thank you. That completes all of the questions that were submitted online. So Erik, I will hand back to you for any final comments. Thank you.

Answer

Erik Skullerud (Executives)

Thank you so much, Frazer, for helping with that. And thank you to all of you that are sticking with us and that are supporting us, both you here in the room and those online. I don't think any of us could have predicted the kind of impact we are seeing, both from omicron and what we're going through, with regards to geopolitical issues. But we truly appreciate the partnership with you, investors, and you, our owners. And trust me when I say, we do everything we can, 24 hours a day, to do as good as we can for Betalutin and for you.

So thank you for the collaboration, the conversation, and we look forward to seeing you the next time around. Thank you.

22.02.14. Nordic Nanovector ASA- Shareholder/Analyst Call

Presenter Speech

Jan Egberts (Executives)

Good morning, dear shareholders. Welcome to the Extraordinary General Meeting of Nordic Nanovector. My name is Jan Egberts, and I'm the Chairman of the Board. With me here today is our CEO, Erik Skullerud; and our CFO, Malene Brondberg, as well; as well as the company's Counsel, Fredrik Haavind.

We assume that all shareholders and proxies present are registered and that the voting slips have been handed out. If someone still hasn't registered, I ask you that this is done now by the venue's entrance. The company's issuer of securities account manager, Nordea, is present and is assisting us to register shareholders and proxies.

First of all, the presentation of the record of shareholders. A record of the shares that are represented in the general meeting shall be attached to the minutes. Nordea has finished the registration, and 24,811,761 shares of a total of 115,935,523 shares are represented at today's general meeting. That means that approximately 21.4% of the company shares are represented here today.

The first item on the agenda is the election of the Chairperson of the meeting and a person to co-sign the minutes. I'd like to suggest that I will chair the meeting as the Chairman of the Board of the company, for this reason, but also for the fact that more and more of our shareholders are international. The meeting will be conducted in English. The minutes of the general meeting shall be signed by the Chairperson and at least one other person elected by the general meeting amongst those present.

I'd like to suggest that Fredrik Haavind is elected to co-sign the minutes. Are there any other suggestions? I'll keep a pause for about a couple of seconds. If there are no other suggestions then, hereby, I've been elected as Chairperson of this meeting and Fredrik Haavind as the person to co-sign the minutes.

The first item on the agenda is the approval of the notice and the agenda. The notice and the agenda have been sent to all shareholders with a known address. The information and documents concerning the general meeting are published on the company's website. Thus, the general meeting is convened in accordance with the Articles of Association and those rules applied for listed companies. We therefore assume that no one has any objection to this notice. I'm waiting again, a little pause to see if there are any comments. Since there are no comments and there seem to be no objection, the general meeting is declared duly convened hereby.

We have at this time completed the constitution of the general meeting, and we'll now go to the matters on the agenda. The first item on the agenda, the only item on the agenda, is the Board authorization to increase the share capital related to the repair offering.

The first matter on the agenda is authorization to the Board to increase the share capital related to a repair offering in the company. The proposal has been published on the company's website. The company has recently carried out a private placement. The purpose of the proposed Board authorization is to allow the company to carry out the repair offering, if appropriate. Such offering would allow existing shareholders who have not been allocated shares in the private placement to participate at the same terms and ensure equal treatment.

The Board has intended to implement the repair offering unless the trading price of the company's share over time is lower than the subscription price in the private placement and a subsequent repair offering hence becomes redundant, which is subject to the sole discretion of the company's Board of Directors.

The repair offering will, if implemented, be directed towards the company's existing shareholders as of 19th of December 2022 (sic) [19th of January 2022], as registered in the Norwegian Central Securities Depository on the 21st of January 2022 who are not allocated shares in the private placement. The subscription amount for the shares issued in the repair offering will be the same as for the private placement, which is NOK 14. Are there any objections to this proposal? I don't hear any objections at this moment.

So therefore, we have received a total number of 24,468,837 advanced votes and voting instructions for the proposal and 342,924 against and 0 abstain. This general meeting against that number of votes is considered to have adopted this resolution.

We've now been through the agenda. Therefore, this Extraordinary General Meeting in Nordic Nanovector has been completed. Thank you all very much for your support, and hope you have a great day. Goodbye.

21.11.30. Nordic Nanovector ASA- Special Call- R&D Day

Presenter Speech

Jan Egberts (Executives)

Good afternoon, ladies and gentlemen. Welcome to our Nordic Nanovector R&D Day. My name is Jan Egberts, and I'm the Chairperson of the company, Nordic Nanovector. Unfortunately, I was really looking forward to meet you all in person today in Oslo. But I guess, unfortunately, because of the -- all the corona-related travel restriction, that's not possible. However, we'll make the best out of it with using the more modern technology, it's the webcast and obviously, we will also be available for more intimately answering all your questions.

Obviously, corona had a major impact on our company. We have kept you updated about our recruitments, which suffered quite significantly in the first half of last year, which really starting to pick up now, which is very encouraging. Over the past months and years, we have been sharing a lot of information about our progress with PARADIGME, the clinical program with Betalutin.

I think it's now also very important to kind of switch gear a little bit and share what our organization has been doing over that period in earlier-stage R&D projects because I think there's a lot of very interesting things we'd like to share with you.

Here today with me are -- is Erik Skullerud, our CEO, with his team, and they will share with you some of the progress I just mentioned that we have made. We're also very privileged to have Professor Dr. Leo Gordon with us today, who is going to share his experience as a clinician with some of these patients. Professor Leo Gordon, he's the Abby and John Friend Professor of Cancer Research and Professor of Medicine. He's also the Co-Director of the Hematology Malignancy Program, the Division of Hematology Oncology at Northwestern University School of Medicine. So very pleased with all the people, and I think you're going to be very impressed with the progress we have made over the past 1.5 years.

So having said that, I'd like now to hand over to Erik, who, together with his team, will share you some of the projects I just mentioned earlier. Erik, please go ahead.

Presenter Speech

Erik Skullerud (Executives)

Thank you, Jan. And also from my side, a warm welcome to all of you. It would have been great to have been in Oslo, just like we were a couple of weeks ago. But as Jan just pointed out, there are a lot of issues on travel at the moment. So we're joining you from different places around Europe. There's a couple of us that are sitting in Switzerland. There's a couple of us that are sitting in Belgium and some of us are sitting in London at the moment. And obviously, Dr. Gordon is sitting over in the U.S. So it's really a global conference that we are about to embark on.

I don't know how many of you there are, but we are equally happy to see all of you. As a matter of, first, giving you a little bit of a snapshot of the agenda, if I could have the next slide. We are obviously going to go through quite a few things during the presentation. We're going to start with -- I will give you a couple of reflections on where I see us moving to as an organization, as a company. As you will know, I joined the company 8 weeks ago. I've had a chance to thoroughly get familiar with the organization, with the people and with the exciting pipeline that we have. So I'll give a little bit of a background on where we want to get to.

We will then introduce Professor Gordon, who will be talking about follicular lymphoma treatments, the treatment paradigm and the unmet medical need. And that will be followed on by our new incoming CMO, Dr. Pierre Dodion, who will also talk to you about the Betalutin program. But this time, we will tell you a bit more about our plans on Betalutin as a product and eventually Betalutin as a pipeline of its own. Because I think it's fair to say that there are several indications that makes this asset really interesting moving forward.

Marco Renoldi, my Chief Operating Officer, will share with you a program that we're in the midst of working on our commercialization and the potential how we overcome barriers to success. And it's a really interesting project in the sense that here we take, first, the U.S., but then also other countries, and we look at what are the barriers

that we need to get across over and above your normal commercialization barriers. This is a really interesting project that we are collaborating with other big industry partners on.

Lars Nieba will give you an update on how we're moving forward, both with our supply chain and our manufacturing. For those of you very familiar with biologics and radio immunotherapies, you will know that the process that you bring these products through your manufacturing is just as important as the clinical development itself. And we will [update] how we're doing that. So we'll share insights with you on that.

We will also, and then finally, as our last part of the presentation, jump into a couple of presentations that will be aimed towards our pipeline. Our CSO, Jostein Dahle, will do a part of this. And Maureen Deehan, our Head of Strategy and Business Development, will also take you through each -- a couple of assets. So I think we have a very interesting program ahead of us. If I can have the next slide, please?

And just to share with you, first of all, this is our management team. And as you will recognize here, we have an extremely experienced group of people that we're working with. They have been in large pharma corporations. They have worked with small biotech. Several of them has also worked as consultants and worked in 2 companies. So a wide experience, both in number of companies and also the expertise. And I'm really proud to be leading this group of people.

Also today will be the first time, as mentioned, you will meet our incoming CMO. You'll see at the bottom here, Pierre Dodion. And let me also now give a big thanks to our outgoing CMO, Christine, done a fabulous job for us, and we're really happy with what you have done, Christine. And she is in the midst of a transition to Pierre.

Next slide, please? So first, a little bit of an update on PARADIGME. I've seen, over the last couple of days, quite a few questions from you online. Are we going to give an update on PARADIGME and on the inclusion? I'm assuming that all of you will now be familiar with the program itself. This is what we have become famous for over the last couple of years. We have spent a lot of time on updating you, and you will see the study design in front of you. So I'm not going to go through any more than that.

I am going to use a little bit of time on the lower line here where you see what we reported in our last quarterly call, 102 patients included or enrolled in the study. This is now 10 days or 8 business days ago. And today, I'm able to add on to this number. But let me spend a few minutes on just telling you a story around the last 2 weeks.

So we've had 2 patients that have been in later stage screening and inclusion, if you want, into the study in this time frame. Both of these looked really good until approximately mid last week, end of last week. One of the patients in late screening fell through on one of the inclusion criteria and, as such, had to be dropped from the study. The second one, I'm happy to announce, is virtually being treated as we speak. They have their first medication happening in about 36 hours from now and has been cleared through enrollment. So the new number for us now is 103. That's 1 more patient included over the last 8 business days.

So that is the status of PARADIGME. We will mention PARADIGME on a couple of locations in the presentations to come. But I think it's fair to say that today's focus is more going to be around what are we doing, to Jan's point earlier, over and above. So next slide?

The starting point of this is really our own proprietary CD37 platform. As you will be familiar with, this is something that we have worked on since the inception of the company. CD37 is a really important target in beta cells. And for you to believe that this is a viable and an interesting strategy, let me make a couple of comparisons.

On a beta cell, which is basically the main attack point for cancer treatments in hematological cancers, you have CD20 and you have equally numbers of CD37 antigens. What does that actually mean? Well, if you believe that companies such as Roche, that has made a huge impact by understanding and developing the CD20 platform, if you believe that, that is possible for others, I would suggest it's definitely possible for us. We're the leading CD37 company arguably around the world at the moment. You see over that line, we have 5 different assets in our development, 5 different attack points, if you want, towards CD37 as a target, all with different attack points, attack angles and different ways of altering -- or attaching, sorry, to the target -- to the CD37 target.

Obviously, Betalutin is the one that is the furthest on the development horizon. But during the presentations today, as I mentioned earlier, you're also going to hear more about the other 4 and we're going to give you an update on where we are with them. But just to make it very short, Humalutin, the next one from the left, is a

product that really fits very well into our life cycle thinking as far as Betalutin is concerned. This could be a fast follower in hematological indications. It has a slightly different backbone, and we'll speak to that in a second. And it is a product that we have developed until IND stage.

Alpha37 is -- has the similar antibody as Humalutin, but a different payload associated with it. And Jostein will talk both about Humalutin and Alpha37 a little bit later on.

The last 2 over on the right-hand side here are, if you want, our 2 new babies. It is on the far right, the CAR-T program that we announced just a couple of weeks ago. Maureen is going to touch upon this program in much more detail a little bit later, but we are super excited about this program. Why? Because we are, in this case, able to collaborate with arguably one of the most distinguished research institutions in the world, especially when it comes to CAR-T. This institution, University of Pennsylvania, were the ones that initially developed the CAR-T technology, licensed it out to Novartis and is the base for the Novartis product the way that we see it today.

The last of our assets is a pure humanized CD37 antibody. And this is in early-stage development. We are really interested in how this is going to take us forward as this is a product that may give us also inroads into other indications. And as you can see in the vision statement on top here, over and above what we have done so far in hematological cancer, we are also expanding this vision and including immunological disease or autoimmune disease as something we want to focus on. So not only do we have 5 different molecules/assets in development, we also target wider disease areas as we move forward.

It is pretty obvious that we cannot do this alone. So on to this strategy, we're also bolting on an additional development strategy, if you want, in the sense of seeking partners for these different molecules. You will probably be aware that we have such collaborations with Orano Med on Alpha37. As mentioned earlier, we announced a collaboration with University of Pennsylvania for the CAR-T molecule. And we're actively looking for other partners as well in parallel with the commercialization partner -- partnerships that we're looking at for Betalutin. So this is something that we don't need to spend additional resources on but we use what we have.

And again, if you think about how much resource are we actually spending on this today, the vast majority of our resources is focused on PARADIGME and on Betalutin. That is where our priorities are, and that's what we have to deliver first. But I hope you agree with me that the vision that I put forward to you right now is clear. It has a focused strategy behind it based on the CD37 platform. And when we are successful in bolting on partnerships to this, it is something that is also going to create future value for you as shareholders.

Next slide? I'm not going to spend a lot of time on this because other speakers will touch upon this in more detail. But as you can see here, from left to right, you have the same molecules. And from top to bottom, you have, kind of, how do you describe the different CD37 therapies that we have under development. If I could have the next build, please?

Three of these are really based on our heritage radioimmunotherapy background. It is something that we are really good at. It also shows you that although we're starting from the CD37 attack point, we equally have a chance of adding on additional nuclear payloads on them as well. It also shows you, from left to right, that we are evolving the antibodies somewhat that we are using from a murine to a chimeric in these 3 boxes. And again, Maureen will touch more upon this in detail, what does that actually mean.

You can also see here that we're using IV as the administration form for these 3 assets. And finally, they're mainly focused on to hematology, although arguably, you could say that an asset such as Humalutin may also be used in immunological disease. But for now, we have focused on hematology for the development of all of these 3 assets.

The next, please? For the antibody, the humanized CD37 antibody, this will obviously be targeted towards subcutaneous use like most other antibodies. It will have a wider area that it could be used in the sense that here, you have a product that potentially could be used in hematology but also in autoimmune disease. It can also be used in addition to our other assets in hard-to-treat tumors, you could imagine as a baseline treatment, Betalutin, for example, and then iterative treatments with an antibody to enhance the efficacy of the radiopharmaceutical itself.

And finally, if I could have the last build, the CAR-T program, which again focused on hematology, and are also, I would say, cutting edge as far as oncology/hematology treatments are concerned. What we obviously hope here is to add value for you as shareholders, but also to actually take the next step in development of CAR-T

treatments. This is for us a next-generation treatment when it comes to CAR-Ts. Again, Maureen will talk more about that in her presentation.

Next slide? So as a last slide, before I hand over to Professor Gordon, I just try to depict here where are we with these different programs. You are all aware of the third line development that we're doing for follicular lymphoma. The row below is the first step towards a Betalutin as its own pipeline, if you want. We obviously have shown interesting results from the Archer-1 study.

We are currently talking to regulatory authorities for what we would need to do as a confirmatory Phase III program based on our BLA approval for Betalutin in third line. That discussion is ongoing. Pierre will talk more about what that looks like and what we are doing moving forward. But the next time we speak to the FDA is towards the end of first quarter 2022.

And we have plans that we'll share with you today around how we're moving forward on our DLBCL strategy. You have both programs, the additional 2 radio immunotherapies here, both Humalutin and Alpha37, both of them targeted in -- towards other NHL indications. And there, we are now -- Humalutin is already at the pre-IND stage. We are just finalizing the final steps for Alpha37 as well in the same frame of getting this to a pre-IND stage. And I've just shared with you some of the top line details for the humanized antibody as well as the CAR-T program that we are embarking on with University of Pennsylvania.

So with that, I will stop, and I will introduce Professor Leo Gordon to you. We're very, very honored Professor Gordon that you have been willing to spend your time with us today. And for those of you who don't know Professor Gordon, I think most people online would be familiar with your background. He is an Abby and John Friend Professor of Cancer Research, a Professor of Medicine, a Co-Director for Hematological Malignancies Program at the Division of Hematology and Oncology, Northwestern University Feinberg School of Medicine in Chicago.

We're very honored to have you here, Dr. Gordon. Thank you for taking time for this and floor is all yours.

Presenter Speech

Leo Gordon (Attendees)

Thank you so much. It's a pleasure. It's an honor to be with you. So I think -- can I have the first slide? Thanks. So my task today really is to review with you some of the treatment algorithms in patients with relapsed follicular lymphoma and to really kind of find perhaps a niche or find an unmet medical need for those patients.

Can I have the next slide, please? So in order to do that, I thought it would be worth discussing a little bit with you some features of follicular lymphoma, talk a little bit about the incidence of this disease, where it fits in the spectrum of the non-Hodgkin's lymphomas and the spectrum of the B-cell non-Hodgkin's lymphomas. Talk a little bit about how one makes the diagnosis, going about making the diagnosis under the microscope and at the bedside. Talk a little bit about certain biological features which might be important and might predict for a favorable or an unfavorable course. And that has a lot of impact, I think, on where we go with second and third line treatments and whether -- when and if to expect the need for second and third-line treatments.

We're going to talk about management algorithms clearly for relapsed patients in second and third line, but I thought it would be important at least to review with you some of the first-line options because the first-line options sometimes -- there are many choices for first-line options, and they will impact what we do in second and third line. I will try to focus somewhat on patients who are a little bit older or might be too frail for very intensive therapies or for some of the newer treatments that I'll also mention, CAR-T, stem cell transplantation, things of that sort. I'll talk a little bit about the evolving landscape, what else is out there, what's going to be there and focus on some recently approved agents, perhaps PI3 kinase inhibitors which are being used more and more in patients with follicular lymphoma.

So next slide. So this -- on this slide, this is sort of a pie chart of where follicular lymphoma fits. We can see that it's probably the second most common type of B-cell lymphoma. We estimate probably closer to 80,000 cases of non-Hodgkin's lymphoma in the United States in 2021. Most of those are B-cell non-Hodgkin's lymphomas. And this is the sort of, for the most part, the pie chart representing the B-cell lymphomas, diffuse large B-cell lymphoma. DLBCL is the most common type. Follicular lymphoma makes up maybe 22% to 25%, maybe a little bit more now of the B-cell lymphomas.

Some of the discussion we'll have, although we're focusing on follicular lymphoma, many people feel, and I'm among those that patients with marginal zone lymphoma, although maybe a somewhat different biology and has very similar presentation and the treatment algorithms for marginal zone lymphomas, over the years, have mimicked the treatment algorithms for follicular lymphoma. And so some of the things that we do in follicular lymphoma may also apply to marginal zone lymphoma.

Next slide, please? So as I mentioned, it's the second most common lymphoma in the United States. We have grades which are determined by what the cells look like or what the biopsy specimen looks like under the microscope. I will say that the recent practice of making diagnosis by fine needle aspirates or even by small core biopsies has limited our ability to make accurate diagnosis, and that's something, while very popular, at least here in the U.S. in hematology oncology, it's along with our pathology -- hematopathology colleagues, that's something we kind of try to discourage as much as we can. We often have to repeat biopsies in patients that are seen in consultation for second or third opinions.

The grading can be difficult, and that's why we need more tissue and needs -- I think I would not say may need, but I think does need hematopathology expertise and review. We think of grade 1, 2 and 3a lymphomas as the indolent type, the type that we'll talk about today, the follicular grade 3b we tend to view as similar to DLBCL, to diffuse large B-cell lymphomas, and that sort of sets it apart as a different category.

So while we will say that advanced stage follicular lymphoma is not curable with standard therapy, this is a disease that people can live with. They may lead a normal life span with follicular lymphoma and may die of other disorders or other causes. So in many ways, when I -- at least when I discussed this with patients that we're seeing, I might compare this to diabetes or compare this to other chronic disorders. And they may not be life-threatening. And in fact, when we see people for the first time, when the diagnosis is often made incidentally on a CAT scan that's done for other reasons or by physical exam on a routine visit, we stress the fact that this is something that actually may not need intervention right away.

Can I have the next slide, please? So this is from the NCCN Guidelines, which we put together every year and, in fact, update many times a year. This just gives us some clinical features that we're using for prognostication. And there are 2 major criteria that are basically determined at the bedside, the so-called GELF criteria, which was developed in Europe. It was developed for clinical trials for now the [Lisa group]. And basically, these were eligibility criteria for clinical trials. I think this has begun to be used or has been used over the years as a way of predicting perhaps a worse outcome and maybe are specific indications for treatment.

I don't know that we use them that way all the time, but there are features there that I think are important. The number of nodal sites, the involvement of -- the number of lymph nodes that are involved. Any nodal or extra nodal, that means a mass outside of a lymph node greater than 7 centimeters often is an indication for treatment. The presence of B symptoms, of fever, sweats and weight loss. The presence of a large spleen, although I will say that we see many patients who have a large spleen who don't necessarily require treatment. The presence of pleural effusions, fluid in the lung, or peritoneal ascites, fluid in the abdomen, might be an indication for treatment. Cytopenias, low white blood count or a low platelet count related either to the large spleen or to infiltration of the bone marrow.

And then the presence of malignant cells in the peripheral blood, and many people view as an indication for treatment, although I will say that we followed patients for many years, sometimes with some cells in the peripheral blood. And if we do flow cytometry, many patients will have abnormal cells in the peripheral blood and that by itself does not mean that they absolutely need to be treated. But these are some of the criteria that are used.

The so-called FLIPI criteria developed by my colleagues in France with -- and different iterations of this. Age, greater than 60; Ann Arbor stage, greater than III or IV, that is more advanced stage disease; hemoglobin level, anemia, less than 12; an LDH, lactic dehydrogenase level, which I find very useful and important in management of patients with both large cell lymphoma and follicular lymphoma as an indicator of more aggressive disease when that is above the upper limit of the laboratory normal, that is a negative prognostic factor, greater than 5 lymph node sites.

And if you can see, the right part of this chart gives you some indication of the lymph node areas and how to measure those. I will say that although the FLIPI criteria are extremely useful for clinical trials, at the bedside, it's not commonly used, I think, to sort of make decisions about treatment. I think we tend to use a [indiscernible]

I would say, which includes many of the FLIPI and GELF criteria. But I don't think that most people are charting the number of lymph node sites at the bedside to make decisions about whether patients need intervention or not.

Next slide, please? This gives you some idea of what I talked about earlier about the grading. Basically, the grading of this disease is determined by how many large cells are present. The more large cells that are present, the more like large cell lymphoma this is and the more aggressive it might be. And you can see follicular grade 1 and grade 2 with small numbers of large cells. Grade 3a on the bottom -- on bottom left and grade 3b on the bottom right gives you an indication that if there are sheets of large cells, the more large cells, the more it's tending toward large cell lymphoma. We tend, as I mentioned, to treat grade 3b as we treat large cell lymphoma. So most of the discussion that we'll have today has to do with follicular grade 1, grade 2 and grade 3a.

Next slide, if I may, please? So this is how the diagnosis can be made with immunophenotyping, that is specialized flow cytometry techniques that are used to distinguish follicular lymphomas from some of the other B-cell lymphomas. And there's 2 antigens which are really helpful, CD5, cluster designation 5; or CD10 helps us make that distinction. Patients who have CD5 positive disease tend to be more likely to have margin -- mantle cell lymphoma or chronic lymphocytic leukemia, small lymphocytic lymphoma. Patients who have CD10 are more likely to be diagnostic for follicular lymphoma. CD10 is an antigen that's present in the germinal center of the lymph node, and the germinal center of the lymph node is where we think that follicular lymphoma originates.

So these are helpful. And I won't go into any more detail about these, but I think the diagnosis, although it can be tricky sometimes, with an experienced hematopathologist with an adequate amount of tissue, this diagnosis can be made pretty readily.

Can I have the next slide, please? So this is just like a very high, if you will, aerial overview of what our -- some of our goals are. We'd like to -- if we decide that patients need treatment, and I will say probably maybe as many as 50% or 60% of patients that we see initially don't necessarily require treatment because they're not symptomatic. They don't have bulky disease. They don't have any of the criteria that I just showed you.

But in those patients who do require treatment, the goal is to get a good quality remission. If we can get a complete remission, that would be ideal, to reduce the tumor load and induce an initial response, to maximize that response by sometimes using some kind of consolidation. And a fairly controversial area in hematology oncology is whether patients with follicular lymphoma should have maintenance treatment or not. And that's -- and I'll show you some data on that. That's -- it's an evolving discussion. And actually, and I'll show you in a minute, has been impacted quite a bit by the pandemic, by COVID.

Next slide, please? These are data from Gilles Salles from France, now at -- in New York at Memorial Sloan Kettering. These are the data from the so-called PRIMA study. The primary endpoint of this was 3 years, and the study was basically randomizing patients who were treated with chemotherapy upfront for follicular lymphoma, randomized 1:1 to receive a maintenance treatment for 2 years with Rituxan given every 2 months versus observation.

And if you look at the progression-free survival end point at 3 years, there's clearly a statistically significant difference at, say, 36 months between Rituxan maintenance and observation. And this has led to a fairly widespread use of maintenance therapy. What this study did not find, however, was, is there a difference in survival? And up until now, there has not been a difference in that trial in survival in patients receiving maintenance therapy.

Next slide is a meta analysis published by Vidal et al in the European Journal of Cancer in 2017. And with all the caveats of meta analyses in place, I will say that they did find, if you look at sort of the left graph, an improvement that was seen at about 6 or 7 years in overall survival in those patients who received maintenance therapy in green compared with those who did not in red.

So quite a bit of debate. I will say that the pandemic has made a major impact on the decisions for maintenance therapy. Just some point of interest, we know that a patient who has COVID, a normal individual gets infected with COVID, in about 20 days will clear if you do multiple PCR swabs. Patients on Rituxan take 100 days to clear.

So while Rituxan is among the safest drugs that we use in oncology, when it comes to COVID, it's probably one of the most dangerous drugs that we use because it limits our B cell immune response. And so we have adjusted,

I think, at least in the U.S., and I think this is true around the world, decisions about maintenance treatment, and we have been more reluctant to recommend maintenance treatment if there's not going to be a major difference in overall survival. And we have even adjusted our decision-making about when to initiate treatment. I think we've moved that sort of line that we cross about needing treatment over to the right in the era of COVID. And -- so that's, I think, something important to remember.

Next slide, please? So these are -- we get to update these, as I mentioned, NCCN Guidelines and sometimes I find it hard to follow the algorithms in the NCCN Guidelines myself. This is just one way to -- another way to look at it. If you look at the top, there are some patients who present with early-stage disease, say, a single lymph node or a lymph node area. In general, the recommendation has been those patients should be treated with radiation, involved site radiation because data from the Princess Margaret Hospital in Canada suggests that you wait 10 years, you follow those patients, 50% or 60% of them may still not have recurrent disease.

So we think that radiation might be curable in a group of patients with very early stage disease. And any time I mention radiation, obviously, we always think about how this could translate to radio immunotherapy. But radiation, involved site radiation, I think, is important.

Some people might use immunochemotherapy with Rituxan or perhaps chemotherapy with or without radiation. I think that's reasonable, but I think in really truly early-stage disease, radiation is probably the preferred treatment. You might, however, observe patients if there -- if the radiation would involve an area that might not be amenable to -- or safe to give. So I'm not sure I would necessarily give somebody with a mediastinal, behind the sternum, presentation involved site radiation for stage I disease. Those patients might be observed.

And if the disease then progresses in the yellow vertical bar here, then they can progress either without transformation. They may stay follicular lymphoma or they may progress with transformation in the green box on the right if they're transformed to large cell lymphoma. And overall, about 30% of patients will transform to large cell lymphoma if followed long enough clinical trials. And those patients should be treated as large cell lymphoma, clinical trial, chemotherapy with rituximab, possibly with radiation. And then those patients then are candidates perhaps for allogeneic or autologous stem cell transplant or even now CAR-T therapy with the 3 agents that are now approved in large cell lymphoma.

If patients have either bulky stage II or more commonly advanced disease stage III or IV, as most patients with follicular lymphoma present, if you look at the brown box on the left, and then the brown box in the middle, clinical trial, of course, if the clinical trials are available. Bendamustine and Rituxan has, I think, replaced R-CHOP, Rituxan and CHOP chemotherapy is the most commonly used regimen in follicular lymphoma based on the data from the German studies. Rituximab alone, probably my most commonly used regimen in patients who might need treatment and have stage III or IV disease. The R-squared regimen, that stands for Rituxan and Revlimid (lenalidomide), an IMiD which is active in this disease. And sometimes local radiation and then I think most commonly, observation.

I will say once you've made the decision to treat, that's when we talk about whether we should do maintenance or not. There were data from actually my colleagues from the Netherlands in the early FIT trial using radioimmunotherapy as consolidation, using Zevalin as consolidation. And since this is a discussion of Betalutin, I'll say, and I'll say this many times, whenever I mention radio immunotherapy, it's a bit of a pipe dream because we don't have radioimmunotherapy anymore. Zevalin is, at least at the moment, not available, at least in the U.S., and I don't know if and when it will become available. So either consolidation or extended dosing maintenance therapy with Rituxan with the caveats that I mentioned during COVID.

And then if you look at the bottom left in the gray box, elderly or patients who are -- we don't think can tolerate aggressive chemotherapy, may be treated with Rituxan alone, and that's a commonly used regimen that's what will be my probably first-line treatment for the most part. Chlorambucil or Cytoxan, these are oral -- can be oral alkylating agents or perhaps radioimmunotherapy, again, if we had it. There were data from the group at the University of Michigan with an I-131 radioimmunotherapy where -- that was given safely and with excellent results. But again, that's not available either. So that's a general overview.

Can I have the next slide? I wanted to focus on the patients who we didn't think were candidates for aggressive treatment, just to come down on this. Again, Rituxan or -- which is again my first choice, chlorambucil or radioimmunotherapy were available, that can be followed by either observation or Rituxan as a maintenance treatment. If patients then progress, either after just their initial induction therapy or after a maintenance therapy, once again, they can progress with transformation. And I think a re-biopsy with a good sample of tissue, but not a fine needle aspirate but a biopsy can make the distinction most of the time between transformation to large cell lymphoma, DLBCL or just progression with follicular lymphoma.

If they're transformed, then we should be treating them like large cell lymphoma. If they're not transformed, then we have some options. Some of the things that we didn't do in first line or we thought we couldn't do in first line, we might begin thinking about now doing in second line. So rituximab, lenalidomide or Revlimid and Rituxan are R-squared, once again, radioimmunotherapy if available, possibly PI3 kinase inhibitors, local radiation or sometimes best supportive care.

If they don't respond or progress at that point, really that is an unmet need and I'd even say the first relapse is an unmet need. Shall we think about resurrecting radioimmunotherapy? Shall we think about radio immunotherapy in combination? These are patients who might not be candidates for something like CAR-T therapy, although we've seen and in recent data that patients who are older, say, over 65, and treated with CAR-T have a similar outcome with similar toxicities to patients who are younger. So I think it's not out of the question, but more difficult.

Next slide? So just to go over once again for first-line therapy, bendamustine-Rituxan, Rituxan-CHOP, Rituxan with CVP, basically CHOP without the Adriamycin, Rituxan and Revlimid, R-squared or obinutuzumab, which is a different monoclonal from Rituxan, probably maybe with a little bit more efficacy in chronic lymphocytic leukemia and suggestion based on some recent data that it might have more activity than Rituxan actually together with lenalidomide. And then for patients, again, who are -- may not be able to tolerate Rituxan alone, chlorambucil and Rituxan and possibly radioimmunotherapy.

Next slide, please? Consolidation or extended doses, Rituxan maintenance with the caveats, obinutuzumab maintenance as in the so-called GALLIUM trial where it was given after chemoimmunotherapy, obinutuzumab was given for 2 years of maintenance. And other options of a shorter maintenance course. In Switzerland, they did the initial Rituxan and then the Rituxan every 8 weeks for 4 doses. So basically a shorter course of maintenance therapy.

Next slide? So I think one thing to point out about second-line treatment, there have been some recent data that sort of substantiated I think most investigators feeling that if patients relapse within 24 months or early after their initial treatment, the outcome may not be as good. And those -- and that's been confirmed in a trial that Carla Casulo published from sort of a data analysis of -- sort of a large data subgroup of patients and then was substantiated by the Mayo Clinic Group that patients who have progression of disease at 24 months, or the so-called POD24, have a worse outcome.

So in general, second-line treatment is whatever wasn't done in first line. So if you gave R-CHOP first line, then bendamustine-Rituxan; if you gave bendamustine-Rituxan, then R-CHOP or R-CVP or Revlimid and Rituxan, possibly Revlimid and obinutuzumab. And in more frail patients, single agents, I think, is the order of the day, Rituxan alone, obinutuzumab alone, chlorambucil alone, Cytoxan alone or possibly, again, radioimmunotherapy alone as a single agent.

Next slide? So this represents the current thinking and state of the art, if you will, for the POD24 group. These are patients that I mentioned who relapse within 24 months. There is a large intergroup trial led by the Southwest Oncology Group, comparing either obinutuzumab, the alternate monoclonal -- anti-CD20 monoclonal antibody with CHOP if patients had prior bendamustine and with bendamustine if patients had prior CHOP. The second arm is umbralisib, one of the PI3-kinase inhibitors, we'll talk about in a moment. And the third arm is Revlimid, the IMiD plus obinutuzumab.

Just to remind you, I've talked a little bit about Revlimid, where that came from. So Revlimid is an IMiD. It's -- you may be familiar -- you probably are familiar with, its cousin, thalidomide, which was used in the '50s and '60s as a sleeping aid and led to birth defects -- significant birth defects. It was kind of obviously put on the shelf for many years, but resurrected again as thalidomide and then the 2018, '19, '20 version lenalidomide. And what was forgotten about thalidomide early on is that it had major immunologic effects, enhanced T cell function and

had effectiveness in B cell disorders. And so that's why it's used and it's a very active agent. So this is the current landscape of POD24.

Next slide is talking about landscape. This is -- basically gives you some rough estimate, we won't go into these in any detail, about some of the agents that are being either approved -- were approved or in the pipeline for follicular lymphoma after second line. These include some of the bispecific antibodies. It includes some third and fourth generation BTK inhibitors, Bruton's tyrosine kinase inhibitors, which would seek to improve upon the results with ibrutinib, which is down on the bottom left in a red dot on the slide with only about a 30% response rate, disappointing response rate in follicular lymphoma. So I think people are trying to look at the next generation of BTK inhibitors to see if we can improve the response rate. And this gives you some idea of what's being tested. What's approved is in blue and pipeline therapies are in red and in orange.

Next slide. Third line and subsequent treatment. PI3 kinase inhibitors, copanlisib, duvelisib, idelalisib and umbralisib is fourth line. I'll talk a little bit about those in a moment. The EZH2 inhibitor, tazemetostat, it's approved now by the FDA in third line if patients have the EZH2 mutation that can be relatively easily tested for on tissue specimens. But interestingly enough in an unusual FDA approval, what -- if patients are wild-type, not mutated, the clinician has the option to use this drug if they determine that there are no other options for treatment. And how that's defined, I think, is [truly] loosely, obviously, and in the eye of the clinician.

So basically, I think tazemetostat is available and approved for anybody with follicular lymphoma, whom the clinician feels has no other good options. And then CAR-T therapy based on data from the ZUMA-5 study, which I'll show you in a moment, axicabtagene ciloleucel, or Yescarta, is now approved in the U.S. by the FDA for follicular lymphoma and certainly has some promise.

Next slide. We'll go to third line approved and pipeline therapies, a similar matrix with ibrutinib now being tested together with the checkpoint inhibitor, nivolumab, on the bottom left, and then some of the other drugs, the PI3 kinase inhibitors, I mentioned, duvelisib, umbralisib and idelalisib. And then on the right part of the slide, you'll start to see some of the CAR-T agents. The allo agents are -- now people are beginning to look now at off-the-shelf allogeneic CAR-Ts. And I would say, not for necessarily elderly or infirm, but these are patients that might go to transplant if they're younger and healthier, but the allo CAR-Ts and the autologous CAR-Ts may be reasonable options for those patients, even older patients.

Next slide. So the PI3 kinase inhibitors, the first generation idelalisib; second-generation umbralisib, another experimental drug; and then dual PI3 kinase inhibitor, duvelisib, are the ones we'll touch on briefly.

The next slide. Umbralisib is inhibitor of PI3 K delta and casein kinase 1e and a difference in structure and other characteristics from idelalisib and duvelisib, which are approved in follicular lymphoma. This is the most recently studied and generated quite a bit of excitement.

Next slide. We'll show you the study that generated that excitement. The issue is that this drug has to be given until unacceptable toxicity or in the study, of course, withdrawal of consent. The primary endpoint was safety, the maximum tolerated dose and some PK, pharmacokinetic, data. Secondary endpoints were what we're all interested in, overall response rate and duration of response. I will point out something if you look at the bottom of the slide, and this I'll bring up as we talk about these in a minute, infection, Pneumocystis jirovecii, prophylaxis was permitted but not mandated. I think it should have been mandated.

Next slide gives you a waterfall plot of the responses. And you can see and if you focus on the pink, in follicular lymphoma, you can see that there were reasonably good responses, better than 50%, say, in a significant number of patients, but most of the responses were between 5% and 50%. That's really quite meeting the mandate for at least a partial response.

So next slide. So this summarizes some of the PI3 kinase inhibitors, the competition, if you will, for -- or some of the competition for radioimmunotherapy. It's given daily orally, but grade 3 to 4 hepatotoxicity is reported. Diarrhea and colitis in about half the patients -- more than half the patients. About 10% of patients had grade 3 or life-threatening neutropenia. Skin reactions in a small number and about 10% of patients had PJP or cytomegalovirus infection. And so I would advise that everybody on these drugs should be on PCP prophylaxis with Bactrim, at least, and should be checked on a monthly basis for activation of cytomegalovirus infections,

just like we check our allogeneic bone marrow transplant patients. And these drugs interact with CYP3A inhibitor. So there's a fair number of drug interactions that we have to be aware of with this drug.

Next slide. Duvelisib. Similar. It's twice a day dosing, but hepatotoxicity, diarrhea and colitis, pneumonia, skin reactions, infections again with PJP and cytomegalovirus. And again, concerns about the use of concomitant drugs, which are CYP3A inhibitors, for example, azoles. And if you look, there are many, many drugs over-the-counter that are CYP3A inhibitors that can interfere with duvelisib.

Next slide. Copanlisib, recently presented -- published by Martin Dreyling from Munich with exciting data, except this is a drug that's given intravenously on day 1, 8, 15 and then every month -- well, actually, 3 weeks out of every month forever. It's just an IV drug given every 3 weeks out of 4 forever until progression. Hyperglycemia is an unusual -- and hypertension are unusual complications. But again, infections with PJP and cytomegalovirus and, again, interaction with certain other drugs. So the activity of this is 50%, 60% responses and maybe 30% complete responses.

And when people -- we've been in meetings where people take a poll of what would be your choice of agent for relapsed follicular lymphoma, everybody says PI3 kinase inhibitors. And then everybody says, what would be your choice if you didn't have to give it for the life of the patient on an IV basis 3 out of 4 weeks, and I would say radioimmunotherapy.

So next slide. Histologic transformation. I mentioned earlier, these patients can transform and they may be candidates for CAR-T therapy, we'll finish in just a moment. I wanted to highlight this a little bit because I think this is here to stay. And I think exciting data, the chimeric antigen receptor, which is where CAR comes from, is basically mimicked after the normal T cell receptor.

And this has evolved where there is now at the -- if you look at the right side of the slide, the scFv is the place where the -- in the next slide, I'm sorry. Yes. So this mimics the T cell receptor. So the chimeric antigen receptor on the right, the scFv, is the place that recognizes the target antigen for the most part, CD19, but studies now with CD20, CD22, all of the approved drugs are CD19 targeted and follicular lymphoma is ubiquitous positive for CD19. So a perfect target. And people are now manipulating the co-stimulatory signal in yellow on the right, whether it's CD28 or 4-1BB or OX40 impacts on how active this construct will be.

Next slide? I wanted to show you the data on ZUMA-5. These are data that Caron Jacobson from the Dana-Farber presented recently. If you look at the overall response rate, 76% -- 92% overall response rate in 104 patients. If you look at the follicular group, it's very similar. This is all patients. It's made up follicular and marginal zone, but in the middle part of this graph, follicular lymphoma, 84 patients, 80% complete remission rate, 94% overall response rate. And so excellent data.

Next slide? The duration perhaps is not as good as we'd like. Starts falling off at about 10, 11, 12 months. The advantage of this treatment, just like radio immunotherapy, is it's one and done. It's a onetime treatment. And there probably are some patients that are going to be cured we hope by this approach. And so I think this is here, and I think it's actually -- since there are preclinical data suggesting synergy between cellular therapy like CAR-T and radiation, I would envision some trials where radio immunotherapy might be combined with CAR-T therapy.

Next and last slide. So this is just what we saw earlier. We tried to do is talk about the incidence of this, the diagnosis, little bit about biology and talk about first, second and third line treatment with a bit of a focus on patients who are older and perhaps couldn't tolerate more aggressive treatment. The evolving landscape, I think many agents out there, I certainly think doing this for many years now that there is a role that has been missed for radio immunotherapy, either as a single agent or perhaps in combination with other agents. And some of those might be the recently approved agents, such as CAR-T therapy. So I want to thank you for your attention, and I appreciate the opportunity to talk about this. Thanks very much.

Presenter Speech

Erik Skullerud (Executives)

Thank you so much, Dr. Gordon and -- for that highly educational and interesting presentation. I know you have patients to tend to. You have your rounds. So we'll not be able to do a Q&A today, but really appreciate your insights. Thank you so much.

Presenter Speech

Leo Gordon (Attendees)

Thank you very much. I appreciate the opportunity.

Presenter Speech

Erik Skullerud (Executives)

Next, we'll let our new incoming CMO, Pierre Dodion, give you some insights around our program on Betalutin post third line FL. So Pierre, I'll let you take it on from here. All yours.

Presenter Speech

Pierre Dodion (Executives)

Thank you very much, Erik. And while we are loading the slides, I would like perhaps to express my -- the privilege to be able to speak to all of you. As you know, I joined the company relatively recently and I've really -- I'm really impressed by the number of activities, interesting activities that have been conducted and that will be pursued in the future. I'm looking forward to collaborating with all of you with my colleagues at Nanovector. And also, of course, with the investigators who are participating to our clinical program.

So task this afternoon will be to evaluate the potential of Betalutin beyond what we are already doing, i.e., the PARADIGME program, which, as you know, is conducted in the third-line setting in follicular lymphoma. So if you move to the -- next slide, please? This is a schematic conceptual cartoon, trying to illustrate where we could go. The blue box represents symbolically the current activities in third-line follicular lymphoma and one expansion pathway is quite clearly to go to earlier lines in the treatment paradigm first and second line, but also possibly down the road in the first-line setting.

On the other side, we could also expand and this is shown by the curve pointing to the right top corner. We could expand to diffuse large B-cell lymphoma, DLBCL starting with advanced disease, i.e., patients in the third-line setting but, year ago, nothing prevent us to expand further to earlier stage of DLBCL. And of course, DLBCL has a special place in the overall landscape of non-Hodgkin's lymphoma because as indicated conceptually by the slide, this is the largest non-Hodgkin's lymphoma subtype.

And finally, nothing prevent us to move as well to smaller indication and representing here the particular case of -- among others, but particular case of marginal zone lymphoma. So let's address first, follicular lymphoma. If I can have the next slide, please and the next one -- move to the next slide, please? Very good. Thank you.

So the treatment -- could you go backwards by 1 slide? Great. Thank you. So we are focusing our interest on -- in terms of clinical development on the patients in the second line setting and more specifically on frail patients. This has been discussed in details by Dr. Gordon, but typically, those patients, elderly patients, patients with co-morbid conditions, typically, do not tolerate aggressive treatments like combination chemotherapy. And very often are treated with single-agent treatment, in particular, single-agent rituximab. Hence what I'm showing here is that single agent rituximab for these patients is not at all a bad option. If you look at the efficacy data on the left side, you can see a complete response rate of 5% to 15%, a median progression-free survival of approximately 14 months.

So it does work to some extent. But clearly, there is ample room for improvement. And the curve on the right side is an illustration coming from one of the most important study in this field testing single-agent rituximab in red versus the combination of rituximab plus lenalidomide, the so-called R2 program, which was presented by Dr. Gordon in his presentation.

Next slide, please? The other attractive feature of rituximab is that overall, this is a well-tolerated drug. You have in the top part of the slide, the list of adverse events that can be induced by rituximab, things like infusion-related

reactions, fever, lymphopenia. But the most important point is that in the vast majority of the cases, up to 90%, these events are actually mild or at times moderate.

And at the bottom of the slide, I'm also drawing your attention as it has been done by Dr. Gordon to the fact that besides rituximab, there are other single agents that are being used in that setting, for example, chlorambucil, with or without rituximab, cyclophosphamide with or without rituximab and ibritumomab tiuxetan. So in some of this rituximab does work, and this certainly used in these frail patients, the second-line setting. It is reasonably well tolerated, but there is clearly ample room for adopting better treatments.

If we move to the next slide, we have a nano vector piloted the combination of Betalutin plus rituximab in this patient population. This has been performed within the so-called Archer-1 study. So we are talking here in terms of patient population of follicular lymphoma were received at least some of them more, but at least one prior regimen and with the primary objective to evaluate the safety and tolerability of the combination of Betalutin plus rituximab. And of course, we have also looked as a secondary objective to preliminary antitumor activity.

In the middle of the slide to have the study scheme, in the middle box, you can see the administration of Betalutin followed by preceded and followed by rituximab as per the FDA approved regimen. And then followed by continuation of rituximab in those patients who achieve at least stable disease or partial response or complete response. The results of that study are summarized in the bottom of the slide. And actually, we have generated quite attractive data with actually all the 7 patients achieving a response. And this includes 5 complete responses, not bad at all for patients -- population of patients with resistant disease. And these response seems to be quite long lasting. 6 patients have still an ongoing response. And out of these, 5 patients have passed the 2-year or 24-month assessment.

Furthermore, the combination of Betalutin plus rituximab showed actually a very good safety profile, not really different from that of single agent Betalutin. So the data suggests a pretty good -- a pretty attractive level of activity with an excellent safety profile. And quite obviously, these results play an important role in forming the design of our confirmatory Phase III study in follicular lymphoma.

So coming to that, a particular study, if we can move to the next slide, please? We have been evaluating several options for the next phase of the clinical development of Betalutin in pace with follicular lymphoma in the second line setting and more specifically in frail patient who are not eligible for aggressive therapy. And for those who are curious, you can see at the bottom of the slide, a partial list of these aggressive treatment options. These are pretty much identical to those mentioned by Dr. Gordon. You can see there CHOP with or without rituximab, the combination of bendamustine, et cetera.

So if I consider all patients in the second-line setting, some of them will be eligible for these aggressive treatment regimen, but many others will not. And these patients not eligible for aggressive therapy are those who will be randomized in our study between rituximab alone, the standard of care and the combination of rituximab plus Betalutin. The primary endpoint is likely to be progression-free survival.

The beauty of this approach is that this program will be -- will serve, number one, as confirmatory randomized trial as part of the possible post-approval commitment that we might receive from FDA in the third-line setting based on the PARADIGME study results. But as I said, will also constitute a data set that could lead to the approval of Betalutin in combination with rituximab in the second-line setting. So that realizes typically the label expansion that I was talking about in my introduction.

As mentioned by Erik in his introduction, we are in close contact with regulatory agencies, in particular with the FDA to finalize the various elements of this study design. So more to come, but suffice to say that we are very excited by this approach.

Next slide, please? Let us turn ourselves now to DLBCL or diffuse large B-cell lymphoma. Next slide, please? Just a quick reminder, as already mentioned, DLBCL is the most common form of non-Hodgkin's lymphoma. And about 30% of the non-Hodgkin's lymphoma, at least in the U.S., are DLBCL. And it is typically an aggressive form of lymphoma that involves the lymph nodes as well as other organs.

I'm not going to go into the details of the treatment of DLBCL. Suffice to say that for newly diagnosed patients, the goal is truly to cure them. And this is typically achieved by a combination approach combining multi-agent chemotherapy, the so-called CHOP regimen combined with rituximab. Many patients also receive high-dose chemotherapy followed by stem cell transplantation. Unfortunately, many patients despite this aggressive

treatment still relapse and moved to the so-called second and third line setting. And despite many, many years of clinical research, the treatment of these relapsed patients remains a challenge. Therefore, this group of patients is a significant unmet medical need.

You have at the bottom some indication about the commercial opportunity for second and third line of DLBCL. And you can see that this is by no means a small group, about 23,000 patients per year for second line, 11,000 patients per year in the third line, and these are the data for the 6 key markets, EU-5 and the U.S. So that is approximately 50% more than the market of second line follicular lymphoma. That is just to show you the importance of the DLBCL patient population.

Next slide, please? This is intended to give you a very brief snapshot of the treatment approach for DLBCL as Dr. Gordon focus mainly on follicular lymphoma. As I said on the previous slide, the first-line treatment is typically a combination of chemotherapy and rituximab. In the second-line setting, there is a quite long list of agents with relatively poor activity. This may be changing now with the introduction of newer regimen, but it remains also an area of intense clinical research. And I will show you in a moment some recent data about 2 particular classes of newer agents. And then in a third line setting, the situation is even worse and it's typically an area of clinical research.

Next slide, please? I'm sure that many of you have heard about CAR-T cell therapy, bispecific antibodies. And I'm mentioning these 2 classes because they represent examples of treatment with, yes, quite substantial activity. If you look in the middle of the slide, you can see there, the objective response rate, the complete response rate, progression-free survival data, overall survival data. And when one is talking in refractory patients or relapse patients about complete response rate of 40% to 50%, 2-year survival of 50%. One cannot deny that this is indicative of pretty good activity.

However, at the same time, the toxicity of this agent is quite substantial, and this is featuring the bottom part of the slide, Grade 3-4 toxicity failures or cytokine release syndrome, neurotoxicity, infection, neutropenia. And you can see that virtually for all of these, we are talking about ranges between 5% and 20%. Accessibility may also be an issue. These treatments are not necessarily given in every single medical center and also the financial burden in terms of acquisition costs may be quite tremendous. I'm sure that you've all heard about the cost of CAR-T cell therapy.

Now you may perhaps remember what Dr. Gordon said about a third class, i.e., the PI3 kinase inhibitors. And in fact, I could have easily added third column about the PI3 kinase inhibitors as a class because it's providing pretty much exactly the same picture. Some very good activity but also quite substantial toxicity. And quite obviously, yes, one would wish to be able to administer these treatments to every single patient in the third or second line setting, but the reality is that elderly patients are simply unable to tolerate these quite aggressive treatments.

Next slide, please. It's just providing more details about what I said as an overall approach. And I'm not going to spend too much time here. But fundamentally, in the second line setting, you can see that there is no one combination that has been approved, tafasitamab plus lenalidomide combination. CAR-T cells are moving along as well as bispecific antibodies. But clearly, there is still a need for better combination therapies and very importantly, that have an acceptable safety profile, especially for frail patients.

And in the right column, I'm providing data on the third line setting, again, some information about CAR-T cell treatment that we already discussed. Some information about drugs called polatuzumab and loncastuximab. But bottom line is that, again, these refractory patients, particularly in the third-line setting may very well represent a unique and very attractive spot for Betalutin, especially in elderly and frail patients, and therefore, provide us a way to enter the DLBCL segment.

Next slide, please? Just like in follicular lymphoma -- I may have the next slide, please? Previous one? Yes, apparently. Yes. Thank you very much. We have also initiated clinical activities in the field of DLBCL. This particular study is named LYMRIT 37-05. And in fact, we have performed a Phase I study in 18 patients with relapse or refractory DLBCL patients, 16 of them were evaluable with the goal, quite obviously, to investigate the safety profile to determine the maximum tolerated dose in these patients and also to detect initial signs of activity. And you have the kind of dosages that we've explored in -- as part of this study in the 4 boxes that are displayed on the slide.

Next slide, please, is actually showing the critical results of that study starting from the bottom. Importantly, we have been able, indeed, to establish recommended Phase II dosage. And the exact numbers for lilotomab and Betalutin are indicated on the slide.

In terms of safety and tolerability in the high top corner, we found that Betalutin is actually very well tolerated and complete in a consistent manner with all previous studies. And then finally, and importantly, as illustrated in the left top corner, we did see interesting clinical activity. In particular, we reported 2 complete remissions at 2 highest dose levels, again, considering the kind of patient resistant refractory DLBCL review that is very encouraging.

Next slide, please? Where do we go from there? Well, one very attractive option in our mind is to combine Betalutin with other agents. And this has been also -- this has also led to successful development for some of the drugs, 3 of which are listed on slide, tafasitamab on the top, polatuzumab in the middle, naratuximab at the bottom. You can see in the middle, the kind of efficacy data achieved with single agent, and we are showing here the overall response rate, 26%, 56% and 22%, respectively.

And then on the right, you can see the clear increase in terms of activity when these drugs are combined with patented drugs, in particular, tafasitamab with lenalidomide, polatuzumab with rituximab and bendamustine, and finally, naratuximab with rituximab leading to a response rate of 60%, 63% and 50%. So at times more than the double of the response rate achieved with the single agent.

If we move to the next slide, we think based on all those considerations that -- the most important, the most attractive option is to explore a combination of Betalutin in the third-line setting in the form of an exploratory Phase II study. To be complete, we have explored other options, in particular, escalating the dose of Betalutin further which, by the way, could be actually achieved as part of the proposed Phase II study or exploring Betalutin is consolidation agent. These options are there. But again, we feel that the combination approach is really the best one.

And coming with that to my next slide, which basically recap that, again, you can show the next slide, please, that third line DLBCL in frail patient is really the focus of our clinical research in these patients. We are working on the identification of ideal combination partners, taking into account both efficacy -- existing efficacy data with also tolerability data. As I said, we could very well increase the dosage of Betalutin, and we are engaged in multiple consultations with external experts to optimize the study design. Thank you very much.

Presenter Speech

Erik Skullerud (Executives)

Thank you so much, Pierre. Two pieces of logistical information before we move to Marco. So first of all, we're going to have a break after Marco's presentation, so that we can get a little bit of coffee or bio-break for people. And secondly, if you have questions, please free to submit them, and we will handle that at the end of the session for everyone. But without further ado, I want to move to Marco Renoldi, our COO, who will speak to you about one of the initiatives more on the commercial side that we are developing at the moment. Marco?

Presenter Speech

Marco Renoldi (Executives)

Yes. Hello. Good afternoon, everybody. I think it would be a shame if we were unable to use the great clinical development work that the company has done so far and make it available to patients. For that reason, over the past few years, we've invested time, resources to understand both the drivers and the barriers to the integration of radioimmunotherapy into the continuum of care for lymphoma patients in preparation for launch. So I will share today the findings from the most recent initiative. May I have the next slide, please?

I think, as we all know, radioimmunotherapy is a targeted approach to cancer care, with the potential to improve both progression-free survival and quality of life in many tumor types. And we're proud to have generated data with Betalutin that makes us confident that radioimmunotherapy can make a difference also to NHL patients. But on the other side, we are also aware, and I think Dr. Gordon mentioned, that some radiopharmaceutical therapies are underused despite the significant potential they can offer. So our effort has been targeted to understand the barriers to adoption and most importantly, to find solutions.

Some of these barriers, we are well aware are not necessarily related to the product. Rather, they are systemic. And so the solution, the mitigation can only be obtained through policy interventions, which require a coordinated effort. And for that reason, we are, indeed, partnering with medical societies, patient advocacy groups and also with other biopharmaceutical companies that operate in this space.

May I have the next slide, please? In 2019, a U.K.-based health policy organization, named HPP, started a very interesting project with one specific goal to raise awareness around targeted radiopharmaceutical therapy, which they called radioligand therapy. And actually, radioimmunotherapy is 1/4 of radioligand therapy, and Betalutin is one example of radioimmunotherapy. And the key findings of their preliminary research are shown in the blue chart on the right of this slide.

And what they found -- what HBP found with this research was a set of barriers to integration of radioligand therapy into cancer care. I think it's reassuring to see that what HPP found out really validates the previous research we had done in this space. The same barriers we had previously identified and had started to work on. And I will just name a few, which I believe are particularly relevant.

Number one, the low awareness of this technology amongst the younger generation of physicians. Number two, the insufficient number of authorized users, for example, nuclear medicine specialists who can deliver the medication. Number three, the unclear referral models through which patients are basically referred from hematologists, oncologists on to nuclear medicine specialists.

Next slide, please? For the above reasons in late 2020, we decided to partner with HPP. We felt they had done a really neat job. We decided to partner with them and together with another important pharmaceutical company, we decided to co-fund to provide funding support to their follow-on project. The goal of the new project was to develop in collaboration with a series of international experts from both the U.S. and Europe, and Dr. Gordon was one of them, an assessment framework.

Basically, one assessment framework per country that would allow the evaluation of the readiness level in each specific country to integrate novel radioligand therapies, radio immunotherapies, but most importantly, because that's what is important to guide any required changes.

Next slide, please? The readiness assessment framework is designed to generate thorough situation analysis for the U.K. and one for the U.S. This situational analysis contains a clear articulation of the barriers, requiring policy interventions, but in addition, a series of background document that explore in depth specific domains. To name a few, governance, regulation and reimbursement, service provision and so forth. If I can make a parallel, it's almost like a CT scan.

So the situational analysis identifies the problems and indicates the most laser-focused approach for removal of the problems. So you will agree with me that this is a unique tool as we prepare to launch our product because it will ensure that eligible patients can benefit from the treatment.

Next slide, please? I would like at this point to share with you a glimpse, just a very high-level overview of the most important findings of the U.S.-based situational assessment. You see on the left, certain barriers, which were spotted. And for each of the barriers, a clear set of intervention plans was identified. You see that on the right. We call them policy implications or policy interventions. And this is the beauty of this approach that we can identify areas, barriers where we can directly act upon. And I'd like to focus on the 3 ones which are highlighted in red on the left -- on the right column.

Number one, our effort to ensure that treatment guidelines include any approved radioimmunotherapy as soon as technically possible. And so we hope that as we prepare to file our BLA with the FDA, we will be able to ensure that guidelines include Betalutin for treatment of lymphoma patients. Second, to ensure the awareness of this treatment collaborate and partner with patient advocacy organizations to create very patient-friendly information, so the patient are aware of this novel type of treatment and appreciate the advantages that one only administration can provide to them. And number three, last but not least, supporting medical societies to develop easier, more streamlined referral and treatment pathways.

And our goal is very simple. Our goal is to create a multidisciplinary approach so that hematologists who normally see the patient and nuclear medicine specialist who need to receive these patients for the treatment with

radioimmunotherapy can have a seamless dialogue and we can ensure a consistent approach across different settings of care, both in academic sites and in the community practice.

Next slide, please? I think we are proud of this project. We are proud to partner with HPP. We are proud to be a co-funding partner with another important pharmaceutical company because we are together in an effort to drive policy change. I think we believe that creating a more receptive environment to radioligand therapy or radioimmunotherapy, whatever you want to call it, will ultimately benefit patients because those who are eligible for these therapies will be granted access.

Next slide? So I hope I've been able to share with you the most important findings from this project. I wish to thank you for your attention. And I'd like to suggest for those of you who are interested to learn more to please visit the website, radioligantherapy.com. Thank you very much.

Presenter Speech

Erik Skullerud (Executives)

Thank you so much, Marco, again, for this great presentation. I hope you're starting to get a feeling, the multitude of different areas we're working on the different dimensions that we're working on. Before we break for a short break, let me take this opportunity to give a big thank you to Marco. Some of you will not know, but he is going in retirement as of the 1st of January 2022. And he has obviously been a cornerstone in a lot of the efforts that we have done as a company since I believe, back in 2014, Marco. So a big thank you for that.

We obviously wish you all the best for your retirement. But I'm equally happy to also say that you have decided to stay with us for 2 days a week on a consulting basis, so we won't lose your great knowledge and your great contribution. But for now, thank you. All the best for your retirement. We're going to take 5 minutes break, guys. I'll be back at 3:45. I know some of you have to fill up on popcorn and Coke. I believe I saw in social media. So feel free to do that, and we'll be back in 5 minutes and continue with Maureen's presentation.

[Break]

Presenter Speech

Erik Skullerud (Executives)

All right. Are we back online? I think we can move on with the next few presentations. So I hope you can hear me out there? Yes. Great. Thank you. So we're about to get started again on the second part of our presentations for today, a little mistake from my side just before we went into the break. We're going to move to our manufacturing/supply chain now and have Lars give a short update on what we are doing with that and how we are progressing with that. This is an important part of how we develop our readiness for the upcoming BLA as well and then move to Maureen after Lars. So without further ado, Lars, all yours.

Presenter Speech

Lars Nieba (Executives)

Thanks, Erik. I tried to look like Maureen, but it didn't work out. That is why we had to change. So -- but seriously, thanks. Good afternoon, everybody. It's pleasure for me to be here on stage and to walk you through our journey to BLA and to launch readiness.

Can I ask, next slide, please? So what does CMC stand for chemistry, manufacturing and controls. So what does it cover? It covers all aspects from production, so including quality and regulatory. So why is CMC important? Now the easy answer in essence is what Erik also mentioned earlier is, without the substance, you can't treat the patient. But seriously, CMC has become more and more important for regulators and many successful clinical programs failed to receive immediate approval due to CMC issues.

We, at Nordic Nanovector, are working hard to avoid this. CMC is important to us because it impacts our patients. It is important to our IP and of course, later on for our margins. We have regular meetings with the health authorities, and it is really an integral part of our company. So that is why the overall CMC strategy is really important for our overall success. As you know, we have no own manufacturing capabilities.

Let me have the next slide, please? But here are our key partners. So that covers more or less where we are active in. So we are a Norwegian company. We have 2 partners in Oslo and one is Diatec, the other one is IFE. We do have a partner in Germany, which is ITM. We have 2 partners in Spain with Liof and 3PBio. We also have partners in the U.S. with Macrocyclics and we are in close interactions to finalize the contracts also with Cardinal Health for our later on distribution. So what you can see, our supply chain is already pretty global.

Can I have the next slide, please? So let me walk you and give you an overview about our journey to launch. So first of all, the PPQs, what is PPQ stands for? Its process, performance, qualification. It is a requirement to demonstrate and validate the robustness of our process and very importantly, in a suited facility, which is GMP conform.

So next in line is then that we have to prepare all of our documentation for submission, the so-called BLA preparation, and we have to prepare our facilities for a so-called preapproval inspection. In parallel to that, we have to set up our commercial supply chain.

We have to define all of our business processes to that to be able to supply in all countries. We have to define, for example, something like top policies having the right planning systems in place and so on and so forth. And where, of course, Marco and Erik are very keen on is that we are already at time of approval for an immediate launch so that we can really supply and give the medication to our patient. And last but not least, as I mentioned, it's also important for our margins. We already start focusing today on our efficiency and effectiveness of the entire supply chain to not only have a robust process but also to reduce costs.

May I have the next slide, please? So I know it's a reminder for most of you. Here's our manufacturing process. As most of you are aware of, we have 2 independent products. The one is called lilotomab and the other one is called Betalutin. Let me start first with lilotomab. So we start with our production in Oslo at Diatec, where we produce the crude. We then moving further to the drug substance, to purification at 3P in Spain. And then we do have the filling at a company called Liof. So that is our final product for lilotomab.

For Betalutin, we do have the first step -- the first 2 steps are the same. We then add DOTA, chemically to it, which is supported -- which is brought by Macrocyclics to Spain. And we then do have the filling for the so-called lilotomab-satetraxetan at Liof and then we couple it with lutetium, which is coming from ITM in Germany, and we do have our final product done at IFE with Betalutin. So what you can see is that is our overall manufacturing process, which we are currently validating.

Can I have the next slide, please? And as mentioned before, it is not only important to have a good and robust process. It is also extremely important to have good facilities for the so-called pre-approval inspection, of course, but also in general, for producing GMP. Let me go and give you an impression about where are our partners.

So let me start with Diatec monoclonals in Oslo, I wanted to say here in Oslo, but unfortunately, we are here in Switzerland and instead of being, of course, in Oslo. And what is Diatec? We have developed together with Diatec, a robust production process. And we have invested together into the production facility, which is GMP certified by the Norwegian Medicine Agency. We have Class B and C room. So overall, I think we are making very good progress here for both the process and the facility.

Can I ask the next slide, please? Moving on in our value chain, we move to 3PBio, which are in Pamplona in Spain. The facility itself is GMP certified by the Spanish agencies, for the manufacture of biological products and also the release of sterile products. But more importantly, for us, 3P has invested into a new state-of-the-art facility, which we just visited, which really looks great and our product is produced now in the new facility, which is really good news for us.

Let me walk you to the next partner, next slide, please, which is Liof, which is about 80 kilometers away from Pamplona. And also there, Liof is GMP certified by the Spanish Health Authorities and for aseptic filling and release of sterile products. Liof has a state-of-the-art filling line, and it was already inspected by the FDA in a pre-approval inspection, and also there have very good quality, what we are getting.

Now let me -- let us move back to Oslo. Can I have the next slide? IFE. IFE has also done a lot of work over the last years. This has invested into a new manufacturing line for our Betalutin production. The picture here is showing actually, the very new line, where we are very proud of. Our product will be manufactured in that line.

And of course, IFE is also GMP certified by NoMA. So overall, I think we have not only a robust process, but I think also all of our partners have really good facilities in place and where we can do a lot of work in.

Now going to the next slide. And as mentioned in the beginning, the one thing as a process and the facilities, which is also very important, is really to bring the product to the patient and that is the supply chain. Now how have we set that up and what is important to look into in the supply chain if we are setting up a commercial supply chain? And what you can see here is, how we will move our product from place to place. Now we started Diatec with the crude. We will go by plane then to Spain, that it is and that we can produce there, see bulk drug substance. And then we will move it to Liof, which is 80 kilometers away, again, by plane back to Norway. And then we would -- and we have to bring it from IFE very fast into the U.S. As you know, we only have about 7 days of shelf life after the production.

So -- and we have a very strong partner chosen in the U.S. for commercial supply chain. We want to move ahead with Cardinal Health, which do have a lot of radio pharmacists, and they are very active in the U.S. and very well known for that, and we are happy to have them as a partner. And from there, we can bring it into various administration sites in time.

As the supply chain is not only is that what you also need to be aware of that you have to look on critical raw materials, your safety stock policy, your secondary sourcing and so on and so forth. Underneath, you can see some of these very important. But of course, it's only a snapshot, a glimpse on where we are looking for. One thing is, for example, the monoclonal antibody medium for production at Diatec. The other part, of course, is the DOTA that it is in time at 3P. What some people are forgetting is the primary packaging. You need to think about we have vials and stoppers, which looks very basic. But of course, we have to have enough room for them. Because if we don't, then we can't fill. So all of that, we would need to look into it.

There are other premier packaging sources. There's also some additions to some buffers like Recombumin and all of that needs to be looked on. And of course, lutetium always have to be fresh there in time. And we are working very close, not only with ITM, but also, of course, thinking about second suppliers and so on and so forth.

And finally, at the administration side, what you should also not forget is infusion filters. And there's a long list, which we are currently looking on and how we prepare ourself to be ready for the launch and the commercial supply.

And can I the next slide, please? Now where are we? You always hear a lot from [Malene], where we are, that CMC is working on the PPQs and so on and so forth. Now we are fully on track with our process, performance, qualification. We are also on track in preparing for our BLA submission. As you have seen, we have already started to set up the commercial supply chain because it takes also a while if all of, say, things are really in place for the launch. So, of course, we haven't done the launch, but we start to prepare for it. And where everybody is interested later on is to having good margins. And we are already thinking about how to improve our cost of goods. So that is at conceptual stage.

With that, I hand over back to you, Erik.

Presenter Speech

Erik Skullerud (Executives)

Thank you very much, Lars. I think as you can see, one thing is the clinical development, the PARADIGME study. It walks hand-in-hand with our CMC, our manufacturing, development. This is really a hand in glove. It is a matter of really ensuring that on one hand, we get the clinical results that we have. But on the other, that we also do the right things in order to ensure that the product gets developed and produced, manufactured well. So this was a bit of a glimpse into what Lars and his group is working on at the moment.

Now we're going to switch gear completely. We're going to let Maureen take over and talk to you about our 2 most recent little babies, on first the monoclonal antibody that we are developing, a humanized antibody. And on the other, our CAR-T co-development or our collaboration rather with radio University of Pennsylvania. So Maureen, on to you.

Presenter Speech

Maureen Deehan (Executives)

Many thanks, Erik. Yes, I'm very, very excited now to have the opportunity to give you some headline information on where we are with these discovery programs.

Next slide, please? Can I have the next slide, please? Apologies. Thank you. So this is a build slide. So B cells also known as B lymphocytes are a type of white blood cell, and these play an extremely important role in adaptive immunity. Hit the button, please. There are multiple antigens present on B cells, CD19. Next, again, please? And you've heard both Professor Gordon and Pierre talk about these today and also -- hit the button again, please.

CD37. So yes, CD20 is very well recognized and as we all have heard of rituximab. Rituximab was actually approved in 1997 for cancer. And you've also heard today about some CD19 therapies, such as Monjuvi and the CAR-T therapies, Yescarta and KYMRIAH.

But at Nordic Nanovector, we focus on CD37 because it's also a major antigen on B cells. You will see from my subsequent slides that other people are active in this space. But where we really have an advantage is that we've been working in this biology for over a decade.

Next slide, please? So now I want to talk to you about the B-cell development process, which is shown in the upper most panel of this cartoon. And you can see from the far left from the stem cell and the bone marrow to the far right in the plasma cells, there's multiple stages that are involved. And when you look at the middle panel in this figure, you can actually see that individual B-cell lineages can be associated with particular B-cell malignancies as shown in green.

And what I'd like you now to focus on, please, is in the bottom panel where we show levels of CD20 and CD37 expression and CD19. And what's really important is that CD37 expression in the B-cell lineages overlaps identically with what you see from CD20. So you see expression from the pre-B-cell to the early plasmablast, where the CD19 is expressed broader. And why we think CD37 is a better choice of candidate is that, you don't really want to be with the therapy knock out all of these early Pro-B cells because it's still important to be able to mount an immune response. So CD37 expression is very attractive for a novel therapeutic.

Next slide, please? What I want to do from this slide is just also to remind you that despite the fact that CD37 is almost exclusively expressed on B cells, that there is also an immunomodulatory potential, that there's also an impact on other important immune cells such as macrophages, T cells, dendritic cells and neutrophils. And now there's a lot of literature that really explains that CD37 has an important role not only on the B cells, but it can also impact these other important immune cells.

Next slide, please? So to date, you've heard all about our important role in working on radioimmunotherapy. Now with the radioimmunotherapy, what we do is, we use the CD37 antigen as a docking station. So the radioimmunotherapy molecule is an antibody with the chelator and the radioisotope. And essentially, what happens is that the radioimmunotherapy comes along, docks onto the CD37 receptor. And then the radio activity can be incorporated within the cell and also kill other cells in the environment.

Now this is a very clever and effective way of targeting B cells. But what I want to do next is explain to you how now by exploiting a humanized anti-CD37 monoclonal antibody approach, what we actually do is, we target the CD37 receptor pharmacology.

Next slide, please? And so to do that, I just want to do a little bit of a recap, refresher on antibodies. So this is a diagram of an antibody structure. And an antibody is composed in green of 2 identical heavy chains and in blue, 2 identical light chains. And through disulfide bonds and noncovalent interactions, you have this typical Y shape that you can see in the figure. So that's what you'll recognize as an antibody. And I want to bring your attention to the 2 circles on the top, the variable region, which circles around those square boxes and then in the bottom in red, the constant region.

Next slide, please? Okay. So as this next slide is -- becomes visible, what I want to do next is to talk to you about the different types of monoclonal antibody. So what you can see on the left-hand side is that there are mouse murine antibodies, monoclonal antibodies. And the first murine monoclonal antibody approved was in 1986, and

it was an anti-CD3 antibody for a kidney transplant indication and also Betalutin, our antibody component of Betalutin, Lilotomab is also a murine antibody.

Then when we move across to the chimeric antibody, you can see in the cartoon I explained previously. What you can see here is in the chimeric, the area that I called the constant region in yellow is actually now from a human and the blue, which is the variable region is from the mouse. Then moving to the right, when you actually have the situation where more of the variable regions are human and you have less than in the chimeric, that is the humanized antibody. So you have predominantly a human structure. And could you hit the dot, please? And again? And also again, please?

And really, what this means is why we're really excited about having a humanized antibody to complement what we have is because with murine antibodies and potentially with chimeric, there is the increased chance of having immunogenicity. So therefore, that dose limit you because there is a risk if you give multiple injections. So one of the key reasons why we are pursuing a humanized anti-CD37 monoclonal antibody is because it will support multiple injections which will be important for some acute indications, but it also moves us into a market for chronic diseases because we know that in the chronic disease situation that often you have to repeat your administration. So this is why we are particularly excited about this approach.

Next slide, please? So we've been working on this program, and I now want to just give you an update on where we are. So we've generated multiple anti-CD37 leads with different vector functions. That means different killing mechanisms. And I'm going to talk to you -- I described that a little bit better in the next slide. Where we are from the process is that we are finalizing our lead candidate selection. And that is based on a range of criteria, including in vitro activity, in vivo activity, manufacturability assessment because Lars wants to make sure we choose the antibody with the best characteristics to take forward for production. And also, we are ranking our leads based on other anti-CD20 and other anti-CD37 antibodies.

So now in the slide that we're looking at, in this cartoon on the left-hand side, that's your typical Y-shaped antibody that I've explained to you. And I want to let you know that these monoclonal antibodies have got 4 mechanisms by which they can kill a tumor cell when they engage. So if we start at 11:00 on the blue tumor cell, what you can see happen is, you can see the antibodies inverted. You see the arms are now interacting with the receptor -- CD37 receptor on the tumor cell. And the tail is sticking out. And what can happen is, this type of engagement causes receptor signaling of a lot of death signaling pathways. So you can have a direct death effect.

If we move around in clockwise, then you see a process called antibody-dependent cellular phagocytosis. And what happens here is that the tail SC interacts with the cell, the green cell called a macrophage and it tells the macrophage, eat me. So then the macrophage is involved here and starts to eat the tumor cell.

Moving around to 3:00 on the right-hand side is also another process called complement-dependent cytotoxicity. And what happens here is that the antibody engages with a protein called C1q and causes this cytotoxicity. And then if we move down to the bottom left, the fourth process is called antibody-dependent cellular cytotoxicity. And what happens here is that the antibody engages with other immune cells called natural killer cells. And what happens is, it can elicit these natural killer cells to release granules, which kill the cell.

So we filed a patent for -- on our leads. And where we are just now is, as I told you, we're choosing our lead candidate. And because it's commercially sensitive, all I can tell you at the moment is that we have come up with a series of leads, which -- where we've optimized each of these killing functions. And I can let you know we've come up with some really interesting molecules. But where we are just now is that because it's commercially sensitive, what we will do is we look forward to presenting further data to you in 2022 on the lead candidate that we've selected.

Next slide, please? So in oncology, I'm using this slide really to point out to you that for a monoclonal antibody, the top 10 therapy areas for monoclonal antibodies are shown in this figure. So you can see here that for oncology, almost 4,000 monoclonal antibodies are being developed for oncology indications.

Next slide, please? So the reason why we are developing the humanized anti-CD37 is because we want to utilize this antibody and the benefits it has to strengthen our radioimmunotherapy platform and namely to strengthen Betalutin because we believe you've heard from Pierre, he's got ideas about how to do some combination treatments with Betalutin and some of these more aggressive and difficult-to-treat tumors where we know that a single injection such as we see in follicular lymphoma might not be enough. So Betalutin could be a good

induction therapy, but because, again, the fact that it's based in a murine antibody, we really feel that we might not be able to give multiple administrations.

So where this monoclonal antibody will prove extremely beneficial in oncology is that, we'll be able to treat some of these difficult-to-treat subsets of patients such as the relapsed refractory DLBCL patients are also it gives us the opportunity to try to go to earlier lines and to have a treatment for frontline NHL. So we could use the humanized monoclonal antibodies. The maintenance therapy after administration of Betalutin with the aim of extending both the rate of response as well as the durability. So therefore, you heard Dr. Gordon talk about it, and you also heard Pierre and that's this idea here, but we could actually use the monoclonal antibody as a maintenance therapy.

Next slide, please? So we have the opportunity in oncology, but because B cells also have an important role in immunology and in fact, immunology is the second highest therapy area for monoclonal antibodies, we intend to also explore this market opportunity and also because autoimmune diseases, in particular, have been predicted to be -- have a market share of $150 -- sorry, $150 billion in 2025. So we truly believe that this is an area that we should explore for our humanized anti-CD37 antibody.

Next slide, please? And why? Why do we have reasons to believe that we should do this? Because of some analysis that we did a couple of years ago in-house, with Clarivate Analytics, where we worked in a program where they looked at CD37 expression in a whole range of different autoimmune diseases. And what we came up with was the 5 listed on this slide as being areas where CD37 is expressed at higher levels. So we have Sjogren's syndrome. We had severe asthma, colitis, psoriasis and systemic lupus erythematosus. So what we are doing now is considering doing further data mining to really look to see other sensible immunological diseases that we could target from both a scientific and clinical rationale basis.

Next slide, please? And also, we want to look at what the large pharma, Erik mentioned this earlier. So large pharma have been extremely successful in their anti-CD20 approach to extrapolate into autoimmune diseases. So we want to look and see if there's any lessons learned for us in CD37. And in this slide, I just want to recap for you where the CD20 molecules are playing currently. So rituximab has a marketing authorization for RA but also for other immunological diseases. And in fact, rituximab is in clinical trials for progressive multiple sclerosis.

Obinutuzumab, the kind of second generation anti-CD20, is not currently an FDA approved to treat lupus but may be described off-label, but it's also being looked at for lupus nephritis because it's one of the most serious complications of the lupus condition.

And in addition, moving to the right-hand side, the Novartis molecule, ofatumumab, is in clinical trials for progressive multiple sclerosis and also rheumatoid arthritis. So again, what we will do is utilize the expertise that the larger pharma are working in this area, too, to really come up with a sensible plan. First indication will be for an oncology but to look to further extrapolate into some of these other autoimmune diseases.

Next slide, please? And it's not just those that share opinion in the value of CD37 as a target. There are other companies also active in this area. So GEN3009, the Genmab molecule, which I'm sure you're all aware of. It's a biparatopic duohexabody molecule, and that was recently partnered with AbbVie and needed Phase I/II for hematological cancer.

And in the summer this year, we became aware of another molecule from a company called Sound Biologics, PSB-202, which is actually CD37, CD20 bispecific antibody, and that's a Phase I for hematological cancer. And the molecule that I'm sure you've heard you're most aware of because it's been around longest is the CD37 ADC from Debiopharm, which was in-licensed from ImmunoGen, and that's currently in Phase II for hematological cancer. So again, different molecules are in clinical development that targets CD37, but our molecule will have a different properties, and we will be able to share that target product profile with you in 2022.

Next slide, please? So again, just a summary, the patent has been filed. The lead candidate selection is ongoing. And as I explained, the first indication will be hematology, and we have an IND date planned for 2023.

Next slide, please? So on my last couple of slides, I want to talk to you now about our CD37 DOTA CAR-T cell approach. We're working with you, U Penn. Erik already told you earlier. One of the reasons we were particularly enthused about working with U Penn is that they are the pioneers of a CAR-T cell therapy. And of course, the first CD19 CAR-T cell came out of that U Penn and that was the first CAR-T licensed by Novartis. So we know they're an excellent group to be working with.

Next slide, please? So the collaboration aim is to harness that CAR-T experience and also to utilize the CD37 expertise that we have at Nordic Nanovector and as I explained to you over a decade of experience there. We're also interested because the CD37 CAR-T cell landscape is less competitive. You heard Dr. Gordon already say there's a lot of molecules that are CD19 CAR-Ts.

So we think this is a good space to play in. And also, we believe that the U Penn technology may have an important safety feature, and I'll describe that in the next slide. And what's exciting for us in this collaboration is that we will have the option to license in this CD37 DOTA CAR-T cell therapy.

Next slide, please. Okay. And the next slide is really just to highlight the unique properties of this technology. And if you can hit the button on this. Thank you. So the U Penn have an immune -- sorry, a universal immune receptor T cell, UIR T cell. And what this is, if you think back to what Dr. Gordon said, he said, essentially, you have this single gene Fv molecule, and you have CAR and T-cell signaling elements fused to it. And you also heard that he said that new generations are really working in the T cell signaling part. So the difference here with this UIR is in addition to having the binding domain, the T cell signaling, there's also a DOTA binding domain. And DOTA is a cumulate molecule. So what happens is that the patients in this -- the blood is taken from the patient. The white blood cells are collected. And basically, the T cells are collected. And this construct is introduced into the T cells. And then they can be infused back into the patient. And unlike the CAR-T cell technologies that Dr. Gordon and Pierre has mentioned to you earlier today, normally, when you do that, when these T cells are put back into the body, they start to proliferate. But with the technology we are using, they cannot because they have a DOTA binding requirement.

If you could please hit the build again, please? So what happens for us -- and again, please. So what we have in our system is that we have an anti-CD37 DOTA antibody. So again, taking you back, the T cells are in the body, they can't do anything. This anti-CD37 DOTA antibody is injected in. This antibody binds to the CD37 cells on the B cells. And the DOTA is exposed. So then the T cells can engage with the DOTA, and then they can start to proliferate. So this really does have the opportunity to mitigate existing limitations. And you saw some of this already mentioned, a series of adverse events by Pierre.

So what this means is by being able to titrate in the amount of antibody you use, you can regulate the degree of T cell proliferation. And what that means is that you can have some control over potential toxicities, such as cytokine release syndrome and also neurotoxicity that some patients experience with these agents. So this project has just started. We're really excited to see what data we have. And in conclusion, we're excited to be able to present on both projects next year to you. And I really hope as investors that you're excited to see that we've got some new molecules with new angles, new target product profiles. And hopefully, these new molecules will complement what we already have in our platform and also build on it.

And that all that leads me to do now is to thank you very much for your attention.

Presenter Speech

Erik Skullerud (Executives)

Thank you very much, Maureen, for that in interesting presentation.

I hope you appreciate our 2 latest additions to our pipeline. We are excited about this. We believe this adds very nicely to what we already have.

But in order to complete that picture also from what we already have, I'd like Jostein Dahle, our CSO, to take you through an update on Betalutin as well as Alpha37.

Jostein, please?

Presenter Speech

Jostein Dahle (Executives)

Yes. Humalutin is a CD37 targeted therapy for the treatment of non-Hodgkin's lymphoma.

Next. In Humalutin, we have used a chimeric version of the lilotomab mouse antibody that is used in Betalutin, the NNV3 antibody. It binds equally well to the CD37 antigen as lilotomab. The blue part of the antibody is

human, while the red part is marine. So 70% of the most sequences have been removed. And therefore, the antibody has lower immunogenicity potential, higher therapeutic effect and longer half-life in blood than lilotomab. For Humalutin, we used the gold standard lutetium DOTA peculation of lutetium 177 as in Betalutin. The intellectual property rights are covered by a composition of matter patent and a combination patent application. GMP processes have been established to manufacture NNV3 and Humalutin for clinical trials. And our regulatory dossiers have been completed. So Humalutin is our next-generation anti-CD37 radioimmunoconjugate that is tailored for treatment of non-Hodgkin's lymphoma.

Next slide. In our most therapy experiment, NNV003, in the orange curve, was more effective than lilotomab, in the blue curve. In this study, we injected 100-microgram of the antibodies 2 times a week for 4 weeks to each mouse. So we used quite high doses, but they were tolerable. The mice were injected intravenously with REC-1 mantle cell lymphoma cells before the treatment started, and we got 100% survival while treatment with NNV003 and 60% to 70% with the lilotomab, while all the mice in the untreated control group died because of cancer between 50 and 70 days after start of treatment. Human antibodies bind very well to most effector cells, and like Maureen talked about. And that is why we get an effect in this therapy experiment, while most antibodies do not bind to human effector cells. So in humans, or patients, we do not expect and also we haven't seen any therapeutic effect of lilotomab, while we expect to see an effect of NNV003. This higher therapeutic effect of NNV003 than of lilotomab might enable use of NNV003 for both pretreatment and pre-dosing. So we don't need to use rituximab like we do for Humalutin.

Next slide. With a radiolabel antibody, Humalutin, we use much lower doses of antibody, only around 4 microgram as compared with 800 microgram in the experiment with only naked antibodies on the previous slide. So here, we also have exactly the same mouse model as in the previous slide. it's actually a leukemia model since we inject cells intravenously. And we actually do not expect so good effect of Humalutin in this model because the range of the beta particles is too long for treatment of single cells in the blood. It's better suitable for larger tumors. You can see in the green curve that when we treated only 4 microgram or 0.167 milligram per Kilogram of NNV003, we still get some effect of the naked antibody, around 40% survival. So it's quite potent on its own in this model. The greater is the untreated control group. And you see that all the mouse dies within 70 days of the cell injection in this experiment also. The orange curve shows the effect of a nonbinding antibody and the red curve shows effect of nonbinding antibody labeled with lutetium. And as you see, there's no effect of these 2 treatments. They just follow the gray control curve. In the light and dark blue curves, you see the effect of treatment with Humalutin. There was a significantly increased survival compared with the control groups, but the effect was not significantly higher than the effect of NNV003. Okay. So we could have increased the dose as you might think, but we have used skid mice in this experiment, and those mice are inherently very sensitive to radiation. So therefore, we couldn't go higher than 100 megabecquerel per kilogram.

Next slide. So in this experiment, we have changed to another mouse type, new mice, that tolerates radiation much better, so we can go up to 500 megabecquerel per kilogram. In addition, we have changed our subcutaneous tumor model with tumors under the skin on the few flanks of each mouse to resemble a lymphoma tumor. Even though we have used the same cell line here, REC-1 cell line again and much higher doses of the NNV003 antibody. We get no effect of the naked antibody in this model, as you see in the 2 green curves, and also no effect of the nonbinding antibody of a radio label nonbinding antibody in this aggressive model. You see it's much more aggressive than we have it on the flanks, when we have tumor cells on the flanks than when we inject intravenously, or the mice dies because of cancer after around 30 days of the cell injection. The reason for no effect of the antibody this time is probably that it only binds to the outer surface of the tumor and do not reach the inner cells of the tumor, which then grow as they want. The better part, it goes from Humalutin, on the other hand, they reach the inner tumor cells. And here, you really can see the benefit of the cross-valuation that 1 beta particle can hit multiple tumor cells. So therefore, the effect of Humalutin is significantly higher than all other treatments in this aggressive tumor model.

Next slide. A way forward for radio immunotherapy can be in combination with other drugs. In this study, we have looked at the combination of Humalutin with olaparib. Humalutin results in DNA damage and Olaparib inhibits DNA damage repair. So this should potentially be a very good combination.

Next. So a beta particle from Humalutin induced a single-strand break in the DNA. And next, the cells will start to repair the break by recruiting a protein called PARP to the damaged side. But then, next, Olaparib will inhibit PARP, and we get that unrepaired bulb, double strand break, and the tumor cell dies.

Next. So that is the double strand break. So next, we tested the combination treatment in 7 different NHL cell lines and found the combination to be robustly synergistic in 4 of 7 cell lines.

Next. Conditionally, synergistic in 2 cell lines and antagonistic in 1. We have not been able to find out exactly why the combination was not synergistic in a DOHH-2 cell line, but this could, for instance, be related to different DNA repair pathways involved in this cell line.

Next slide. In preparation for clinical development, we have made a GMP-grade companion diagnostic for Humalutin. It is based on the NNV003 antibody label with the PET trace of the zirconium 89. That emits a positron instead of an electron, and can therefore be used for PET dosimetry instead of using Humalutin. The benefit with this is much better image quality, lower radioactive dose to the patients and shorter imaging protocols than when using Humalutin itself. So far, we have shown that imaging with 89 zirconium and imagery can accurately predict whole body distribution of Humalutin in mice by comparing data for the 2 molecules. We have developed a GMP procedure for manufacturing. And the molecules are ready to be used in the clinic to predict radio immunotherapy distribution in patients. With clinical 89 zirconium and NNV003 imaging, we can help identifying response to Humalutin, we can predict Humalutin mediated toxicity to help in healthy tissues, and we can optimize those regimens for Humalutin.

Next slide. So the key takeaways are that Humalutin has lower immunogenicity, which may allow for multiple dosing. We have developed a robust GMP manufacturing process and completed preclinical and CMC dossiers. A high therapeutic effect of NNV003 than of lilotomab may enable use of NNV003 as pretreatment. And we have shown therapeutic effect of Humalutin in different animals models and a synergistic effect when combined with the PARP inhibitor Olaparib. As zirconium 89 and NNV003 companion PET diagnostic has been developed for dosimetry studies in the clinic.

Next slide. So in the second part of the presentation, I will present the status of our pipeline candidate, Alpha37, for treatment of chronic lymphocytic leukemia and non-Hodgkin's lymphoma.

Next slide. Alpha37 also consists of the chimeric anti-CD37 antibody NNV003. But this time, we have conjugated it with the chelates TCMC, which chelates Alpha particle generating chelates lead-212 much better than DOTA. So this is a collaboration project with Orano Med. Lead-212 is an Alpha particle, generating radionuclide with a 10.6% hours half-life. An alpha particle consists of 2 neutrons and 2 protons and has a charge of plus 2. So it interacts very strongly with biological material, and therefore, you only need 1 to 2 alpha particles to kill a cell. An Alpha particle has a very short range of less than 100 micrometer. Alpha particles are therefore optimal for treatment of disseminated disease like CLL.

Next slide. NHL has already been covered by the other speakers, but I would like to go a little bit into the treatment and unmet medical need in CLL. So CLL is currently mainly treated with the Bruton's Tyrosine Kinase inhibitor ibrutinib, both in first line and second line of treatment, but anti-CD20 antibodies in combination with chemotherapy and with the BCL-2 inhibitor venetoclax are also used in first line. Venetoclax is also used along in second line. And anti-CD20 antibodies are also used in combination with venetoclax or in combination with the PI3 kinase inhibitor, idelalisib, in second line. So there are already many treatments available for CLL.

Next slide. However, there are still large unmet medical needs in CLL. In a new report by Decision Resource Group, treatment options against new targets and with new mechanisms of action for the high-risk patients with p53 mutations were highlighted as an unmet medical need. Alpha37 is a new treatment with a different target and a unique mechanism of action that currently have oral treatments. One unmet need is also discontinuation of ibrutinib therapy because of adverse events and intolerance. So a well-tolerated radioimmunotherapy can be an alternative treatment for these patients. Another unmet need is a lack of complete response, especially in old and frail patients, in the high-risk patients and in patients treated with chemotherapy. And as you know, CLL cells are very radiation-sensitive, so -- and they also have a very high CD37 expression. So radioimmunotherapy will potentially give higher complete responses. The kinase inhibitors are oral therapies, and they pose compliance issues because the patients have to take the tablets every day until disease progression. A single injection with radioimmunotherapy will secure compliance. And then we are finished with the treatment. So there are absolutely unmet medical needs in CLL that can be met by radioimmunotherapy.

Next slide. Market analysis shows that there is a significant opportunity in second line and third line setting of CLL, the total of around 27,000 patients. There are around 10,000 high-risk patients with p53 17p-mutation in second and third line. And there are around 11,000 patients in first and second line that discontinue ibrutinib therapy. The available treatment options in high-risk and ibrutinib refractory patients are not satisfactory. So the entry indication for Alpha37 should be in these 2 settings because here the unmet need is high and the regulatory pathway will probably be easier.

Next slide. Therefore, the preclinical development strategy was designed to evaluate effect of Alpha37 in ibrutinib resistant and ibrutinib sensitive mouse models. In an ibrutinib-resistant mouse model, mice were treated with daily high doses of ibrutinib. And you can see in the green curves, there was no effect of ibrutinib because the curves overlap with the gray curve, which is the untreated control. So this data confirms that the model was ibrutinib resistant. The lead-212 label cetuximab, it's not binding to the cells. And there was a small effect of this treatment, as you can see in the purple curve. The effect of Alpha37 was very high in this experiment, with 100% survival when we treated with 15 microcurie of Alpha37, as you can see in the yellow curve. The orange curve shows treatment with 20 microcurie Alpha37. And here, the treatment became a little toxic, so the maximum dose should be 15 microcurie for these mice. NNV003 did not have any effect in this experiment, as you can see in the blue curve, because we used TCMC conjugated antibody, and that destroyed the binding to the effector cells. The data indicate that Alpha37, our next -- the data indicate that Alpha37 has potential in ibrutinib resistant refractory third line CLL.

Next slide. Okay. So then we tested on ibrutinib sensitive model. We treated mice that had been intravenously injected with tumor cells, with increasing doses of alpha37, and with the nonbinding antibody, cetuximab, labeled with lead-212. This model is about 5x more sensitive to ibrutinib. Median survival was not reached for Alpha37 treatment. And after 27 weeks, the survival was from 70% to 90%. For the controlled treatment, the median survival was only around 7 to 8 weeks. You can see in the purple curve that there was no effect of the nonspecific cetuximab antibody, 212-lead in this experiment and no effect of the NNV003 TCMC conjugate either. The data indicate that Alpha37 can have -- next, the data indicate that Alpha37 can have potential in ibrutinib sensitive second-line CLL.

Next slide. So in the end of 2019, we started a project for Phase I trial and got Eurostars funding for it as well. The goal of the project was to finalize the package of work and documentation that is needed for starting a clinical trial. We are getting very close to reaching that target now and have only the last part of the finalization of the GMP methods for production of the antibody conjugate and Alpha37 itself and the documentation around this left to do.

Next slide. So the key takeaways are that Alpha37 is an alpha particle emitting anti-CD37 targeted therapy for CLL. It is superior to ibrutinib and effective in both ibrutinib resistant and sensitive mouse models. The preclinical data and the unmet medical need suggest to focus on high risk and/or ibrutinib resistant refractory CLL as the entry indication, because here, the unmet-need is high and the regulatory part may be shorter. There is a clear unmet medical need and market opportunity for Alpha37 above and beyond this entry indication. Yes. Thank you.

Presenter Speech

Erik Skullerud (Executives)

Thank you, Jostein. So in conclusion of today, first of all, a big thank you to the team for giving these updates. I hope you share our excitement over what we're trying to achieve with our wider CD37 platform. Again, we have seen examples of this in the past. We have seen other companies do similar things to what we are starting the journey that we are on.

And let me give you one other example. There was a company called 47, who did very similar things to what we are doing, but for a CD47 rather than CD37. This company got acquired by Gilead and is now a big part of Gilead's success. So I think, again, if you look at where we are, our attack points, our unique area of focus, it's a good starting point. Hopefully, we have also been able to give you a feeling for the different parts, the different angles that we have, these 5 different molecules that we can use to target the receptor in different ways, both some that have been in development for a while and others that are fresh off the bats that we have great faith in for the future. And the third part is, in the area of which diseases we can targets for patients, we have already done a lot of work in hematological disease. But we are also looking at how we can expand this to autoimmune

or immunological disease. And that is where molecules, such as our humanized antibody, will find its place, in the sense that these diseases will likely need iterative treatments over time. And as such, a humanized antibody will be a better fit potentially than a radio immune therapy.

So all in all, again, thank you for taking the time today. Thank you for joining us on a day that seems fairly lackluster in other ways, with the stock markets around the world going down significantly on the base of news that we saw this morning from Moderna. So obviously, we're interested in that part of how the world is working as well. But we hope that all of you are safe. We hope that all of you are enjoying what we've been able to share with you today. And we look forward to your questions. So I'll probably now -- let's open the channel for questions. What we'll do is I'll try to answer as many as I can, but I will obviously add on people in the team as we need over the next few questions. So if I may ask for the questions, please.

Answer

Frazer Hall (Attendees)

We'll get started with the Q&A session. [Operator Instructions]

So just to begin with, we have a number of questions around PARADIGME. But the first question is asking, why are you not publishing the preliminary complete response, partial response and medium duration of response data together with top line data for PARADIGME?

Answer

Erik Skullerud (Executives)

Yes. So thank you for that question. This is obviously an equation of what data do you have available when we have our preliminary results. And that will purely be on the primary end point. More analysis will need to be done for the secondary endpoints, and this will take time. Hence, we can only give updates on the preliminary end points when we initially give the results. We will not have the data in a detailed enough fashion to say anything about these other end points upfront. And again, feel free to look at how other companies are doing this. This will be exactly the same as any other company that is finishing their pivotal trials. Unfortunately, this has to take time.

Answer

Frazer Hall (Attendees)

The next question relates to screening numbers and is asking, since you've previously mentioned in presentations the number of patients in screening, can you give us a rough estimate on how many there are in screening at the present time, given your previous statements that the patient pool is one of the most promising that you've seen with regards to PARADIGME?

Answer

Erik Skullerud (Executives)

Yes. I don't think we have given any numbers as such. But we stand by our comments around that we see we see a good number of patients in screening. As I mentioned in my update on PARADIGME when we did our Q3 update, it takes about 3 months for us to get from the first time we see a patient until they are officially included. So again, as an example of what I just mentioned previously today, the patient that we are enrolling as we speak has been on our radar for quite a while, but it's only now that we are able to say that they're actually included. There are several other examples of this, but we have not nor will we talk about the exact numbers. And again, the example I used on the patient that actually did not enter this study is hopefully a good example. And I hope you understand why rather than going in and talking about all of these numbers in detail, we would probably not give you a very confident answer if we were to do so, because they fluctuate a lot. And some people go into the study, a lot of people also do not go into the study. And again, that is the nature of doing clinical research. Some patients will find their way into the study, others will not. But from a totality point of view, we do see a lot of patients in screening also as we speak.

Answer

Frazer Hall (Attendees)

Just moving on to a question around enrollment for PARADIGME. Given the current enrollment update that you've given for PARADIGME at this point in time, how confident are you in still meeting the time line with guidance for top line data in the first half of 2022?

Answer

Erik Skullerud (Executives)

So as mentioned in the update as well, we are 8 days post our Q3 update. We are still as confident as we were in our Q3 update. And with the additional patients, I think for those of you that are more into run rates. You also see that we continue on the same road as we have been in the last few months. And may I also remind you that the quarter that we have ahead of us, last year, we included 14 patients. I'm not saying that we're going to do that again, but it should also tell you that these numbers are fluctuating, and we may very well have such a number also coming up in this coming quarter.

Answer

Frazer Hall (Attendees)

And a further question on PARADIGME relates to the impact of COVID. And is asking specifically whether you can provide any color on the ongoing impact from COVID. And in particular, are you seeing missed follow-up appointments within PARADIGME? And is there any issue in terms of the enrolled patients becoming infected with COVID, which can impact outcomes from the study?

Answer

Erik Skullerud (Executives)

So my first comment, I will reiterate what I said in Q3 as well. So far, we have seen limited impact of COVID on patient numbers in the study, and we continue to see that similar picture. I think it's also fair to say that due to the emergence of the Omicron variant, I think many of us are still waiting or all of us are still waiting to see how this will pan out. But again, as mentioned in the Q3 report, we saw a similar picture of rising numbers last year in Q3 and into Q4 of COVID patients. We saw more patients included in late Q3 and into Q4 last year. And as such, we don't see necessarily that this would change this year. But again, I would put a caveat on that, that the new strain of the virus may affect it, but we don't know that yet nor have we seen it yet.

Answer

Frazer Hall (Attendees)

The next question relates to the confirmatory Phase III study following Archer-1, and asks, will this study be done by Nordic Nanovector alone, or were will be a financial or medical partner, and possibly, with the supply of rituximab for completion of that study?

Answer

Erik Skullerud (Executives)

A very good question. And there is obviously a lot of unknowns to the answer of that. #1, will there be a partner? As we get the results of PARADIGME and assuming that what we believe will be the case, we will have partners. If they will be part of the confirmatory Phase III, it's still too early to say. That will depend on the deal that we will be doing. On the second hand, with regards to rituximab itself, obviously, there are different providers of rituximab. You have a whole lot of biosimilar companies at the moment. So from a purely from a costing point of view, the cost of doing this study now probably will be less than what it would have been just a few years ago. But again, it's too early to comment exactly on what this is going to look like. It depends on the PARADIGME results. It depends on partnership deals. It depends on what those are going to look like, the structure of them, et cetera. So that's all we can say really at this stage.

Answer

Frazer Hall (Attendees)

The next question, again, relating to PARADIGME is, can you say something about what you think would be an acceptable overall response rate to target in order to meet the endpoint for the study and get an approval for Betalutin?

Answer

Erik Skullerud (Executives)

Short answer, no, we can't. And from competitive reasons, we wouldn't necessarily talk about that either. This is something that -- in looking at our clinical data, and eventually, our strategies, this is something that we would need to internalize, analyze, and therefore, optimize as we go to market eventually as well.

Answer

Frazer Hall (Attendees)

We'll move on to a couple of questions on Alpha37. And the first of those is that, at the previous R&D day, Jostein expressed the view that the data -- the early data around Alpha37 were some of the most promising data that he had seen. And the question is, is this statement still valid? Can you explain how the company intends to benefit from moving the program forward?

Answer

Erik Skullerud (Executives)

Well, I'll let Jostein talk in a little bit about if he still stands by his statement. I know he is extremely excited about Alpha37. And whenever we have a conversation, he keeps on reminding me about that. I think it's fair to say, this is a molecule that we have a very good partner on, and that should speak for itself with regards to the results of it. Secondly, this is an Alpha emitter, not a Beta emitter. And as such, it is differentiated from other products in our pipeline. But Jostein, with regards to how excited you are about the data, do you still feel that way?

Answer

Jostein Dahle (Executives)

Yes. I think it's the best data I have seen. So the data hasn't changed. So it's extremely good data.

Answer

Frazer Hall (Attendees)

Great.

Answer

Erik Skullerud (Executives)

Thank you, Jostein.

Answer

Frazer Hall (Attendees)

And just as a follow-up question on Alpha37. Can you give any guidance on the time line for being ready for IND approval and the start of clinical studies with Alpha37?

Answer

Erik Skullerud (Executives)

So I think Jostein alluded to this. We are really nearing the end point of the data package that we would need. Our estimation, and we are in close dialogue with our partner, Orano Med, on this. We had a big meeting as late as this last week, is that we believe that we'll be able to do this in the first half of 2022. It may even be earlier. But in this sense, it's a little bit too early to say. As you did see in Jostein's slides, we do have a few more steps to complete, but we're making extremely good progress as we speak.

Answer

Frazer Hall (Attendees)

And moving on to the CAR-T CD37 program. Can you describe in any more detail at what stage you're at with regards to the collaboration with U Penn? Are there any in vitro and in vivo studies that you can discuss at this point in time? And when might we expect to hear some of the first results from these studies? And just following up on that, is there any time line for how this program is likely to progress and going forward into clinical development? Can you put any time line on that at this early stage?

Answer

Erik Skullerud (Executives)

So with regards to the collaboration itself, the expectation is that we'll be able to give some indication on where we're going in the next 12 to 18 months. What that exactly will look like is more -- we will assume that we will kind of show what is the molecule, what does it look like? We may even be able to give some early stage results. I believe Maureen said in her presentation that when we get to the R&D day 2022, we will likely have an update for you. More specific than that, can I not be at the moment. We did publicize the deal, was it? 2.5, 3 weeks ago now. So we're -- it's obviously very early days. But we're -- were suggesting that at least in the next 12 to 18 months, you will see something around the -- around what this is giving as results. Was there a part of the question I didn't answer, Frazer?

Answer

Frazer Hall (Attendees)

No. I think that's fine. Thank you, Erik. There are a few questions around your ongoing discussions with partners. And essentially, these questions really ask, can you give any further updates at this point in time to any of your ongoing discussions with these partners?

Answer

Erik Skullerud (Executives)

So I would say we -- like I said in the Q3 call as well, we have several conversations ongoing. And I reiterate what we said back then as well. We can't talk about which companies we're talking to, what kind of companies we're talking to. But for obvious reasons, we're hoping for different types of deal, and I said that in my introduction, different types of development deals, depending on the molecule in question and depending on geographic area in question for Betalutin or for other parts of our portfolio.

Answer

Frazer Hall (Attendees)

There's one further specific question, just regarding the announced retirement of Marco, just asking, do you have in mind who his successor will be at this stage?

Answer

Erik Skullerud (Executives)

I have in mind, but that's where it will stay for now.

Answer

Frazer Hall (Attendees)

That completes most of the questions that we have online at this stage. There is one further question that is directed at Dr. Gordon, which he may wish to answer in his absence, which is asking, which patients would you use Betalutin assuming the data holds up from the Phase IIb readout from PARADIGME?

Answer

Erik Skullerud (Executives)

Well, it should probably be directed at Dr. Gordon. What I will say this, and I said it in my introduction for why I joined the company as well. I have very seldom seen a company that has been as prepared when it comes to how we have characterized the patient where the unmet medical need is, and how we therefore are able to target this unmet medical need. It's very, very seldom that you can see that in a company that are in Phase IIb. That usually comes much later. So I believe the organization way before my time have done an incredible job in outlining exactly that. And I also do believe that, that is where patients should benefit the most for it. So that's where I would hope that most physicians would prescribe it. But I don't want to put words in Dr. Gordon's mouth. It is probably something one would follow up with him directly on.

Answer

Frazer Hall (Attendees)

And then just a general question, which asks, could you give any outline as to the anticipated news flow that we might expect over the coming year other than for PARADIGME?

Answer

Erik Skullerud (Executives)

Yes. I would look at this space. We -- I hope -- let me take a step back. I've spoken to several of you, several investors via e-mail, in Norwegian and in English, I've spoken to some of our biggest investors around what are they expecting from us. And one of the things that they have told me over and over again is be more transparent, give us updates when you can. And as an example, I believe today is the first time that we have ever gone out with an update on PARADIGME outside of the quarterly updates. This is our intention moving forward. That's not to say that we're going to give updates every single week on what's happening with PARADIGME or anything else for that matter. But we will try to the best of our ability to communicate more with you, our investors, and to give updates continuously. But I'm not going to promise that we're going to give updates on PARADIGME inclusion every day or every week or every month for that matter. I believe that -- and again, I hope I've been able to make that point, inclusion for PARADIGME is going up and down almost on a weekly basis. So to try and do this more often than the quarterly updates, I believe, would be foolish of us.

Secondly, with regards to other news items and what you should expect from us is we want to keep an open communication with markets. We want to ensure that you get the updates when we have the updates. At what exactly will come when, I will not be able to say now. I'm still 2 months in the job. And I know that people around me are working very hard on creating results as much as they can. But you have my commitment, that we're going to do the best that we can to communicate as much as we can, we do.

Answer

Frazer Hall (Attendees)

We're really reaching the last set of questions now, Erik, which really center around the competitive landscape, and are asking, first of all, can you give a broad overview in terms of an updates around the competitive landscape? And then there are a couple of specific questions which relate to how you view the indicated risk benefit profile of bispecifics, such as the CD3, CD20 at bispecifics, and relate to some other more recent data from competitor programs, and in particular, a PI3 kinase called Zandelisib from MEI Pharma, where evidently some data has been released earlier today. But broadly speaking, could you give an update on the competitive environment? And are there any specific comments around the bispecifics?

Answer

Erik Skullerud (Executives)

Yes. So again, thanks for that question. With regards to the competitive environment, we mentioned this again in Q3, in our Q3 updates. And what we see both in the last few weeks' worth of data, the last year worth of data, and what is expected over the next year worth of data is that the positioning that we have chosen initially for Betalutin in the space of follicular lymphoma, it is still an area of significant unmet need. What have we seen get into this area already? We have seen CAR-T products. But as Dr. Gordon said, he would, and our impression is also that his colleagues, other prescribers will mainly use this in younger patients. There are still significant toxicity around these regimens. And although progress is being made in how this is managed, I think he gave a clear indication that this was only for a smaller group of patients. The other part of the CAR-T treatments in general is that they are extremely expensive, about $0.5 million per injection. And as such, this is a significant burden for payers to play -- for payers to pay. And as such, again, it will remain an area of high selection when it comes to who's going to receive these kind of products.

From a PI3K point of view, I think, again, Dr. Gordon, and I believe he presented the vast majority of data that exists in that space. On one hand, far from the same type of efficacy as what you have seen with CAR-T, but on top of that, a significant toxicity as well. That seems to be the case also in the -- some of the -- at least of the later PI3K inhibitors. I'm going to ask Marco in a second to talk about the data that has come out today on MEI. I haven't been able to read through that myself, to be honest. But I think, again, it kind of confirms what we have seen with other PI3K inhibitors as well. And the last group of -- or there's 2 more group of products that Dr. Gordon was touching upon as well. One is EZ2H inhibitors. Here, you obviously have a highly selected group of patients that can utilize the drug in the sense that you have -- you only have significant response rates in patients that have the mutation in the gene, to begin with, and that's about 15% of patients. And finally, with the bispecific antibodies, again, I think he was also pointing towards the risk benefit in the sense of, yes, good response. But on the other hand, and I believe Pierre also talked about this, significant toxicity associated with them. So as such, I know it's a long answer, but hopefully, if you look at all of these potential competitors, I think we're very well positioned. And I would add to that as a final point, personally, I don't see CAR-Ts as a direct competitor, nor do I see bispecific antibodies as a direct competitor. And that basically leaves us with the PI3K inhibitors as a competitor. Again, I believe Dr. Gordon confirmed this.

With regards to the latest one, maybe I'll ask you, Marco, to talk a little bit of what you have seen in that data.

Answer

Marco Renoldi (Executives)

Yes. Thank you, Erik. I think we've seen the data provided by May Pharma earlier this morning about their Phase II TIDAL trial. And I think the results were not unexpected. The data, the efficacy data are aligned to the upper end of the efficacy range we have seen with the PI3K inhibitors in the past, and actually not very different from the dapples-to-apples that we have generated with Betalutin in our LYMRIT 37-01. So an overall response rate in the 70% range, if I recall correctly, the press release, and a complete response rate in the 35% range. I think the median duration of response was not reached, so not provided by the company. But I think what is important to remind is the side effect profile this agent is still associated. So 10% of the patients in the trial were discontinued due to side effects. And we saw Grade 3 and Grade 4 adverse events, which are very typical of the class. So we don't see any really different feature in terms of the safety profile of Zandelisib. We -- I read about those events that led to discontinuation in the GI tract, so diarrhea and colitis. I read about pneumonitis. I read about [indiscernible]. So a safety profile which is very much reliant on the safety profile of the PI3K inhibitor class. It's a good class. It's a class of agent that are effective. But is this the right drug for the patients we're trying to serve? We don't think so. We don't think so. Umbralisib came to the market with a similar promise. But it was associated exactly to the same type of adverse events, the prior PI3K inhibitors were associated. And the market uptake to date seems to confirm that physicians understand that and patients as well.

Answer

Erik Skullerud (Executives)

Thank you, Marco.

Answer

Frazer Hall (Attendees)

Thank you, Marco. Thank you, Erik. That concludes the questions that we have that have been submitted online. So I'll hand back to you for any concluding remarks, Erik.

Answer

Erik Skullerud (Executives)

Yes. Just a big thank you partly to the team here internally for their development of material, their presentations today, and the dialogue with all of you that we've had today. Secondly, to all of you out there that have dialed in to listen to our presentations, our discussions. We hope this was what you were looking for. As mentioned, to begin with, we're looking for a transparent communication with all of you. We're looking to give you updates as often as we can. We're looking forward to a new R&D Day in 2022 to give updates on the different projects that we have outlined today. And thank you very much for your support as investors, and looking forward to the onward journey. Thank you so much.

21.11.18. Nordic Nanovector ASA, Q3 2021 Earnings Call, Nov 18, 2021

Presenter Speech

Erik Skullerud (Executives)

[Audio Gap]

So I started my career in Bayer, worked mainly in Scandinavia but was situated in Sweden back then. Seven years later, I moved to Amgen, moved also to Switzerland and spent about 16, almost 17 years with that company in different positions around the world. I've done everything from strategic marketing roles, worked in different therapeutic areas, oncology, in bone disease, nephrology, in cardiovascular. But I've also been in different countries in management roles. As an example, Australia. I've been in the Netherlands, I've been in Greece. So I've become a little bit of a global nomad as far as my personal life is concerned. I have a wife and 2 kids. They are born outside the country. So as much as it pleases me every time I get to go back to Norway, I also have a life outside due to an international family. So in that sense, great to come back and be part of a Norwegian company. And also want to talk a little bit on why I've joined Nordic Nanovector. First of all, I think we could all agree that this is exciting time for radiopharmaceuticals. We've all seen late results coming out from other companies that are extremely encouraging, both from survival and from results we see the emergence of an increasing amount of radiopharmaceutical companies around the world, in the U.S., in Europe, in Asia, in China, et cetera. There's a lot of interest of the area.

Personally, I've been involved with Nordic Nanovector since 2016 in a consulting fashion. As I mentioned, I started my own consultancy company in Switzerland and worked with small- to medium-sized biotech companies, Nordic Nanovector being one of them.

So the first job that I did was I participated and worked with the management team back then in what ended out as the target product profile. And already then, I could say that here you have a very interesting asset. And very seldom have I seen a company that's so early in the whole development of the product, actually set out to truly understand the patient, to target a specific part of the patient segment and couple that with the unmet medical need. And that's the other reason for joining Nordic Nanovector. I feel that this is a very well-prepared company when it comes to what eventually will become the commercialization effort. There's an asset at the center of this that has shown very encouraging results, whether it is on response rate. At this stage, public data is suggesting around 70%, complete response around 32%. And it's very seldom that you see this in oncology products.

So in that sense, very, very much looking forward to working with these assets and working with the team and bringing this to the market. But there's more behind the company and more as a rationale for me to join as well. I personally feel that with the focus and the rightful focus on PARADIGME, a lot of the other parts of the pipeline have gotten very little attention, and there's a lot of other gems in that pipeline as well. So another reason for joining the company. And finally, the more you're outside Norway, the more you get to appreciate the great country this is. So when a company out of Norway comes and tap you on the back and say, hey, would you want to join us, would you want to take up a leadership role, number one, it's humbling and you really appreciate it, but number two, I'm really proud. So I'm invested with my mind, I'm invested with my heart.

A little bit of what we'll be talking about today and what the highlights have been in the last quarter. We're today reporting 102 patients that are involved in the -- or enrolled in the PARADIGME study. You will know that we're targeting 120 patients. Last quarter, we reported 94 patients. So we have added another 8. In that sense, you may also say, well how does that compare to what we're expecting. And I want to go into that a little bit later in my presentation.

Apart from myself, we have also appointed a new CMO, Pierre Dodion, who comes with an incredible record. And I'm really looking forward to working with such a distinguished medic. He has 30 years of experience in the pharma/biotech industry and is exactly the type of profile the company needs with the partnership around commercialization moving forward.

We have also, in the last couple of weeks reported -- sorry, I have 2 important announcements. The first one is with regards to the Health partnership. This partnership is one step further when it comes to our own commercialization. A lot of you that follow pharma will always look at how well does a company launch. Very often, what gets missed out is the lack of an understanding of the competitive environment, number one, but these days, even more importantly, a lack of the barriers to entry from a governmental and a payer point of view.

This specific initiative is targeting a better understanding and a better enablement of radiopharmaceuticals and uptake of radiopharmaceuticals. I would urge all of you to have a look at this in the sense that this is not just us that is doing this, this is an effort across companies. We're working with some of the biggest in the industry around getting this right. And we believe that this is going to be a key success factor for our commercialization on its own.

And finally, we're very excited to also announce a collaboration with the University of Pennsylvania around the CAR-T technology. Most of you, for sure, will understand the CAR-T technology in general. But this is obviously, if you want, the next frontier when it comes to oncology treatments. It is using the body's own immune T cells in a response to the disease itself. And we're, as far as I know, the first that are starting a development around the combination of our proprietary CD37 technology in collaboration with the University of Pennsylvania. We'll speak a little bit more about this as well a little bit later.

But let's talk a bit about our new CMO, Pierre Dodion. When it comes to commercialization, you want to build a team that is focused on a thorough understanding of the industry, the key success factors and have experience in having done this in the past. Pierre joins us, as I mentioned, with about 30 years of experience. He has experience from small biotech companies, such as Innate and Ariad. He has experience from big pharma, such as Roche and [Aventis.] This combination for us speaks to, number one, a great understanding many years in the industry. He's also adding a lot of clinical development experience, but more importantly, translating that into what eventually becomes medical affairs and the whole scientific communication part, a key success factor in how you commercialize pharmaceuticals in the first place. He joins us from Alacrita Consulting. And he has already worked with us since April 2021. You will hear much more about the work that he has contributed at the upcoming R&D Day. And so for example, Pierre has worked with us on what will eventually will become the confirmatory Phase III study that we will be doing as part of filing our BLA for FL in third line.

The second line, by the way, or the additional indication that we hope to get with the confirmatory story -- study, by the way, is in second-line FL. Again, we'll talk more about that later.

He has started his onboarding already and will take over Christine Wilkinson's responsibilities fully as of January 2022. And it's great to already have him on board as this will ensure a transition of responsibilities that will be optimal for us.

So let's talk about PARADIGME and use a little bit more detail around the numbers because I know a lot of you are looking at the numbers and setting your expectations that way. As you know, in 2020, we did significant changes to the protocol. And you also saw throughout 2021 that we have increased enrollment rates. Also this time around, if you look at numbers in general, what we reported last year was 3 patients, 3 patients in Q3. This year, we're reporting 8 patients in Q3. We'll get back to that in a second. But on top of that, you have also seen that we have started implementing several initiatives in order to accelerate it even further.

Right now, we're focusing on 4 different things. Number one, we have done a continued and will continue to do a segmentation of the different centers that are participating in the study. And there's basically 3 segments that you can look at. One, are the ones that have enrolled, are enrolling and will, therefore, be enrolling. And that's our primary focus. Then you have another at the other end. You have several centers that since the beginning, for whatever reason, have not contributed, have not shown much interest in screening or in contributing, and these are centers that we're closing down. And the third are centers that now post corona is we're also seeing an increase in the number of patients that are in screening. They're making increased efforts in participating in the study. So these are also focus centers for us.

Secondly, coming out of corona this summer, we have asked all of our customer-facing, for a lack of a better word, personnel whether it is Nordic Nanovector or in our clinical research organization to really focus in on face-to-face and direct communication. Our belief is that in this sense, we're actually fairly early on. We know that a lot of other companies bigger and smaller are still working on technology-based communication. And what we hear from the people that we're working with in the field study nurses and study investigators is that they truly appreciate this face-to-face contact again. And while all of us have been focusing on the numbers of patients from a COVID point of view and the disarray that has created, the flip side of that in the health institutions that we are working with is that we have new study nurses, we have new study investigators. So the additional face-to-face and a refocus on retraining the centers, reengaging with them, gives us a double whammy, if you want.

The third is around how we speak to these centers and really also doing that in a segmented fashion. What are we saying to those that are doing a really good job for us, what are we saying to those that need further encouragement and what are we saying to those that are, for whatever reason, not willing to participate anymore. But still, we need to have a good relationship with. And finally, the fourth dimension in all of this, and Marco Renoldi mentioned this in our last quarterly update as well, we're rolling out a digital aspect of this strategy as well, both because during COVID, it's been hard to keep people aware and up-to-date and therefore, engaged in the study, and we're using the digital terms for that. But the other is also creating additional awareness around potential patients. On one hand, this means that we get more patients into screening, and that's the good news, if you want. And we see that. We also today, as Renoldi said last time, have more people in screening than what we've ever had in the study. The flip side of that is it takes longer from when you get the patient involved in the first place until they're actually enrolled. The average time that we're looking at today is above 3 months from the beginning of that process until they're actually enrolled in the study. While when we did this, without the digital side, it would have gone faster, and it would have taken approximately 2 months on average for a patient to get enrolled. That's just to give you a little bit of a feeling for -- we see good news in this, but we also see some challenges that we have to continue managing.

From a numbers point of view, and this is probably the one thing that most of you will be looking for. So I said 102 patients, 8 new patients, we did 3 patients last year. So we see an increase. There is seasonality in this, so for those of you that are expecting 14 next month or next quarter, I would say, yes, we're expecting it to be higher than what we see in this quarter, but we don't necessarily to be that they're going to be as high. That being said, if you look at what we have guided on, and we continue to keep our guidance on end of the first half of 2022, we also have to take into consideration that we need 3 months of follow-up before we will have the first possibility to say we did or we did not meet the primary endpoint. And that is what we're looking for as a first result, right?

So if you use that as an example, that will put us into, and let's assume that at the end of H1 2022, you would have the numbers. That means that the last patient has to be included by the end of March 2022. On that basis, we are now middle of November. We have 4.5 months left of inclusion before we have to deliver and be done with the study enrollment. That means that we need approximately 4 patients per month in order to do that.

If you then triangulate this, but what have we done in the last year? In the last year, at this time, we reported we had 59 patients in the study. Today, we're reporting 102. We have increased by 43. 43 over 4 quarters is about 3.8 to 3.9 on a monthly basis. Or if you want, it's about 11 patients per quarter, 3.8, 3.9 per month. In other words, where we are now is where we need to be, but we're adding a bit of a stretch on top of that, obviously. But still, we are where we need to be. And if we continue at the rate where we are today, plus a little bit of a stretch, we will be where we need to be at the end of March 2022, and therefore, be able to deliver the results by the end of H1 2022. That is why we are confident with regards to the numbers.

The final part in that equation is what can we expect from corona? Because obviously, you have seen that has had an impact in the past. It will continue to have an impact. But again, if you look at last year as the predictor of what this year could look like, you see similar numbers around Europe and around the world from new cases point of view, that should not be a surprise to any of us. That being said, we would also expect a similar impact on the health care systems as we had last year. From a macro point of view, we would expect a similar impact in general. That's the third reason for why we feel confident about the numbers that we are reporting today and our prediction for still being able to give the results at the end of H1 2022.

So post having delivered on that, what is it that we now need to continue to focus on? Our first priority is obviously the PARADIGME enrollment and needs to continue to be PARADIGME enrollment. But over and beyond that, we have to ensure that we also, from a business development point of view, execute on our business development strategy. We've had a lot of questions in the last few quarters, what's the status of your business development strategy? And we have, we are and we will continue to talk to partners. I had a question a few weeks ago, okay, so how many are you speaking to now versus how many you have spoken to over the last year or so? It's hard for me to say because I don't know the history that well. But from what I've seen, it's a constant drip of new interest. For those of you that have followed pharma and biotech over the last few years, you will also know that when it comes to the kind of potential partnerships we're looking for, at least big pharma has a tendency of waiting until they see the results. And increasingly, they are doing so because they have the money to wait for it.

So if you look at it from our point of view, this is the time when we really need to have to start to gear up with the conversations in order for us to have the optimal partnership when we eventually need it. What is that partnership going to look like? It will differ, it will differ depending on the region. I think nobody would expect us to go into China or Southeast Asia. So there, you would look at some kind of a licensing partnership potentially. In the U.S., do we need a partner? Well, if you look at the data and if you look at what have others done and done successfully, a partnership is definitely not out of the question. And if you then look at Europe, finally, there are hybrid solutions. So what are we looking at? We're looking at everything. We're looking at all of the different options, and we'll be opportunistic. But obviously, our responsibility is to you as shareholders, we're looking for the best possible partnership solution and the best possible commercialization solution for Betalutin.

And in the event of positive results, we are already talking to the FDA. The next time we'll be speaking to them is in Q1 2022 about both filing strategies and what comes beyond. So we're also preparing for that side of things. These interactions and due to the accelerated approval and the Fast Track designation, we have a possibility of being much more in contact with the FDA. That is the benefit that you get from this designation. And over and beyond that, we will also utilize the rolling submission for approval, which means that we don't have to give the whole file at the same time, we can also drip feed that as we go through. So also from a regulatory point of view, we're making all the preparations in order to be able to file and to get the approval as quickly as possible.

Why are we doing this? And to just reiterate what you will have heard before, this is an area of significant unmet medical need. And especially when you go to the later stages, when you get [second line and] third line, these patients become increasingly elderly. They get increasingly frail, they have increasing comorbidities. So the patient at the stage where we will be launching and where we will be competing are already in a fairly frail [fashion.]

What do these people actually ask for? What do these patients need? They need a treatment that over and beyond everything else is mild from a safety point of view, that is convenient from an administration point of view, but still gives efficacy that they need and expect. And that is where we feel [that it is specifically situated.] Just to remind you, in this population, about 70% in third line exhibits what I have just said. They're elderly, they're frail and they have comorbidities. In second line FL, about 50% are elderly, frail and are exhibiting these characteristics. So we feel that we have found the right spot for Betalutin. And this is why our focus in NHL. We continue to believe that this is the right focus.

So from a competitive point of view, if you look at what has actually happened over the last couple of years, and you look at this picture from left to right at the horizontal side and you look at age and frailty of the patients, you look from bottom to top on the horizontal line, and you can see the first line, second line and third line treatments. And although the competition is heating up in the first and the second line space, when you get into third line, you see up in the right-hand corner, a fairly open space. And this is obviously where we intend to put Betalutin as a starting point. This is still an area, even when you look at new competition, an area of high unmet medical need. It's an area where, yes, you have had a couple of new launches either through CAR-T or EZH2 inhibitors or there are a couple of PI3K inhibitors as well entering this field. So there are new competitors coming in.

But what do these have in common? Number one, for example, the CAR-T treatments are only really available for a few very fit patients because of the potential side effect profile. So although the efficacy profile for CAR-T is definitely impressive, the safety profile means that only a few of these patients can actually take the treatment. They're not really a competitor for us. The same thing holds true for also the EZH2 inhibitors. Only 15% of these patients has the genotype that actually is needed for them to respond to the treatment in the first place. In other words, again, only a few of the patients in this field can actually get the treatment. And the same for all of them, the safety profile, what I was mentioning for these patients safety is really important. They don't have necessarily the safety profile that is expected. They're all associated with quite a lot of toxicity.

And then when we speak to our customers, we're also getting extremely positive feedback on the way we intend to position Betalutin, whether it is, when they look at the efficacy profile, from 37-01, where both the duration of response, the overall response rate and the complete response rate is definitely something that they are appreciating, something that they feel as extremely compelling and that they see significant advantages of. And

that combined both with the onetime administration and you're done and the favorable safety profile means that they are also appreciating the profile we're putting out Betalutin with into the marketplace eventually.

And finally, if you look at payers and they obviously have an increasing importance, anyone that is following this space will appreciate that if you don't get the payers on site, you don't really have anything to work with. So here, you see that they are talking about this as a moderate to important improvement. What does that mean? On average, we score this from 1 to 5. They're scoring Betalutin around 3.7. And that, if you look at other products in the oncology field is significant. It is very, very, very seldom that you get above 3.5 unless you have something really impressive to talk about.

Finally, 2 slides on new initiatives, one around the HPP initiative. I spoke about that at some length in my introduction. But again, this is for us a further step in truly understanding the competitive field and the market that we eventually will enter. It's about talking about barriers to entry. It's about working with other fellow industry colleagues in building down these barriers and ensuring that we get the success that Betalutin deserves. So far, 2 big pieces of work has happened, one with regard to the U.S. environment, our primary focus for launch, the other one with the U.K. Further countries are underway. And by the time we launch, we expect that most of the Western world, if you want, most of our focused markets will have been mapped and therefore this toolkit will be available for us also to utilize when we launch.

The other one is related to, as I mentioned, the CAR-T collaboration with University of Pennsylvania. You will have heard of CD20 CAR-T therapies that are already in the market, and you have also heard about the discussions and the excitement from the scientific community around CD20 CAR-Ts. You have also heard about question marks around the safety of these products. And although the scientific community is working on and getting better at utilizing and therefore managing with these products, it is also pretty clear to say that there is still significant room for improvement. And by partnering with arguably the most renowned entity in the world on CAR-T technology, these were the guys that innovated the CAR-T technology to begin with. We feel that we have the optimal relationship in taking our proprietary CD37 technology into science and therefore developing a really interesting asset down the line.

We do have the first right of refusal with regards to buying this back and to commercializing it worldwide. So we're extremely excited about the science here, we're extremely excited about the potential asset and the potential outcome, and we're looking forward to this collaboration tremendously.

So I think with that, I will let Malene take over and talk about the numbers. Malene?

Presenter Speech

Malene Brondberg (Executives)

Thank you very much. I hope you can see me I might step out of this, I'm not that tall as you know. So good morning from me as well. I will very quickly run you through the financials for this quarter.

So if you look at this slide, you can see that we had a cost of 104 in the which is a little bit more than last year. And that is, as you probably remember what I've said previously is that we are -- now because we're finalizing or coming to an end with the enrollment, we're stepping up on both CMC, but also on the clinical activities. And this is what you see here. This is the driver basically. And on the cash position, as you can see, we had in the end of September, NOK 370 million in the bank. And of course, we continue to monitor the -- both our spending and -- how we spend the money, of course, is very important. As I said previously as well, we spent the money where we should spend the money, so on the CMC and of course, on the clinical. And we continue to constantly review our budgets, constantly review the spending and, of course, also budget for next year.

And I think with that, Erik, I would actually hand it back to you. That was very quick, wasn't I?

Presenter Speech

Erik Skullerud (Executives)

Thank you, Malene. So in summary, I wanted to make 2 points. One is first around our continued efforts on creating value and creating value for U.S. shareholders. Number one, we have to meet the enrollment in the enrollment targets for PARADIGME. And as you've heard, we feel confident that we are continuing to do so, and we'll deliver the results towards the end of H1 2022. Secondly, we also feel that we have a highly attractive

product, and we do not see that the market conditions as such have changed significantly towards how we will succeed in the NHL setting with Betalutin. As I mentioned, we're obviously looking towards finalizing PARADIGME. And then we are working very hard on the other work streams that will enable a quick submission and a successful submission to the FDA. And again, we are in continuous communication with the FDA in order to ensure that we do this optimally, we do this in the right way, and we get the approval as quickly as we possibly can.

And finally, I will draw your attention to what we are about to do about 12 days from now on the 30th, we'll talk more about the wider pipeline. We'll give you an update on all the different projects that we are working on over and above PARADIGME, but we thought that today was the focus needed to be on PARADIGME, the focus needed to be on our operational efforts around being successful with the enrollment, and we'll be very happy to talk more about our pipeline and our further efforts on the upcoming R&D Day.

And just as a teaser, this is what we will be talking about on that day. We'll give you an update on our strategy. We are joined by an opinion leader, very distinguished professor from Northwestern University in Chicago, who will be talking about follicular lymphoma and how that is treated, the unmet need and what this looks like in the U.S., our first market of entry. So we'll get the perspective from him. And then we'll get an update around what happens beyond the PARADIGME with Betalutin. Betalutin is about to become a pipeline on its -- excuse me, on its own. And over and above that, the other exciting assets that we have in our pipeline. What's our plans for those? What are we looking for with those? What's the latest data that we have on those, and we're really looking forward to welcoming you back and hopefully also then face-to-face that we can give you an update accordingly. The only caveat is, as always, we're still in COVID, and we will obviously follow the COVID restrictions at the time of when this is happening. But we truly hope that it can be another face-to-face event. Obviously, if not, we will do this as an online event as well.

So I think with that, just leaving the slide of what's going to happen next, which is the R&D Day. That concludes our presentation, and we're ready to take your questions. And maybe we start with the ones in the room here first. So I'll invite Malene and Marco to come up and join me for that session. Thank you very much.

Answer

Malene Brondberg (Executives)

We have a mic here, so if anyone's got a question here in the audience, please go ahead.

Question

Unknown Analyst (Analysts)

You were talking about seasonal variations. Could you elaborate a little more on that?

Answer

Erik Skullerud (Executives)

Yes. I -- so what I was mentioning was with regards to last year, we obviously reported 3 patients enrolled in the same quarter, as this year, we have looked at 8. Now if you look at how patients have come in to PARADIGME over the last few years in that sense, we usually have a third quarter that is fairly slow. We have from -- if you want, from November, December, January and February, have a tendency of being fairly high when it comes to inclusion numbers. Then when you go through into the spring and especially into the summertime, there's less patients coming in. Maybe it's wrong to talk seasonal variability because we're talking about human beings and patients there, but I hope you see -- I hope I see what you mean. Does that answer your question? Any other questions from the room here? Okay. Should we open from questions from online then?

Answer

Frazer Hall (Attendees)

Thank you, Erik. [Operator Instructions] But we'll start with the first question. There are a number of questions around ongoing recruitment. But essentially, we can group these into a question around whether or not you believe there are any specific factors that have delayed recruitments in this quarter over and above what you've

already described. And having said that, we had a very strong screening pipeline in the recent past, could you comment on the current status of the screening pipeline at the moment, please.

Answer

Erik Skullerud (Executives)

So hopefully, we will have answered several of the aspects of this question. I think over and above what are we looking at as potential derailers in the enrollment? It goes without saying that if we're going back into severe corona with a lot of people in hospitals that is going to take resources away from potential also cancer care. But at the same time, with more and more people actually being vaccinated, you wouldn't necessarily expect this to be extreme. But that would probably be the one that could get even worse. I don't think it will, but that's probably the one thing I would look at when it comes to over and above what we have already talked about. I believe we touched upon that as well, and I hope that we iterated with the example given around the numbers that we're actually in a really good place at the moment with regards to inclusion.

Answer

Frazer Hall (Attendees)

Thank you, Erik. The next question regards the procedure from completion of recruitment to readout of the 3-month top line data, could you describe that process in a little more detail, please?

Answer

Erik Skullerud (Executives)

Yes. So first and foremost, keep in mind, it's not something we start when the last patient has been included. This is an ongoing process. And usually, what happens is a patient gets included, gets their treatment, three months later, you do a scan and you look at what has happened with the patient. That is the normal way this would work. Hence, the 3 month follow-up data. When you get that scan, you will then need to look at, okay, somebody needs to look at it, analyze it, make the conclusion, and put that as part of the study results. It goes without saying as this is a continuous process, patients that were in 3 months ago that have had their 3-month scan today, they will be looked at, and it takes a few days for that to happen. But as this goes on, and let put ourselves into towards the end of the study, if we continue to do those 4 patients per month, the 4 patients that we get in, in March will then need to be looked at, analyzed and drawn conclusion of in June. Not all 4 of them are coming on the last day of the month. So this will be a continuous process. Hence, the disruption that you will have from when you have the last patient in the study and done the analysis of, it will be a very short time from when that actual scan is done until the final result is ready, which is then for the last patient out as well, from a pure scan point of view. We obviously continue to follow these patients up, but this is the 3 months that we're talking about.

I know that there has been some confusion with regards to before, how long is this process actually going to take, and maybe from the guidance that has been given from my predecessors they have been somewhat conservative in that sense and said, yes, maybe it's going to take 2 weeks, maybe it's going to be 4 weeks due to the nature of how this is happening, from a monitoring point of view, from an analysis point of view and from a review of the scans point of view, this should not take very long. I hope that answers the question.

Answer

Frazer Hall (Attendees)

Thank you, Erik. The next question is around what if any continuing interactions you've had with FDA, can you elaborate at all on those interactions? And practically, what do they mean in terms of the filing strategy for Betalutin.

Answer

Erik Skullerud (Executives)

So I think I can talk a little bit, and maybe I'll ask Marco to follow on, on that. In the last quarter, we haven't had any direct interactions with the FDA. The latest interactions that we have had is in preparation for when we

submit the BLA. And on the basis of that, the confirmatory Phase III study, we will have to do, what is that going to look like, and how do we best take that forward. Marco, do you want to...

Answer

Marco Renoldi (Executives)

No, I think you covered it well. It's an iterative process. And we have multiple opportunities to interact with the agency, whether through formal meetings or through correspondence when we have a question that we request their advice on. I think we have a very clear idea of what we need to include in our BLA filing as we discussed extensively with them. We will have another opportunity to discuss with them the Phase III study pretty soon, as Erik outlined. But I think it's an iterative process. So it's an ongoing process. And thanks to the Fast Track, we have a fairly easy access to the agency.

Answer

Frazer Hall (Attendees)

Thank you. The next question is on Bayer's copanlisib and essentially, the question is, if Bayer managed to get approval for copanlisib would that affect your ability to file for accelerated approval? And what do you think copanlisib does in terms of any changes to your competitive position?

Answer

Erik Skullerud (Executives)

So thank you for the question. I think it's fair to say that we are looking at the same information that you as investors are looking at. As you will know, there is communication online from the FDA with regard to their guidance to Bayer. What they have said to Bayer is you have to do CHRONOS-4 in order to get a full approval for third line FL. That's the first thing to keep in mind. That's the FDA saying that, not us. It's the FDA saying that.

On the other hand, if you look at CHRONOS-3, which is what they seem to have submitted for, that is in indolent NHL MZL, and it's a combination treatment with rituximab. So even if they were to get full approval for that, our belief and our continued belief is that this is not going to affect our approval or our accelerated approval.

Marco, you want to add anything?

Answer

Marco Renoldi (Executives)

I think you answered the first part of the question very well. So I have nothing to add. I think with regard to the second part of the question, how do we think copanlisib affect the competitive landscape and our opportunity, I think you touched base on this topic during your presentation. Copanlisib, as you know, is a PI3K inhibitor. It has shown some efficacy in third-line follicular lymphoma patient in the range of 60% overall response rate, which is a decent efficacy. But we know the product is associated to side effects which are probably not appropriate for third-line patients who are elderly and frail. And we have seen that the uptake of copanlisib so far in the U.S. market has been very modest. So for that reason, we believe that we have -- we are -- we represent with Betalutin an appropriate alternative to this compound.

Answer

Frazer Hall (Attendees)

Thank you. We also have a couple of questions, which essentially relate to a potential confirmatory trial for Betalutin. And the question is can you elaborate at all on how a confirmatory trial for Betalutin would be designed. You've mentioned historically that it will be in second line FL. Can you say anything further at this stage about the trial design in terms of size, treatment arms or what the comparator will be?

Answer

Erik Skullerud (Executives)

So I would -- with that question, I would love to see all of you back for the R&D Day. As you saw, that is one of the topics that we have put, and we want to give you more information on. So I will leave to answer that question until then. But we will talk more about our strategy around that with the caveat that, obviously, this needs to be agreed with the FDA. We will not have the agreement by then. As I mentioned in my presentation, our next interaction with the FDA on these questions will be in Q1 2022, but we're already making good progress on what we believe that study should look like.

Answer

Frazer Hall (Attendees)

Thank you, Erik. We also have 1 or 2 questions on the CAR-T program. But again, I think it's fair to say that you will answer those at the R&D Day. So perhaps I'll go on and ask the next question, which is essentially around financing and a question that says, given your current cash position, are you able to proceed at the speed you would have wanted to with regard to the proprietary filing work for Betalutin and preparations for the next steps. And also a question around the current cash runway, how long do you expect current cash to last? And what if any plans are there for refinancing of the company?

Answer

Erik Skullerud (Executives)

So if I touch upon purely the first part of that question, and I'll let Malene talk to the rest of it in a second, I think there's 2 aspects to this. Number one, yes, we have the money we need to get through PARADIGME. That being said, we're also a small biotech company, and we will always look for additional money. That is in the nature of being a small biotech company. Otherwise, we wouldn't be in this business. So our continued efforts with the pipeline beyond PARADIGME, what we will do next will always be a question of additional financing. But for PARADIGME itself and Betalutin for its first completion in FL third line, we have a run rate that will take us through the study. Malene?

Answer

Malene Brondberg (Executives)

Well, I don't think I have much to add. We still have money going into the second half of 2022. And I think -- and what we do, of course, as I said before, we look at the spend all the time and then try to spend in the right places. And that's really important. So we are always looking at the [indiscernible] and having discussions how to spend the money on a -- basically on a weekly basis, if not on a daily basis. Because we know, of course, it's the shareholders' money and it's important we spend them the right way.

Answer

Erik Skullerud (Executives)

That's the first question I get from Malene every Monday morning. Are we okay with the spend? And so far, I've been able to say, at least from my point of view, yes, we are. We're doing a good job, Malene so continue what you're doing.

Answer

Frazer Hall (Attendees)

We have 1 last question, which is on Archer. And can you comment on what the preliminary median duration of response is in the Archer study?

Answer

Erik Skullerud (Executives)

Well, as I hope you are all aware and by the way, thank you for that question. It's no doubt that Archer is important for the company. Last June, we reported that there are 7 patients that so far have been treated and it will remain 7 patients. We're not including any more patients in Archer. Out of these patients, they have all responded. The latest update on Archer itself is we have now 5 patients that have been monitored more than 2 years. We had one patient that still is working themselves up to 1 year, and we have one patient that has since in remission, they have continued to progress, sorry. So we have very good data coming out of the study. We're getting more and more data on the longevity of it. But we're still not at the stage where we can say, therefore, the duration of response is but we know that it's long, and we continue to amass data on how long it's going to be. This is a matter of time, and we only need to continue following month by month around how that is doing. Anything you want to add, Marco, to that?

Answer

Marco Renoldi (Executives)

No, we're very pleased that we moved from 3 to 5 patients above the 24 months checkpoint. I think this is great news. It shows that this combination is truly a strong combination for second-line patients. So we're very pleased, and we hope this will continue. We haven't reached median duration of response because patients continue to be in remission. I think this is really good news for patients.

Answer

Frazer Hall (Attendees)

Thank you. At this stage, Erik, we don't have any further questions on the line.

Answer

Erik Skullerud (Executives)

Thank you so much, Frazer, for helping out with that.

In conclusion, let me say 2 things. First of all, I want to say a big thank you, partly to the team that continues to work really, really hard on this. And I hope that we've been able to show you what we're doing and how we're doing things at the moment, also for you to feel confident that we're making the right choices. Secondly, I want to thank many of you. I've had a chance to meet several of you in my first 6 weeks at work. I've been around to talk to several of you investors, and I've asked questions around what are your expectations of us? What have we done well, what are we not doing so well, how can we improve? I want to continue doing that because I believe only in communication with you, can we get better? So please, by all means, if you want to have a conversation with me, I'm all yours, and I really want to do that.

Secondly, a big thank you to the teams that have helped us prepare here today. I hope we've given you an impression of what we're trying to do, what we're trying to do differently. What I've heard from many of you is Erik, please be a bit more transparent with how you communicate. We have tried to do that today. Your judgment if we've been successful in doing so, but I really hope that we have at least come somewhat your way in doing so.

But thank you for coming. It's great to see you all again, post the worst, hopefully, part of corona, and we look forward to seeing you again on the 30th of November for our R&D Day. Thank you so much.

21.08.27. Nordic Nanovector ASA, Q2 2021 Earnings Call, Aug 27, 2021

Presenter Speech

Malene Brondberg (Executives)

Good morning, everyone, and welcome to the Nordic Nanovector Q2 and First Half 2021 Call. I'm Malene Brondberg, Interim CEO and CFO. And with me today, I have our Chief Operating Officer, Marco Renoldi.

Today's earnings release report and the slides for this call are available on our website at nordicnanovector.com. Please note this call is being webcasted live, and a recording will be made available on the Nordic Nanovector website. Questions for the Q&A session can be submitted as usually throughout the presentation through the webcast platform, and we will attempt, of course, to answer as many as those [indiscernible].

Please turn to the next slide. As always, we need to go through this slide. We need to advise you that this conference call would contain forward-looking statements, and such forward-looking statements are subject to risks and the uncertainty that could cause actual results to differ materially from expectations, and more information can be found on this slide.

Please turn to the next slide. Turning to the highlights for the second quarter and first half '21. We continue to make progress announcing our PARADIGME trial with Betalutin in the third-line FL. As we get closer to the finishing line, we are thinking about, of course, how we position and prepare the company for a successful outcome.

As we announced on the 5th of August, we have revised the time line from PARADIGME, and we now anticipate the preliminary 3-month top line data during the first half of 2022. We have to date enrolled 94 patients out of our 120 targeted in PARADIGME, which is up by 11 patients compared to our Q1 call at the end of May.

At our call on the 5th of August, we've reported 92 patients. And you might recall that I said that we had low expectations for August due to it being the holiday season. We're therefore pleased to report that we have enrolled a further 2 patients in August, which, despite the restrictions due to COVID and the delta variant, is an improvement compared to August last year where we actually had no recruited patients.

Following a fundraising during the first half of the year, we have now cash that leads us -- a cash runway that takes us beyond the expected PARADIGME readout and into the second half of 2022.

During the first half, we also reported positive data from our combination Archer-1 trial in the second line of FL patients. We are encouraged by the result of the small study, which confirmed the attractive safety profile of Betalutin in combination with rituximab, also demonstrated promising early signs of efficacy with all 7 patients responding to the treatment, 6 of whom are still in remission. We believe that data and insight from this trial would be important to the design of the confirmatory Phase III trial of Betalutin that is required as part of the accelerated BLA filing process with the FDA. As a result, we decided not to invest further into this plan.

Lastly, we also announced that we will hold an R&D Day in Q4 to discuss Betalutin development and commercialization strategy as well as share insight from our order pipeline. Next slide, please.

So before we go into the operations, let me first remind you why we are here and why we are so committed to what we are doing. So non-Hodgkin's lymphoma is a common cancer affecting more than 150,000 new patients every year, only considering the 7 largest pharma markets. Despite the availability of multiple treatment options, NHL is still associated with a high unmet medical need, both as regards indolent and aggressive subtypes. Our mission is to deliver a novel treatment option that can address this need.

Our current focus, as you are aware, is the treatment of relapsed/refractory follicular lymphoma patients. 40% to 60% of these develop resistance or become refractory to rituximab, which is the mainstay of NHL treatment. In addition, elderly and frail patients may not be suitable for another cycle of chemotherapy or one of the newly available treatments such as the PI kinase inhibitors or the CAR T cell therapy, while -- which, while effective, are associated, as you know, with high side effect burden. So there are unfortunately limited options for these patients.

We believe that the solution can meet their need for a chemo-free, effective yet tolerable treatment, and the unique -- which is really unique, and onetime administration further contributes to improve the quality of life. Next slide, please.

Sorry, I just -- as I highlighted earlier, there are a number of treatment options for follicular lymphoma patients. Rituximab with chemotherapy is, as you know, the standard of care in first line. By moving into second and third line, there are no clear consensus of action, what's best for the patients.

And on this slide, we've tried to capture the different options in the matrix, where the vertical axis breaks down the follicular lymphoma subtypes by line of therapy, while the horizontal axis cluster patients by age groups. So as you could see, it is clear from this chart that there -- in the relapsed/refractory second and third line, there are few therapeutic options. And those that show clinical activity are burdened by high side effect profile, which makes their use unsuitable in elderly and frail patients.

It is important to note that in the third line follicular lymphoma, elderly and frail patients represent approximately 65% of patients. So then left for them is far from, as you know, ideal -- in essence, only rituximab as a single agent, which has a modest efficacy and will have no activity in rituximab refractory patients. Tazemetostat, which is effective yet only in a small fraction, approximately 15% of the third line follicular lymphoma population. Lastly, some other approved agents such as the PI kinase inhibitors, which patients do not wish to take due to the toxicity. Next slide, please.

So we believe this slide adds a very nice -- conveys our aspiration, which is to ensure that Betalutin can truly fill this significant unmet need of the elderly and frail segment of the relapsed/refractory follicular lymphoma patient population. As you know, starting in the third line indication, PARADIGME is designed to support the use of Betalutin in this indication. And it is our goal to then expand its use into the second line upon completion of the confirmatory Phase III trial.

Based on the clinical data so far, we believe that Betalutin could deliver the durable remission these patients long for, coupled with an unmatched tolerability profile and the convenience of a onetime administration. Next slide, please.

Our aspiration is shared by many customers we have interviewed. And when I say customers, we mean clinical stakeholders such as hematologists, medical oncologists and nuclear medicine specialists. They share our conviction that Betalutin potential bundle of -- they share our conviction that Betalutin's potential bundle of benefits, onetime treatment, durable response, general tolerability profile, sets it apart from available competitors and makes it the ideal treatment option for frail and elderly patients who, as a result of their comorbidities, cannot or do not want to receive treatments that would further compromise their life quality. Next slide, please.

Now to the shorter update on PARADIGME, the completion of which remain our primary focus, and we are nearing the end of the recruitment, which we, of course, are very pleased with. We have, compared to a year ago, managed to significantly increase the enrollment rate, which is driven by the improvement of the trial design and the many initiatives we've taken. A good example is our new targeted social media campaign to raise awareness of our trial that has started to pay off. And we are now seeing a good pipeline of potential patients, in fact, better than we have seen before.

This is extremely encouraging given our effort that we have been -- given our efforts have been impacted, as you know, by the spread of the COVID delta variant and continuing restrictions that are still causing problems and affecting our ability to screen, enroll and treat new patients. However, we are not where we wanted or expected to be, which was the reason we communicated we have revised the time line for PARADIGME. And we now expect the preliminary 3 months data readout during the first half 2022. Next slide, please.

Looking forward, enrollment into PARADIGME is coming to an end, as suggested, and we continue our efforts focused on preparing for the filing and commercialization of Betalutin. And we have -- I can tell you, we have a lot to do. For example, for the CMC section of the filing, we are currently working on completion, the process performance qualification campaign, which is required upon filing. This is done to document consistent quality of our clinical and commercial supplies. We are also helping our contract manufacturing partners to prepare for pre-approval inspections. We are also making progress in strengthening our commercialization and partnering strategy and exploring all go-to-market options to enable us to capture the full potential of Betalutin in the different geographic regions.

From a regulatory perspective, our goal is to find a biological license application, also called BLA, which is the FDA -- with the FDA based on the data generated by the PARADIGME trial. It is our current intention to apply for accelerated approval. And this will, of course, require us to have a Phase III confirmatory trial stated at the time of the BLA submission. Next slide, please.

So now I will take you through the key financial highlights for the second quarter and the first half of 2021. We continue our cost control -- we, of course, continue to control our cost carefully. As you know, this has been a focus throughout years, but particularly, of course, the last year with a -- as you can see, a total operating expense for Q2 coming in at NOK 103.9 million, which you can -- if you look at the slide here, and you can see that it's roughly the same as Q1 2021 and also if you go back to the Q4 for 2020, and it is less compared to the same period for 2020.

The total operating expenses for the first half 2021 decreased to NOK 205.1 million from NOK 239.3 million in the same period of 2020. This decrease is due to our, again, careful management of financial resources, which are focused on completing PARADIGME and other development activities needed to support the regulatory filing.

So turning to the next slide, where you can see our cash position, which was NOK 450 million at the end of June 2021. This is, of course, following the successful private placement and the repair offering, which raised approximately NOK 422 million. Here, I would actually like to say thank you to all our shareholders for the continued support. This gives us a cash runway into the second half of 2022 beyond the expected preliminary data readout from PARADIGME, which is an important thing to mention, of course.

So onto the next slide where I would just be wrapping up, and let me just conclude on our outlook. So I would just like to emphasize that we strongly believe that Betalutin is an exciting product opportunity with its attractive safety and efficacy profile from a single, onetime administration and potential for use across the NHL population. Betalutin is also one of the most attractive and advanced radiopharmaceuticals in clinical development, an area of increasing interest in the pharmaceutical industry.

As I said, we are focused on and determined to complete PARADIGME as quickly as possible. So we can report the preliminary 3 months top line data during first half '22. This is a key milestone, and I really mean a key milestone for Nordic Nanovector. And we are really all working hard to achieve this.

In the parallel, we continue the work stream needed to support the filing and the commercialization of Betalutin. These include evaluating partner opportunities designed to maximize the value we can create from this exciting and potentially important product.

Finally, we continue the work towards evaluating the multiple opportunities to expand the market for Betalutin and build on both our proprietary anti-CD37 antibody franchise and our established heritage in radiopharmaceuticals. We plan to talk more, as you know, about these opportunities at our R&D Day in Q4. Next slide, please.

So thank you again for your attention. And before we finish and move on to the Q3 presentation, in the 18th of November, as you can see, is our next event. I also want to just say that we need to have, of course, a date set for our R&D Day, which we expect to set in due course. And we really hope that this event can be an event that you can attend in person because it would be nice to meet all of you again in Oslo.

So once again, thank you very much for your attention. And also thank you very much for all your support and your continued sending questions. And now I would like to open the Q&A session where I know Marco will join me. So I will hand it over to you, [David], please.

Answer

Unknown Attendee (Attendees)

Thank you, Malene. Let me start with the first question. When do you expect to employ a permanent CEO?

Answer

Malene Brondberg (Executives)

Well, that's a -- thank you for that question. It is -- as you know, it's the Board that hires a CEO. And the only thing we can say today is that we are in a -- the Board is in the process. And as Jan said last time, he is -- or they are evaluating candidates. So as soon as possible.

Answer

Unknown Attendee (Attendees)

Okay. Thank you. Could you elaborate on what type of initiatives have been taking place at clinical sites and local clinical sites to speed up recruitment in PARADIGME?

Answer

Malene Brondberg (Executives)

Yes. So Marco, if I start and then you can maybe jump in. So as I said, we have a -- in some, not in all countries, but we have initiated a social media campaign which has given us a good funnel, I would say, of potential patients that could be -- hopefully, some of them may be enrolled, not all of them are eligible, and that is a very strong initiative.

Other things that we are doing, which is, of course, that we are going out to visit the sites, which, of course, is difficult in this environment. And it's possible in some countries at the moment, and in others it's not. And it's not even country by country. It's also different regions by countries that are more open or closed. So those are some of the initiatives that we're taking and continue to take.

And here, I would actually like to say a very big thank you to all our employees, to, of course, the team that's working -- that's been working really, really hard in these times because it is really difficult still out there. Marco, I don't know if you have any further to add.

Answer

Marco Renoldi (Executives)

Thank you, Malene. I'd like maybe to add a couple of other initiatives. We have partnered with companies that are tasked with accelerating the patient enrollment in clinical trials, in particular, with companies that facilitate referral of patients for treatments such as Betalutin, which require the treatment to be handled in a specific setting. And again, we have partnered with a company that basically identified potential referrals in centers that were close to the investigational sites so that we could maximize the potential identification of patients not necessarily reaching the investigational site.

In addition, we increased the number of customer-facing medical teams in addition to the medical science liaison, which, of course, where Nordic Nanovector flag. We've also increased the number of scientific liaison of our contract research organization. So we have had a large number of medical staff that we're in close contact with investigators and reminded of the opportunity to potentially enroll patients.

Answer

Malene Brondberg (Executives)

Thank you, Marco.

Answer

Unknown Attendee (Attendees)

Thank you. The next question is how many patients do you have in screening?

Answer

Malene Brondberg (Executives)

We don't give that number. And [Dave] -- but as I said, we do have a -- we feel a strong pipeline and with potential patients. Of course, it's not -- you can never -- nothing is never given, as you know, with everything in

this world, but we think it looks good. And as also you can see this that third quarter in a row where we actually report a plus 10 patients, which we believe is a very good sign, and it's a good sign that despite -- and this on top of the delta variant, that it is actually working the initiatives that we have taken. Marco, I don't know if you have anything to add.

Answer

Marco Renoldi (Executives)

No, you covered it very well. I have to concur, we -- the pipeline of patients under consideration that we have today is the largest we have ever seen. So we are very confident. As you said, pipeline of patients under consideration doesn't mean that they've all consented. So not all of them are or will enter screening, but we're very confident.

Answer

Unknown Attendee (Attendees)

Thank you, Marco. What is the level of recruitment that you anticipate is required to be able to report the 3-month top line data in H1 2022?

Answer

Malene Brondberg (Executives)

So as you can see today, we have 94 and we -- and the target is 120. And the difference, what we expect every month is not something we will go into because as you have seen in the past, it is a -- it's very, very hard to predict and especially with the delta variant. As I said, we are doing everything that we can, and we will continue to update every quarter on where we are and be as transparent as we can. I don't know, Marco, if you have any further comments.

Answer

Marco Renoldi (Executives)

No, I think you covered it very well, Malene. I think if we continue to show the type of recruitment of the last 3 quarters in a row, so an average of 12 patients per quarter, I think then achieving that target is not only doable but very, very realistic.

Answer

Unknown Attendee (Attendees)

Thank you, Marco. Can you give any more granularity on how long after completing recruitment results will be ready to be released?

Answer

Malene Brondberg (Executives)

Marco, I think you answered that on the -- on our last call. So...

Answer

Marco Renoldi (Executives)

Yes. I think data, in particular, independent review of the scans, are being progressed as we move forward. So I think what happens is at the end of the last month, so when the last -- the patients of the last month will be enrolled, there will be a period of probably 3, 4 weeks for the last patients to be reviewed and cleaned and to make sure we collect the independent assessment. But I think it's almost parallel to the completion, to the enrollment and dosing of the last patient. And again, the 4 weeks' time for the collection of the independent review of the scans will only affect the last 4 patients.

Answer

Unknown Attendee (Attendees)

Thank you, Marco. Do you anticipate to complete the readout before raising additional capital? If so, how confident are you that this will be possible given the current time line?

Answer

Malene Brondberg (Executives)

So as I said, the preliminary data readout is in the first half, and we have a -- money going into the second half.

Answer

Unknown Attendee (Attendees)

Thank you, Malene. Just a couple more questions. What is the preliminary median duration of response for the Archer study?

Answer

Marco Renoldi (Executives)

I can take that, yes. So as Malene pointed out, and I think it's also in today's press release, 6 out of 7 patients who responded in the Archer trial are still in remission. We will, of course, deliver all of the efficacy products, including duration of response from the studies fully reported and presented at a medical conference.

But what we can share today is what type of checkpoint these 6 patients were still in remission had already achieved. So 3 patients have basically passed the 24 months checkpoints, still being in remission. One patient has passed the 18 months checkpoint, still being in remission. One patient has passed the 12 months checkpoint, still being in remission. And 1 patient has passed the 6 months checkpoint, being in remission. So I think -- I hope you would concur with us that these are very good results and seeing that not only all of the patients are in remission, but 3 of them have already passed successfully. The 24 months checkpoint is an excellent result with the type of tolerability that we see from this combination.

Answer

Unknown Attendee (Attendees)

Thank you very much, Marco. And final question. There are a couple of them are essentially, could you provide an update on the partnering situation?

Answer

Marco Renoldi (Executives)

I can take that, Malene. We continue to explore different options for the best go-to-market strategy. And we are open to all options. And to that purpose, we have ongoing dialogues with several interested parties. Of course, we have a priority, and the priority is to choose the option that will enable our company to realize the value potential of Betalutin and to deliver this medicine to all patients who can benefit from it while, at the same time, of course, ensuring the highest return for shareholders.

As you can imagine, the options we are considering include both a stand-alone commercialization but also regional and/or multiregional and global partnership. And we believe these options could also bring additional funds into the business, resulting in a lower need for external financing funds.

Answer

Unknown Attendee (Attendees)

Thank you, Marco. And that concludes all the questions we've received this morning.

Answer

Malene Brondberg (Executives)

Fantastic. Okay. Well, lovely. Thank you so much. Before we say goodbye, I actually just want to say, first of all, thank you to all the shareholders, of course, for the continued support, but also a big thank you to the team at Nordic Nanovector. We have a lot of hard working, and I can tell you, everyone is bringing out their A game. So thank you to all the employees. And we have so much talent and it is a pleasure to work with everyone, and thanks to the leadership team as well. As you can hear, this teamwork, Marco and I, are here together on the presentation.

So with that, thank you so much. And we will, as I said, in due course, announce the date for the upcoming R&D Day in the year, which will be in Q4. Have a good day and also a very good weekend. Thank you very much. And with that, we conclude today's call.

21.08.05. Nordic Nanovector ASA- Special Call

Presenter Speech

Jan Egberts (Executives)

Good morning, ladies and gentlemen. Welcome to the update on the PARADIGME and the new time line for Nordic Nanovector. My name is Jan Egberts, and I'm the Chairman of the Board of Directors of Nordic Nanovector. Today, here with me are Malene Brondberg, our interim CEO and CFO; and Marco Renoldi, our Chief Operating Officer.

First of all, we'd like to share some slides with you, where we'll give you a little bit more detail regarding the current situation. And then subsequently, we have some time for some questions.

So hereby, I'd like to hand over to Malene to take you through the presentation, together with Marco.

Presenter Speech

Malene Brondberg (Executives)

Good morning, ladies and gentlemen. Thank you very much. As Jan said, my name is Malene, and I will take you through a couple of slides, and then I'll hand it over to Marco after that.

As you can see that we announced a -- the day before yesterday evening that we have -- unfortunately, have to come up with a new time line on PARADIGME. That said, we are continuing to focus on, of course, completing PARADIGME as quickly as possible. As you also saw during 2020, we made significant improvements to both the trial design and also how we -- and we implemented multiple initiatives to improve the execution. And with that result, we saw some good improvements in 2021 compared to 2020, but not, unfortunately, as much as we had anticipated.

As of the 3rd of August, we had 92 enrolled patients out of a target of 120, and this is up from 83 as we announced on the 25th of May 2021. We've also made the decision to -- not to invest further funds into our Archer trial. But that said, it's very, very important to say that, that data and insight will help in designing the protocol for the confirmatory Phase III clinical trial because, as you know, it is very positive data we have in that time, and that is important.

We have also decided that we will do, in Q4, an R&D Day. And of course, it is -- with the current COVID situation, it is very difficult to say the exact timing right now. But here, we would like to discuss the position and the next step for the Betalutin development and as well also give an insight into other value-enhancing opportunities we believe we have in the pipeline.

So as I said, we, unfortunately, had to revise the PARADIGME time line. And this is, of course, a very serious situation with the COVID and the -- and we have seen an uptake. But unfortunately, as you also know, the Delta variant hit hard. And where we started first with the Delta variant is here in the U.K. where I'm sitting, because unfortunately, I can't travel into Norway right now, and then it spread throughout. Because we have seen a good trend in the patient enrollment. But unfortunately, the Delta variant didn't help us.

So we did decide to -- unfortunately, to revise the time lines after we had, of course, discussions with our clinical advisers and the CRO, who manage our trial. We have, of course, continued to focus on the increased interest in enrolling patients in regions where we've seen that COVID is under better control. And we are, of course, confident that we can maintain and improve [modestly] the current rate of the recruitment despite the COVID situation.

When that is said, it's also worth mentioning that August is always -- just so you have that in mind when we report in the end of August, where we're going to again give an update on our numbers of recruitment, is always a weak month because of just the nature that in most European countries, that's a holiday season. And of course, unfortunately, with the COVID, that doesn't help.

When that -- all that is said, then the new time line for PARADIGME is that we are targeting preliminary 3-month data readout during the first half of 2022. And with that, I will hand the next slide to Marco, please.

Presenter Speech

Marco Renoldi (Executives)

Yes. Good morning, ladies and gentlemen. Our confidence in the value of Betalutin remains very strong. Not only Betalutin is the most advanced radiopharmaceutical in clinical development, but it's also one of the most attractive compounds in this setting. The reason why our confidence is so strong is because Betalutin targets a disease, a complex disease, where the unmet medical need is high.

Despite new therapies have been made available, quite a few targeted therapies in the follicular lymphoma setting, even on CAR-T, but there is a portion of the relapsed/refractory patient population suffering from NHL and follicular lymphoma, which is underserved by existing therapies. This is the population of the elderly, of the frail patients, with a poor performance status, with serious comorbidities.

These are patients that, as a nature of their age or as a nature of the comorbidities associated to prior therapies, do not tolerate, cannot accept or are not willing to undergo either chemotherapy or even the novel agents that have been approved, the PI3K inhibitors, the CAR-T cell therapies, because both physicians and patients know that while these therapies may be effective, they are associated to a high side effect burden.

And I think it's worth stating that for patients entering into the third line of therapy after devastating prior lines of therapy with chemotherapy, remission is an important goal. But these patients look for more than remission. They look for a better quality of life. They want a more balanced type of treatment that ensure remission but also ensures a more tolerable profile.

And this is exactly what Betalutin can offer. We can satisfy that need for a chemo-free, effective and tolerable treatment. And that's why we believe that we have a tremendous opportunity in this set of patients. And in third line, this is not a niche population. This is more than 70% of the third-line patient population.

But Betalutin is not just the third-line follicular lymphoma indication, even if that's a very promising indication. Betalutin holds multiple opportunities to expand in follow-on indications. You've heard from Malene, we are preparing to start a Phase III, which will enable us to secure a second label in second-line follicular lymphoma. We have now more information on what the next steps will be for diffuse large B-cell. We have multiple opportunities to further exploit the market potential for this compound.

With that, I'd like to hand over back to you, Malene.

Presenter Speech

Malene Brondberg (Executives)

Thank you very much, Marco. And I just want to round off our presentation here just with a reminder about the next events that we have. So as I said, the 27th of August, that's when we report the Q2. I do hope that I will be able and Marco will be able to travel into Oslo. But as right now, it looks difficult, unfortunately.

And we will have the R&D Day, as also said, and we will like to have it in the Q4, just so we have time to prepare. And hopefully, we will see an improvement on the travel, so we can be in Oslo for that day. And then finally, of course, we have the Q3, which will be the 18th of November.

With that, I would like to hand it over to the session of the questions, please.

Answer

Unknown Attendee (Attendees)

Thanks, Malene. So the first question we have is how is the hunt for a new permanent CEO going?

Answer

Malene Brondberg (Executives)

So Jan, I think that's a question for you, please.

Answer

Jan Egberts (Executives)

My apologies, I was muted. We current -- we have a very active search process. We have retained an executive search firm who is helping us, and we are talking to various potential candidates. So that's ongoing.

Answer

Unknown Attendee (Attendees)

Okay. Moving on to some questions about PARADIGME. It says, will recruitment be completed -- will recruitment completed be announced as soon as possible? How long will it take from the last patient dose to top line data? Will this be announced directly to the market or will you wait for a suitable conference?

Answer

Malene Brondberg (Executives)

We will -- if I can start and then I'll hand it over to Marco. We will announce when we have completed the enrollment. And as I said, we will do everything. And the management team works really well together. And they -- and we also, of course, work with the Board to do everything that we can to get it going as fast as we can. And when it gets to the -- what we need from the patients in, we roughly need 3 months, where we then can then come out with the preliminary top line data. Marco, I don't know if you have anything further to add.

Answer

Marco Renoldi (Executives)

No, I think you covered it very well. As you know, we have an assessment of efficacy 3 months after the patient receive Betalutin. We, of course, will clean the patients in stacks as they progress. You can expect maybe for the patients in the last month some additional weeks to clean the data. But in essence, 3 months after the last patient in, we will be able to provide preliminary top line data.

Answer

Unknown Attendee (Attendees)

Okay. Next question. Is it possible to have a 3-month readout after the first 100 patients just to inform the market of the results?

Answer

Malene Brondberg (Executives)

As you can understand, we need to have all patients in, and that's, of course, important. And it's, of course, important that the data cleaning takes place in the way it has to take place, of course. Marco, I don't know if you've got anything further on this.

Answer

Marco Renoldi (Executives)

I think we have agreed with the regulatory agencies that we will do formal analysis only at certain points in time, which is when all patients are enrolled and after a certain amount of time following the enrollment. So we have to comply with what we have agreed.

Answer

Unknown Attendee (Attendees)

Next question. Can you start writing the NDA application when preliminary results from 100 or 110 patients are available, and then include the final 10 to 20 just before submission?

Answer

Malene Brondberg (Executives)

As going back to saying, we need the 120. I don't know, Marco, have you got any further [indiscernible]?

Answer

Marco Renoldi (Executives)

I think we can start preparing for other elements of the BLA application. The BLA application is a very complex endeavor, and our regulatory team is coordinated these massive efforts. This includes nonclinical, CMC and clinical data. And we are advancing all of these workstreams in parallel, and we can certainly give priority to certain areas until when the full clinical data set is available.

And we, of course, since we have received fast track, we even had the possibility of exploring the rolling BLA concept. So yes, what is being asked is possible. We can have different information, documentation being provided at different times. But we will wait until the 120 patients are enrolled to finalize the clinical documents.

Answer

Jan Egberts (Executives)

Just want to be clear, that is the plan. The plan is a rolling admission and we provide the information to the agency as soon as it is available. Again, the data integrity -- what's the point about can you break the code after 100 patients? That's a very important point to the regulatory authorities like the FDA. We really do not want to -- and are very negative towards breaking this code halfway.

Answer

Unknown Attendee (Attendees)

Next question. About 2 years ago, a significant emphasis was made on CMC strategies in respect to BLA readiness and commercial execution. According to public job listings, the company had also made a number of hires in this field lately. However, there has been limited investor communication around manufacturing. Are there any changes to your go-to-market strategy?

Answer

Malene Brondberg (Executives)

Marco, I think I'll hand that over to you.

Answer

Marco Renoldi (Executives)

No. The requirements for BLA filing as far as CMC is required have not changed. We are committed and actually are on our way to satisfy the requirements that the agency, the FDA poses in terms of CMC readiness and all the performance -- process performance qualification activities are on their way and proceeding well. So all that we had described a couple of years ago during one of our R&D day are on their way. And maybe we'll find opportunities to update the market on these activities.

Answer

Jan Egberts (Executives)

Can I...

Answer

Malene Brondberg (Executives)

If I can -- sorry, Jan?

Answer

Jan Egberts (Executives)

Yes. No, the word CMC, for people who have not heard -- or the acronym CMC stands for chemistry, manufacturing and control, which is basically the catch-all phrase for manufacturing issues. So in case people kind of wonder what CMC means.

Answer

Marco Renoldi (Executives)

Thank you, Jan.

Answer

Malene Brondberg (Executives)

Yes. And if I can follow up on that, I can just say and also allude to the fact that I have said that in the last many quarterly calls that we, of course, do continue also with the spending in CMC because I've also said that, that is -- as Marco also said, a very important part of getting ready. So we are, of course, continuing on that path.

Answer

Unknown Attendee (Attendees)

Where in the world is recruitment highest in PARADIGME? And how many patients do you currently have in screening?

Answer

Malene Brondberg (Executives)

We don't give an insight, unfortunately, to each country nor each region, and also we don't give in to the screening. And what we will continue to do is we will continue to update every quarter on how we are going with how the enrollment is going. And as also said before, we have in the areas where that is -- was less hit by COVID, we saw an uptick. In the areas or the countries where we saw a big impact of COVID, of course, we saw that we were more hit. I don't know, Marco, if you've got...

Answer

Marco Renoldi (Executives)

No, I have nothing to add. But COVID has impacted which are the most enrolling countries. And we have seen countries that we are enrolling extremely well and that were hit by COVID, and therefore, decrease their enrollment rate and others came up. So it's really an inconsistent pattern, dictated more by COVID than by our efforts.

Answer

Malene Brondberg (Executives)

Next question?

Answer

Unknown Attendee (Attendees)

Yes. Can you say which 10 sites you've closed due to low recruitment or in which countries they're in?

Answer

Malene Brondberg (Executives)

No, we don't provide that detail. But what is, of course, very important to say is that we do -- we always evaluate what we do. And we do that all the time. And they -- and of course, we would spend the money the best way we can, of course. And of course, we do need to take initiatives if we can see that something is not working. We can

put the money at places where we think that's a better investment, and that is a day-to-day assessment that we do. And because, of course, we're fully aware that it's the money -- it's the shareholders' money. So that's very important, of course. Marco, I don't know if you...

Answer

Marco Renoldi (Executives)

Nothing to add. We optimize to be more effective. That's what we do.

Answer

Unknown Attendee (Attendees)

Next question. Historically, you've referred to the PARADIGME trial as a [indiscernible] trial, but you do not do that anymore. Can you discuss your current thinking on the regulatory process for Betalutin based on PARADIGME? Is it possible to file for an accelerated approval based on PARADIGME? Or do you think you need to complete a confirmatory Phase III trial before filing?

Answer

Malene Brondberg (Executives)

Marco, would you...

Answer

Marco Renoldi (Executives)

We believe, based on our conversation with the FDA that we can file with the data generated through the PARADIGME trial for accelerated approval. At the time of filing with the data generated from the PARADIGME trial, of course, pending results, we need to have a Phase III confirmatory trial started. That is what the FDA requires for any compound filing for accelerated approval with the Phase II study. So that's reality. Of course, we are looking for the data that will determine the robustness of the data. But yes, PARADIGME is -- can be sufficient to file for accelerated approval.

Answer

Unknown Attendee (Attendees)

Thanks, Marco. Next question. Based on the interim results from last summer, do the management and the Board believe that Betalutin will come to market?

Answer

Jan Egberts (Executives)

Absolutely. Yes, absolutely.

Answer

Marco Renoldi (Executives)

The interim analysis confirmed strong activity for both dosing regimens and a tolerability and safety profile in line with expectations. There was a clear recommendation from the independent review committee to go for the 40, 15 dose, which the company acknowledged and which was later discussed with the agency. That's why we have proceeded with a new single agent study for the second part of PARADIGME. But clearly, strong sign of activity. So we are confident that the drug, through the PARADIGME, the rest of the PARADIGME trial will confirm its efficacy level.

Answer

Unknown Attendee (Attendees)

Next question. What year do you estimate that Betalutin will be on the market? Do you have interest from other pharma companies in Betalutin? Would you consider that interest as high?

Answer

Malene Brondberg (Executives)

Jan, will you -- or Marco?

Answer

Jan Egberts (Executives)

Marco, take the timing, I will take the other one.

Answer

Marco Renoldi (Executives)

Yes. I think it's a bit early to guide on approval time lines. I think what we can clearly confirm as we had previously said, anticipated during the quarterly call, we still expect to start the BLA process towards -- in 2022. And of course, the approval of the compound will depend on the review, whether it's a priority review, a standard review by the agency and all formalities. But I think, again, we want to confirm our intent to start the BLA filing process in 2022. I'll hand over to Jan in regard to the partnering strategy and interest from other parties.

Answer

Jan Egberts (Executives)

Yes. So thank you. So our business development team has discussions with various parties. The reality is that these compounds typically do not get any formal agreement with any partner until there are more definitive data regarding the performance of the product. I've been along on the other side of the equation, working for big pharma. And typically, we should wait until a very definitive result of clinical studies. But yes, we are talking to a lot of different people and different companies on an ongoing basis.

Answer

Unknown Attendee (Attendees)

Thanks, Jan. The next question. Given the recruitment issue in PARADIGME, how does Nordic Nanovector expect to market Betalutin and sell it by themselves in certain regions? And as it relate to the recruitment progress, does it not make sense to partner up in all markets?

Answer

Jan Egberts (Executives)

It's a partnering question. So I mean the Board actively is investigating various partnering approaches. The most likely outcome is a mix where in the larger markets, we would have a partner; in smaller markets, we probably would not have a partner. That's smaller, more local markets like, for instance, Scandinavia, I mean that's not definitively decided yet, just a pure hypothesis that we -- where we are. But no, that is likely a hybrid model. Like many of these smaller biotech companies, when they go to market with their first compound tend to have a hybrid strategy. And I would expect -- there's no definitive decision yet, but I would expect to do the same for our company.

Answer

Unknown Attendee (Attendees)

Thanks, Jan. Just moving on to Archer. What are the consequences of stopping further studies of Archer-1 now? Many people see this as perhaps the company's most important asset in terms of valuation. Do you already have enough data to be able to say that Archer-1 will be attractive combination medicine?

Answer

Marco Renoldi (Executives)

I can take that. I think the decision to stop investing resources in Archer is a very positive decision because it means that we have collected enough information from this study. As you recall, Archer-1 was mainly a study to assess the safety and tolerability of the combination of Betalutin plus rituximab, as well as the preliminary activity of the combination. And we have seen that this combination does not alter significantly the profile of Betalutin when it comes to safety and tolerability, which is one of the most important features of its profile.

We've also seen that the combination strengthened the efficacy of the compound. Therefore, we had all the information we needed to inform the next stage of development for second-line follicular lymphoma. As you know, our Phase III, which we have to start at the time of BLA filing, will target second-line follicular lymphoma. So again, we welcome the decision to put an end to Archer-1 as a positive decision because it means we have gathered enough information to inform the next stages of development.

Answer

Unknown Attendee (Attendees)

Thank you, Marco. With rituximab off-patent, how many biosimilar partner opportunities exist for the future Archer-1 combo treatment regimen?

Answer

Marco Renoldi (Executives)

Yes, there are many biosimilars on the market. As you know, biosimilar -- the biosimilar business model is not a model that leverages scientific collaboration. It's a model that leverages tenders, pricing discount, first-entry advantage. Therefore, there is a limited synergy that can be gained from a scientific collaboration with any of these companies. But clearly, the prevalence of the many rituximab biosimilars means that rituximab will remain a significant component in the treatment algorithm. And therefore, choosing, for example, to combine with that compound may have commercial opportunities.

Answer

Unknown Attendee (Attendees)

Thank you, Marco. Is the Phase III study consisting of Betalutin plus rituximab as a combination in one arm and mantle cell lymphoma in the other aimed at second-line FL and third line FL a possibility?

Answer

Marco Renoldi (Executives)

We will probably provide some update on our ideas relative to the Phase III design later in the year once we've had the opportunity to discuss the current proposal with the agency. But in general, I can say that a Phase III study is -- basically compares the drug that we want to assess, in our case Betalutin, whether in combination with another drug or as consolidation to another treatment versus a competitor in one or more NHL subtypes. Again, we cannot comment at this point in time because we are in the process of finalizing our Phase III design, but we want to first have a conversation with the agency. When the company is ready, we will provide more updates with the market. I don't know if Malene or Jan want to add anything to this.

Answer

Malene Brondberg (Executives)

No, no, I totally agree. As you could just see, we have a lot of things going on, and as I said, working to -- first at PARADIGME, of course, to get that completed. And then, of course, we're also, at the same time, as Marco just said, working on the Phase III design.

Answer

Unknown Attendee (Attendees)

How many Archer patients are still in remission?

Answer

Marco Renoldi (Executives)

I do not have that exact number on top of my mind. I believe it's 6 out of 7, but we would need to check with our Chief Medical Officer, who's not on the call, and we'll be able to provide an update maybe at the quarterly call.

Answer

Malene Brondberg (Executives)

Yes. I recall the same number.

Answer

Unknown Attendee (Attendees)

Maybe we should move on to talking about financing questions -- financial questions.

Answer

Malene Brondberg (Executives)

Yes.

Answer

Unknown Attendee (Attendees)

Can you discuss the financial implications of the delay, please? In connection to your last capital increase, you stated that you did not plan to raise any more capital until you had presented the 3-month follow-up data from PARADIGME. Is this still realistic given the recruitment rate, the follow-up time and the company's burn rate?

Answer

Malene Brondberg (Executives)

Yes. Well, as I said, we are -- we will do everything that we can to complete as quickly as possible, and we will let you know when we have completed and we will continue on the quarterly updates. We also said that we expect the preliminary top line data in the first half of 2022. And we have that and we will reiterate that statement also that we have funds going into the second half of -- into '22.

We will, of course, and we do that all the time, as you've heard with some of the initiatives, we've taken a look at the -- at our purchase and try to spend the money where the money should be spent. And of course, it's important that we spend the money so we get the enrollment going as fast as possible. But as I said, it is second half 2022 that we have money and we expect to be able to have the data -- top line, preliminary data in the first half.

Answer

Unknown Attendee (Attendees)

Thank you, Malene. How does stopping investment in Archer affect the budget and the yearly cash flow?

Answer

Malene Brondberg (Executives)

Well, of course, it has an impact, of course, on that. But as I said, the most -- and also Marco said, the most important thing is that we now feel that we have -- we learned what we should from the Archer-1. And that, of

course, is very important. It is -- and that's where we take the decision. Of course, there is a money implication as well, but that is where we took the decision on, that it is the learning that we feel we've now got from it.

Answer

Unknown Attendee (Attendees)

Okay. What is the cost impact of closing the 10 sites in PARADIGME?

Answer

Malene Brondberg (Executives)

It will have an impact. That said, we will also -- some of that money, we will spend them on -- move them into other things, other initiatives where we see that that could have an impact on the recruitment. Because here, the task is really to get that going as fast as possible. And that, of course, means that we are not slowing down on the spending on PARADIGME. Then there will be other areas that, of course, we -- and we do that all the time, look into -- and whether we can find some savings. But not in PARADIGME, that, of course, is the key.

Answer

Marco Renoldi (Executives)

The money will be reinvested in patient acceleration initiatives focused on the other sites that we've seen have worked very well in certain countries. So it will actually give us the chance to make the sites which are more productive, even more productive.

Answer

Malene Brondberg (Executives)

Exactly.

Answer

Unknown Attendee (Attendees)

I think this is most probably the last question. It says, what is the rationale for spending time and resources on preparing for an R&D Day in the current situation? What does the company hope to achieve?

Answer

Malene Brondberg (Executives)

I think it's a long time ago since we last had an R&D day. And the -- and of course, we feel that we have some -- as we've spoken about before, want to give an update on other projects. So it's not just PARADIGME, because Nordic Nanovector is more than PARADIGME. And we would have liked to have it before that, but we can also see with the current COVID situation that it is impossible. And we would like, of course, to have time to plan because as we had in '19, where we had the day on the 17th of September, we had a day where we also had some external experts in, and it just takes time to plan that. And they -- and with the current situation, that's why we placed it at Q4. We would have liked to have it before. I don't know, Marco...

Answer

Marco Renoldi (Executives)

You covered it very well. If I may just add that the company is still viewed through the lens of PARADIGME and third-line follicular lymphoma. And there is a lot of progress we have made in both the clinical development plans and commercialization plans. We are working actively on the design of a Phase III. We have progressed on the understanding of what the next steps of development for diffuse large B-cell, Betalutin is much more than just third-line follicular lymphoma, and we feel that we have updates for the market on this.

Secondarily, we have projects that have merit, that have the potential to represent important contributors to the value creation of the company. And we feel even if we understand the market is waiting for PARADIGME, these elements will be important to improve the appreciation of what this company can provide the shareowners.

Answer

Unknown Attendee (Attendees)

Thank you, Marco. We've just had a couple more questions. What is the preliminary medium duration of response for the Archer study?

Answer

Marco Renoldi (Executives)

I think as I pointed out, we -- I mean where the 6 patients are still on remission. So I do not know when the next plan assessment, median duration of response is due. So I have to refer this question to my colleague, Christine, and we may provide an update in one of the upcoming meetings.

Answer

Unknown Attendee (Attendees)

Thank you, Marco. I think we've covered nearly all of the questions that have come in and most of it -- and I think all of the topics that the questions cover. So I'll hand it back to Malene.

Answer

Malene Brondberg (Executives)

Well, thank you very much. Before I hand it back to Jan. I would just say thank you very much. As you can hear, it's a team effort here. And as Jan also said, we are still searching for a CEO and well under way. And we will do everything, in the meantime, the team that's here, to get the enrollment going as fast as we can. And with that, Jan, I would hand it back to you.

Answer

Jan Egberts (Executives)

Yes. Thank you very much. I think we covered all. Thanks for your attention. And obviously, August 27, we will have our quarterly release, we'll give you some more information. Don't expect too much difference between today and the 27th, but still, it's always an important milestone, the quarterly results.

So thanks so much for your attention and your support. And [though it's] a disappointing meeting, but that's a bit of the reality of biotech. So all the best. Take care.

21.05.26. Nordic Nanovector ASA, Q1 2021 Earnings Call, May 26, 2021

Presenter Speech

Jan Egberts (Executives)

Good morning, ladies and gentlemen. My name is Jan Egberts. I'm the Chairman of the Board of Nordic Nanovector. Together with me here are Peter Braun, our new CEO; as well as Malene Brondberg, our CFO; and Marco Renoldi, our Chief Operating Officer.

First of all, I'd like to emphasize the forward-looking statement. We're obviously a public traded company. So please read this carefully when you're considering investing in our company.

Today, I'm going to cover a couple of the highlights prior to Peter joining us, and then I will introduce Peter and then I will hand over to him.

So kind of before -- shortly before Peter joined us, we had a very successful private placement in February, and in addition, an oversubscribed repair offering in April, which is a very good indication, which raised about NOK 422 million or about USD 48 million in proceeds. It really helped our runway all the way through into the second half of 2022 next year.

As you're aware, we made some very significant protocol changes to the PARADIGME study, which really helped us improve our execution and the recruitment last year. In addition, we released earlier this week some very promising Phase Ib data from the Archer-1 study where we evaluated Betalutin together with rituximab in second-line follicular.

In addition, we had some change on the Board. As you're aware, Hilde, after a number of years, unfortunately, was not able to stand for reelection at the AGM. So she has left our Board, and Solveig Hellebust was appointed as a new Nonexecutive Director at our most recent AGM on April 28 of this year. So some changes on the Board.

And then, finally, obviously, you have read the announcement and some of you have seen Peter in some presentation, but I now would like to introduce Peter to you. And I hand over the presentation from here onwards to Peter. As you know, Peter has over 30 years of experience with Roche, including launching a number of very important products like Herceptin and Tarceva. In addition to some of these marketing roles, he also had some general management roles and some other commercial roles being involved in launch activities. So very relevant experience for our company as an oncology company, and we're very pleased that Peter has decided to join us.

So having said that, finally, I'd like to last -- like to thank Lars Nieba for his energy over last year where we really made a major change and a major improvement to the company.

And now I'd like to hand over to Peter, who will take you through the rest of the presentation. Thank you, again.

Presenter Speech

Peter Braun (Executives)

Great. Thank you, Jan, for the kind introduction. I'm excited to be here on my first quarterly call with Nordic Nanovector, and I'm even more excited to be leading this organization to the next stage in our journey.

Prior to going into the quarterly update, I'd like to take just a couple of minutes to briefly introduce myself and highlight some of the elements that I think are relevant to Nordic Nanovector.

As you can see, a large part of my career has been at Roche, where I rose within the leadership ranks and had the opportunity actually to learn from the best on various dimensions in oncology, ranging from commercial to development and into access. I had the opportunity to lead a variety of country organizations, both in developed as well as developing countries as well as at the global level. I also had -- I also directly led and indirectly drove multiple launches of brands such as Herceptin, MabThera, Avastin and numerous other oncology and nononcology products. Many of these are actually monoclonal antibodies, which are now, indeed, standards of care in the clinic.

Possibly the most relevant part of my career that is relevant to Nordic Nanovector was when I was leading the Herceptin project during what was possibly the most exciting period of its life cycle, and certainly, a product that

I think everyone can agree changed medical textbooks and changed the lives of countless patients suffering from, not only breast cancer, but also gastric cancer. I had the privilege of leading a cross-functional team, which stretched from commercial to medical to clinical science, clinical operations, manufacturing, regulatory and even into diagnostics.

Additionally, as a life cycle leader of Herceptin, which was and still is the lead compound of the HER2 franchise, I was also deeply involved in the early clinical development of the HER2 sisters, those being PERJETA and KADCYLA, and of course, KADCYLA is the armed version of Herceptin. So I'm also familiar with armed monoclonal antibodies.

Since having left Roche, I then dove straight into the exciting world of biotech, which is, of course, more resource constrained. And now since the 6th of April, less than 2 months, I have the privilege of leading Nordic Nanovector.

So I'll change gears now, and I'll share with you why I joined Nordic Nanovector and I think this also serves as a nice summary of why I believe investors, other stakeholders, and then ultimately, patients should also be excited.

First of all, at a high level, radiopharmaceuticals clearly have a key role to play in the treatment of cancer. It serves as an additional modality in attacking this disease. Radiopharmaceuticals have previously been underappreciated. The interest, however, has increased noticeably over the last couple of years. This increase is largely the result of the evolution that we've seen in the technology and the platform, which actually allows now for better targeting, better efficacy and better safety profiles.

So within this context, Nordic Nanovector, and more specifically, Betalutin is playing a key role.

Within the radioimmunotherapy space, Betalutin is one of the most attractive and advanced in clinical development with compelling data in treating non-Hodgkin's lymphoma patients. The first step of this journey is in, as you know, third-line follicular lymphoma patients, particularly in the 70% of those patients who are elderly and frail and resistant or refractory to anti-CD20 immunotherapy.

We've made significant progress in executing PARADIGME. We'll be sharing more information on that shortly. This, of course, is the pivotal Phase IIb trial.

Lastly, Betalutin is but the first step of the portfolio, and we continue to explore how to best leverage the assets that we have in the company as well as the deep heritage that we have in this space.

So our mission is to develop innovative, targeted therapies for hematological cancers where there is a high unmet medical need. As you know, non-Hodgkin's lymphoma is a common cancer and approximately 150,000 new cases are diagnosed every year in the U.S. and the largest European markets. Despite the fact that there are multiple treatment options, there remains a high unmet medical need in both the aggressive and indolent subtypes, particularly in the relapsed setting.

There's essentially 2 things that are driving this unmet medical need in this space. First of all, although rituximab-containing regimens have transformed the treatment of follicular lymphoma in the first-line setting, practically all patients will relapse. And in fact, 40% to 60% will become refractory or develop resistance within 5 years. So there's clearly a need for additional agents that can drive remission in later lines.

Secondly, follicular lymphoma, as you know, is primarily diagnosed in older people, simply due to age and associated comorbidities, compounded by cumulative toxicity and burden of multiple rounds of chemo -- cancer treatments. Many of these patients unfortunately fall into the elderly and frail category by the time they reach third line. The proportion of elderly and frail in this setting is approximately 70%.

This is where Betalutin, with its unique profile, can change the landscape for these patients, offering durable responses balanced with excellent tolerability and maintaining quality of life, all with one administration.

Diving deeper into follicular lymphoma setting, I'd like to contextualize how Betalutin's unique product profile positions it for success. So on this slide, we can see the treatment landscape across multiple lines and across patient populations. I'd like to draw attention to several things on this slide.

So first of all, from left to right, we see that the patients in later lines of therapy tend to be quite elderly and progressively more frail. In the third-line setting, these patients, as mentioned previously, represent

approximately 70% of the segment. If we look at the second-line setting, these patients represent approximately 50% of these patients. In summary, between second and third line, a large proportion of these patients are indeed elderly and frail.

Secondly, as you can see, there are multiple treatment modalities, lots of boxes, either available or under development, ranging from CAR-Ts to bispecifics to PI3 kinases. These treatment options, however, due to safety and tolerability profiles, are often limited to those patients who are still fit and therefore on the left-hand side of this graph.

You will notice that EZH2 inhibitors are portrayed here as an option. It is important to note that they have their greatest effect in patients with the relevant mutation, meaning the EZH2 mutation, which, actually, unfortunately, only represents 15% of the population. The other option that we see here in this setting is rituximab single agent, which is sometimes used simply because there are not many other options that the hematologist can offer. And let's not forget, many of these patients have, in fact, already relapsed or are refractory to rituximab, but there aren't many options, so that's why physicians go with that option.

So this means that patients who are frail and have relapsed or are refractory to rituximab regimens do not have many options.

This is exactly where Betalutin, with its unique profile, could have a very real impact for frail patients in the clinic. It offers durable responses in elderly patients who are heavily pretreated, a predictable and manageable side effect profile, all with a single-dose administration.

This positioning that I just shared with you clearly resonates with customers. So the efficacy seen in LYMRIT 37-01 - Part A was certainly seen as a strength. We saw approximately 70% overall response and median duration of response of about 13.6 months. More specifically, we saw 32% achieve a complete response with a median duration of response of 32 months. This was seen as compelling by HemOncs in the clinic. This is then combined with the manageable safety profile, I'll be going into more details of that shortly, and the simplicity of a onetime treatment.

So in summary, the positioning, as depicted in the previous slide, clearly resonates with customers when they see the LYMRIT 37-01 - Part A data.

So over the next couple of slides, I'll provide a high-level view of the clinical data, so 2 slides on that. And then I'll go into a little bit more detail on the safety and tolerability. And these are, in fact, the reason to believe for the potential for Betalutin.

So here, we see a waterfall chart, which summarizes the data from LYMRIT 37-01 - Part A with each bar representing a patient. The Y-axis is the change in tumor size as a percent of baseline. So lines going down is good. The first conclusion we can draw is that there is a lot of surface area under the X-axis. In fact, 90% of evaluable patients had a reduction in tumor size and derived a clinical benefit from a single-dose administration.

Secondly, Betalutin is clearly active, and we see that follicular lymphoma and marginal zone lymphoma are particularly radio-sensitive.

On this slide, we see another perspective of the efficacy seen in relapsed/refractory patients. Here, I'd like to draw attention to the third line in bold, roughly in the middle of the slide, where we can see that follicular lymphoma patients with 2 or more prior therapies achieved an overall response rate of 70%. Of the 32 who had a complete response, we saw that median duration of response was a remarkable 32 months, again, with a single administration.

So that was on efficacy. Now changing gears in terms of tolerability. Again, the data from LYMRIT 37-01 - Part A shows that the side effects were primarily hematological in nature. You can see this on the right-hand side of the slide. These are transient and reversible drops in lab results such as platelets and white blood cells, something hematologists are clearly comfortable managing.

What's remarkable -- on the left-hand side of the slide, what is remarkable is that this is in a population that has a median age of 68 years and is heavily pretreated. This is certainly gentle when compared to the other clinical options available for later-line follicular lymphoma patients, now I'm referring back to the landscape slide that I shared with you earlier.

So in summary, what we saw over the last 3 slides is our reason to believe that Betalutin offers the potential for durable responses, particularly in relapsed/refractory, elderly and frail patients, a gentle side effect profile, all within a single administration.

So now let's take a look at PARADIGME. So as a reminder, as a result of the LYMRIT 37-01 - Part A data that I just shared with you, PARADIGME, the Phase IIb trial, was designed to determine the value of Betalutin in third-line follicular lymphoma patients. As previously communicated as well, the primary endpoint is overall response rates with secondary endpoints being duration of response, progression-free survival, overall survival and the quality of life. The original design was to randomize across 2 arms with differing doses.

After the interim analysis last summer, the Independent Review Committee recommended to continue only with the 40/15 arm. As a result of this, and of course, in agreement with the FDA, the patient numbers were then reduced from 130 to 120.

Since our last quarterly call, we have added 10 fully enrolled patients. And after we checked yesterday, we have 4 in screening, 2 of whom will be enrolled in the coming days. Given that in Q3 of last year, 3 patients were enrolled, and in Q4, we recruited 14, we now have a similar order of magnitude of patients compared to last quarter, and this is despite the significant COVID restrictions seen, particularly in Europe.

So this slide, I'd like to provide a little bit more detail in terms of -- and context on the PARADIGME trial. What we've seen is that the clinical trial amendments as well as the improved trial execution are clearly delivering results.

So as a reminder, the amendments to the protocol expanded the inclusion criteria to allow for 2 sets of patients. The first set of patients were those who had previously received autologous stem cell transplantation, and the second set of patients were those who had lower platelet counts at baseline. These 2 changes have allowed for a greater proportion of patients to be considered and is what brought us to this higher level of enrollment. Additionally, we, of course, continue to focus on a variety of initiatives that are designed to accelerate patient recruitment.

This higher level of recruitment was despite the significant challenges that COVID restrictions have brought, especially in Q1 of this year in comparison to Q4 of last year, particularly in Europe. As you're likely aware, follicular lymphoma is an indolent disease, meaning that even under normal circumstances, part of the clinical strategy of managing patients is to watch and wait. Now as a result of COVID, ESMO last year issued guidelines, which called upon clinicians to do more watching and waiting to prevent patients from having to come into the clinic. What we have seen and has indeed been confirmed by Q1 calls with other companies that are active in the follicular lymphoma space, the number of patients suffering from follicular lymphoma coming through the clinic has dropped by about 20% to 30%. So as COVID restrictions are lifted, we expect this to have a positive effect on our continued recruitment of patients into PARADIGME.

So with all of the above considerations, we expect to complete enrollment, allowing for top line results to be shared by the end of 2021.

So upon completion of PARADIGME, we have a clear regulatory strategy to gain rapid approval. So our BLA filing with the FDA for accelerated approval will be based on the PARADIGME data as well as the initiation of a confirmatory Phase III trial, which we intend to focus on second-line patients. Our plans would be to do this during the course of 2022.

It is also worth noting that the Fast Track designation granted in the U.S. means that we have a stronger dialogue with the FDA, which we are certainly utilizing.

So coming on to my last slide before handing over to Malene to cover the financials. As I'm sure you've seen in yesterday's press release, we now have additional reason to believe in the potential for Betalutin in addressing the unmet medical need in the follicular lymphoma setting. So just as a reminder, Archer-1, a small Phase Ib trial, was designed to evaluate the safety and tolerability of Betalutin when used in combination with the mainstay rituximab. The secondary objective was to evaluate the antitumor activity of this combination. The study population was in follicular lymphoma patients who had received 1 or more regimens. These are earlier lines of -- and this is an earlier line of patients to those in the PARADIGME trial.

What was seen was that the excellent safety and tolerability was similar to that observed in LYMRIT 37-01 - Part A, also when used in combination with rituximab. What we also saw was that 7 out of 7 patients achieved a response, 5 of whom were complete responders. We now have another data point confirming the activity of Betalutin in patients suffering from follicular lymphoma.

The key insights derived from this trial are certainly hypothesis-generating and is, of course, being taken into consideration as we evaluate the design of the confirmatory Phase III study that I mentioned earlier in second-line follicular lymphoma. The design will, of course, be finalized in collaboration with experts in the lymphoma space as well as in consultation with the FDA.

So with that, I'll pause and hand over to you, Malene. So over to you.

Presenter Speech

Malene Brondberg (Executives)

Thank you very much. Good morning, everyone. So on the next slide, you can see that we have kept the good cost control. If you look at the Q1 this year, we had NOK 101 million in spending, which is lower than last year of the NOK 126 million. And we've kept the -- as I said, the cost control in place. And we, of course, still continue to spend most of the money as we should on CMC and clinical.

You can also see here that with the cash flow, we had a minus NOK 134 million, which is a little bit more than last year, but that's simply just to the fact that we have more bills to pay in this quarter.

And on the next slide, you can see that the cash run rate, which has now, as Jan also said, has extended into the second half 2022 and that's, of course, due to the -- we have the 2 placement or the first of one was the private placement in February, which gave us NOK 361 million; and another one, which was the repair, a very successful repair, which was NOK 61 million. So in total, that's NOK 422 million in gross, which net is NOK 395 million. This means, as I said, that we have cash into the second half 2022.

With that, I would like to hand it back to you, Peter.

Presenter Speech

Peter Braun (Executives)

Okay. Thank you, Malene. So on to our summary slide. So in summary, we are well positioned to win. Radiopharmaceuticals clearly have a key role to play in the future of cancer therapy, and we're well positioned there.

Betalutin is an important and exciting product opportunity, in fact, one of the most attractive and advanced in this radiopharmaceutical space.

We're clearly focused on completing PARADIGME, and we target to have preliminary 3-month top line data by the end of this year. And I hope that you agree that despite the COVID challenges that we've had, we've brought the recruitment levels to another order of magnitude.

And then, lastly, beyond PARADIGME, multiple opportunities exist for us to go beyond Betalutin, and we would build then on the proprietary anti-CD37 franchise that we have and build upon the heritage that we have in radiopharmaceuticals.

So with that, I'll stop presenting and open the floor to any questions that you may have.

Answer

Unknown Executive (Executives)

Thank you, Peter. We do have quite some questions today, and I have tried to group them into some topics. And then we will collect the latest arrivals in the end.

First of all, a lot of questions about the progress. First question is, "What is the rationale for reiterating readout of top line data second half of '21 when patient recruitment is significantly lower than expectations communicated in the Q4 presentation?"

Answer

Peter Braun (Executives)

Okay. I'll -- this is Peter. I'll address that one, and then I'll ask Marco if he has anything else to add.

As was shared, if you look at the Q3 numbers that we had last year where recruitment was approximately 3%, the changes that were made -- the amendments that were made and also all the efforts that went into the operational aspects of the trial last year, we have significantly improved the recruitment rate to another level. So in Q4, we had 14 patients included. So this quarter's numbers of 10, when you include as well the patients that are in late-stage screening, so you can add another 2 because they will be included in the coming days, we're clearly at another level.

Now so -- and that's, of course, within the context of what has been, particularly in Europe, a very challenging environment to include patients that are in the non-Hodgkin's lymphoma space, particularly follicular lymphoma. What we saw, and as I shared in the presentation, what we and clinicians have seen is a significant drop of 20% to 30% of patients coming through the clinic.

So within that context, the number of patients that were recruited and included in the trial is clearly at another level. So we are at that higher level. And as, particularly here in Europe, we pull out of the COVID situation, we do expect to see more patients coming through the clinic and we do expect to be able to capture and benefit from that increased patient flow through the clinic.

So Marco, do you have anything else that you want to add to that?

Answer

Marco Renoldi (Executives)

No. I think you covered it very well, Peter. I would only emphasize that clearly, the impact of COVID restrictions in Q1 in Europe were probably higher than we had anticipated. However, we see the impact of vaccination program are changing the landscape in many countries, starting from the U.K., Germany and Southern European countries.

So we see that the initiatives that we implemented are really bringing a different path -- a different type of patient enrollment. And with the support of the vaccination program and the lifting of COVID restrictions, we have great hopes that in the next few quarters, we will be able to achieve the level -- the desired level of enrollment that everybody expects.

Answer

Unknown Executive (Executives)

Thank you, Marco and Peter. The next question is whether it is possible to do a top line efficacy readout around new year even without 100 -- sorry, even without 120 patients enrolled at that point.

Answer

Peter Braun (Executives)

Well, let me, first of all, reiterate that our intention is to complete recruitment within the time frame foreseen. So that's clear. And the intention is to provide top line data by the end of the year.

I don't know, Marco, do you want to add anything else? No? Okay.

Answer

Unknown Executive (Executives)

Thank you. And how much time do you think you need from readout of top line data from PARADIGME to a completed BLA for Betalutin to be sent to the FDA?

Answer

Peter Braun (Executives)

Marco, do you want to handle that one?

Answer

Marco Renoldi (Executives)

Yes. Of course, in order to have validated data, so clean data that you can use for the regulatory submission, you clearly need, and we mentioned this during the previous quarterly call, 6 to 8 weeks, but this may not be required in terms of providing top line data. So I think you need to consider what is the reason why you are -- for what scope you are communicating the data. But it's about 6 to 8 weeks to complete the cleaning of the data in order to be able to file them for your BLA package.

Answer

Unknown Executive (Executives)

Thank you, Marco. Is there an increase in screening? And how many patients do you expect to recruit each month until readout?

Answer

Peter Braun (Executives)

As mentioned earlier, what we've seen as a result of COVID restrictions over the last quarter is that there was a pullback in the number of patients coming through the clinic. As we pull out of the COVID restrictions, those numbers will indeed increase. And again, I would like to reiterate that we confirm our expectation to be able to complete recruitment and provide top line data by the end of the year.

Marco, I don't know if you want to add anything. No, we're good. Okay.

Answer

Unknown Executive (Executives)

Okay. And can you say something about which countries show the best recruitment? And how was the distribution of recruitment for the past 3 months?

Answer

Peter Braun (Executives)

Yes. As was previously communicated in previous quarterly calls, we don't comment on recruitment by country. What we can say is that there are additional countries that are coming online. So -- but we won't comment on specific country numbers and evolutions within countries.

Marco, anything? No? Okay. We're good.

Answer

Unknown Executive (Executives)

Good. And the next question is whether you can say something about the proportion of trial sites in Europe, higher level.

Answer

Peter Braun (Executives)

Marco, do you want to comment?

Answer

Marco Renoldi (Executives)

Yes. We clearly have a higher number of sites in Europe compared to other regions in the world, whether it's the U.S. or Asia or other regions. But this is quite normal. Most of hematology/oncology trials with any type of drugs do have majority -- the majority of sites in the European region. So this is quite aligned to, certainly, my experience with a series of other oncology companies.

Answer

Unknown Executive (Executives)

Thank you. Then there's another question, "In order to be able to read top line data towards the end of the year, when must PARADIGME be completed by the latest?" So another variation of the same question asked before.

Answer

Peter Braun (Executives)

Yes. Can you repeat the question? Sorry.

Answer

Unknown Executive (Executives)

Yes. "In order to be able to read top line data towards the end of the year, when must PARADIGME be completed by the latest?"

Answer

Peter Braun (Executives)

Again, we'll -- I'll just reiterate that we expect to complete recruitment in such a way that we can provide top line data by the end of the year.

Answer

Unknown Executive (Executives)

Thank you. Then we have a longer question that we have been asked to read out in his whole formulation, and it's about the guided 3-month readout also. "Can you elaborate on how the recruitment is going to increase? Give some specific data and build some confidence for the general investor. Which countries are expected to increase and why? And is it just based on severity of corona?"

Answer

Peter Braun (Executives)

Okay. Marco, can you handle that one?

Answer

Marco Renoldi (Executives)

Yes. I think as I mentioned earlier, we clearly see the impact of vaccination program throughout key European countries, large European countries where we have a fairly high number of sites. I'm talking about the U.K., I'm talking about Germany, talking about Italy and Spain. We feel that with the softening of the COVID restrictions, this country, which have a fairly high number of enrolling sites, will be able to go back to the full ability to enroll patients. And we expect that with their strengthened contribution to enrollment and the impact of the amendment that we approved throughout the participating countries, we can go back to the expected rate of enrollment.

Answer

Unknown Executive (Executives)

Thank you, Marco. By -- with that, I think we have covered the questions that have come in, in relation to PARADIGME and the data readout.

We'll move to Archer. "When do you expect data from cohort 2 in the Archer study?"

Answer

Peter Braun (Executives)

Marco, can you handle that one?

Answer

Marco Renoldi (Executives)

The data that was communicated in the press release issued yesterday includes the data from both cohort 1 and cohort 2. If you recall, we had 3 patients in cohort 1 and 4 patients in cohort 2. And we felt it was appropriate to provide a comprehensive summary of both efficacy and safety.

And as Peter highlighted in his presentation, we had 7 responses out of 7 patients. So both patients in cohort 1 and patients in cohort 2 responded and the responses are still ongoing in all of the patients and at least some of them, I think 4 or 5 of them, have already reached 2 years since the administration of rituximab -- since the administration of Betalutin. Apologies.

Answer

Unknown Executive (Executives)

Thank you. "And is it possible that the 2 PRs in Archer-1 after time -- or over time, I guess, can become CRs? Or is this very unlikely?"

Answer

Marco Renoldi (Executives)

It's difficult to predict. Clearly, as you remember from the design of the study, these patients are on long-term maintenance with an anti-CD20 with rituximab, which is administered again for 2 years.

So it could be that, of course, with the impact of maintenance therapy, these patients could possibly evolve. But it's very difficult for me to address your question. I would need probably a crystal ball to address the question.

Answer

Unknown Executive (Executives)

"Will you actively seek a partner for the next phase of Archer?"

Answer

Peter Braun (Executives)

Jan, do you want to handle the partner question?

Answer

Jan Egberts (Executives)

Yes. No, we're not going to make any specific statements regarding potential partnership discussions. So that's really where like for strategic and -- reasons, we're not going to disclose that information at this stage.

Answer

Unknown Executive (Executives)

Thank you, Jan. The last question about Archer would be, "When do you expect to make a decision regarding the next step for Archer-1?"

Answer

Peter Braun (Executives)

Yes. So maybe just as a summary with Archer-1. What we saw was, again, excellent safety and tolerability that was similar to what we have seen in LYMRIT. And this is within the context of combination with rituximab.

Secondly, we saw excellent data confirming [indiscernible]. Sorry, there's a bit of noise in the background there. I'm not sure. So clearly, the key insights that we derive from this trial are certainly hypothesis-generating, and this is certainly being taken into consideration as we look at the Phase III study that we're evaluating for second-line follicular lymphoma.

So this is going to be feeding and informing the step that we will be taking past PARADIGME. And that design will, of course, be finalized together with experts in the field as well as in consultation with the FDA.

Answer

Unknown Executive (Executives)

Thank you, Peter. We will move to partnerships and commercialization. The first question is, "What is your strategy to get Betalutin approved in MZL the fastest way possible while retaining as much as possible the upside to the company?"

Answer

Peter Braun (Executives)

Okay. Marco, do you want to comment on MZL?

Answer

Marco Renoldi (Executives)

Yes. As Peter highlighted in his presentation, we saw very promising data on marginal zone lymphoma patients. You recall both the waterfall and the actual response rates in the 9 marginal zone lymphoma patients. We had considered last year, if you recall, the possibility to include an arm in the PARADIGME study to enroll enough marginal zone lymphoma patients to further understand the efficacy level and consider a potential development plan. But in the end, we prefer to focus on timely completion of the trial.

Clearly, marginal zone lymphoma represents an interesting opportunity. It is not as large an opportunity as follicular lymphoma, and therefore, we are still considering how we can best maximize this option from a regulatory perspective. Peter alluded to the Phase III, which we are currently planning to activate. It's a requirement to file for accelerated approval. Of course, we will focus on second-line follicular lymphoma. We will explore options to consider how to best move forward marginal zone.

But at the time being, we have no clear plan. But bear with us, and we'll provide further details. We know marginal zone is a radio-sensitive tumor, and we know that Betalutin can provide marginal zone lymphoma patients with a clear benefit. But of course, we need to maximize the path to approval, and therefore, we still have a lot of thought to be given to this topic.

Answer

Unknown Executive (Executives)

Thank you, Marco. We have some questions about partnerships again and commercial strategy. And I think, well, they are a little bit similar, but I'll try to cover it all.

One question is, "The commercial strategy for Betalutin in Asia and Europe is to establish partnership. Or is this work progressing?"

And same kind of question, "Are you -- are there any dialogues regarding a partnership?

"And if Betalutin gets approval, would you prefer to sell the company? Or would you prefer to build a sales organization and sell by yourself?"

Answer

Peter Braun (Executives)

Okay. Jan, do you want to take that?

Answer

Jan Egberts (Executives)

Yes. No, like very similar to what I said before, for very obvious competitive reasons, we cannot disclose specifics regarding potential discussions we are having with one or more parties.

Answer

Unknown Executive (Executives)

Thank you, Jan. Then we have one question about financing. "Will there be another capital issue this year?"

Answer

Malene Brondberg (Executives)

As I said, we have money now going into the second half of 2022. And of course, it always depends on the pipeline and whatever. But we have, as we said, we have money now to the completion of the PARADIGME, and that is, of course, where our focus is.

Jan, I don't know whether you want to say more.

Answer

Unknown Executive (Executives)

Thank you, Malene. Then we have a couple of questions about the same topic related to -- and I think this goes to you, Marco. "MEI Pharma recently received accelerated approval for their agents for 3L based on a sample of 91 patients. Their original population target was 130. Do you view it as possible to achieve AA based on less than 120 patients?"

Answer

Marco Renoldi (Executives)

Can you please repeat? Because we know that MEI Pharma informed The Street that the FDA accepted their application for marginal zone lymphoma. So can you please repeat the question because this is what was reported in the past few days.

Answer

Unknown Executive (Executives)

Yes. I'll try once again. It says, "MEI Pharma recently received accelerated approval for their agent for 3L based on a sample of 91 patients with an original target of 130 patients. And in light of that, do you see it possible to achieve AA based on less than 120 patients?"

Answer

Marco Renoldi (Executives)

Okay. So maybe we'll leave the disconnect on the approval to another date. But what I can tell you, and I'm speaking on behalf of my colleagues in the clinical and regulatory teams, we have had robust discussions with

the FDA on several occasions during 2020 and 2021 when we discussed the different amendments related to new patients to be enrolled in the PARADIGME trial regarding the recommendation from the Independent Review Committee to reduce the trial from 2 arms to 1 arm. On the occasion of these interactions, we also discussed quite some level of detail what would be the required type of efficacy and safety information to file a BLA package amenable for receiving accelerated approval.

So we believe that with the data that we have collected to date, once we have completed PARADIGME and pending data and with the additional wealth of safety data collected in the other trials, we will be able to meet the expectations of the FDA. So I hope that clarifies the question.

Answer

Unknown Executive (Executives)

Thank you, Marco. And with that, I believe we have covered all the questions that have been submitted. So thank you, everyone, for sending it.

Answer

Peter Braun (Executives)

Okay. Good. Then I think there's only one slide left, and that's simply a reminder of the upcoming dates. Yes, you can see them on the screen.

And thank you very much. And I think this was, I hope you agree, a nice quarterly summary and my first one for Nordic Nanovector. So looking forward to hearing you either later today, in the coming weeks and certainly in approximately 3 months. So thank you.

21.04.28. Nordic Nanovector ASA- Shareholder/Analyst Call. AGM

Presenter Speech

Jan Egberts (Executives)

Good afternoon, dear shareholders. Welcome to the Annual General Meeting of Nordic Nanovector ASA. My name is Jan Egberts, and I'm the Chairman of the Board. With me here is the -- our new CEO, Peter Braun, who you will meet during the upcoming announcement of the first quarter; CFO, Malene Brondberg, who you already have met; as well as the company's Counsel, Fredrik Haavind. The company's auditor, [Tommy Ramskauf], from Ernst & Young is here as well.

We assume that all shareholders and proxies present are registered and that the voting slips have been handed out. If someone still hasn't registered, I hope that this is done now by the entry of the building. The company's VPS account, Nordea, is present and will assist us to register the shareholders and proxies.

A record of the shares that are represented in the general meeting shall be attached in the minutes. Nordea has finished the registration. Of 21,530,678 shares of a total of 97,968,014 shares are represented here today at our general meeting. That means that approximately 21.98% of the company's shares are represented here today. The election of Chairperson to the meeting and a person to co-sign the minutes is the first item.

It is suggested that I'll chair the general meeting as the Chairman of the Board of the company. For this reason, the general meeting will be conducted in English language as my Norwegian is very poor. The minutes of the general meeting shall be signed by the Chairperson and at least one other person elected by the general meeting amongst those present. I'd like to suggest that Fredrik Haavind, our General Counsel, is elected to co-sign the minutes. I want to keep a bit of pause to see if there are any other volunteers.

If not, I hereby appoint Fredrik Haavind to co-sign the minutes.

The first item is the approval of the notice and the agenda. The notice and the agenda have been sent to all shareholders with a known address. The information and documents concerning the general meeting are published -- have been published on the company's website. With this, the general meeting is convened in accordance with the articles of association and those rules that apply for listed companies in Norway. We therefore assume that no one has any objection to the notice. I'll give a bit of pause. I'm going to see if there are any comments.

It seems there are no comments. So therefore, the notice is deemed to be legal. We have, at this stage, completed the constitution of the general meeting and will now go ahead with the matters on the agenda. The first item is the approval of the annual accounts and Board of Directors' report for 2020.

The first matter on the agenda is approval of the company's annual accounts and the Board of Directors report for Nordic Nanovector and the group for the financial year 2020, including the allocation of the result of the year as well as consideration of the statement on corporate governance. The annual accounts, the Board of Directors' report and the statement on corporate governance are included in the company's annual account for 2020, which have been published on our company's website.

The company had no revenue in 2020 and recorded a loss for this year -- for the year 2020, from NOK 417.6 million. The Board has proposed for the general meeting to approve the annual accounts and the Board of Directors' report for Nordic Nanovector ASA and the group for the financial year 2020.

Are there any objections to the proposal? Again, I'll give a bit of silence and wait.

I don't hear any objections. With respect to the results, we received a total number of 20,900,798 advanced votes and voting instructions for the proposal and 230,235 against, and 8,578 abstained votes. This general meeting against said number of votes is considered to have adopted this resolution.

The next item on the agenda is the approval of the guidelines for remuneration of the senior executive. Pursuant to Section 16 -- excuse me, Section 6-16A of the Norwegian Public Limited Companies Act, the Board has prepared guidelines for remuneration of senior executives, the so-called guidelines. The guidelines are available on the company's website.

The Board has proposed for the general meeting to approve the guidelines for remuneration of senior executives. Are there any objections to this proposal? Again, I'll keep a bit of silence.

We have received a total number of 20,729,782 advanced votes and voting instructions for the proposal, of which 400,800 were against, and 83,959 abstains. This general meeting against set number of votes is considered to have adopted this resolution.

The next item is the approval of the auditor fees.. The auditor fees for Ernst & Young for the year 2020 is NOK 320,000 ex-VAT. For information on other fees paid to the company's auditor, reference is made to Note 3.7 of the annual account. The Board has proposed for the general meeting to approve the auditor's fee for the year 2020. Are there any objections to the proposal? As usual, I'll keep about 10 seconds quiet.

I have not heard any objections. We have received a total number of 21,205,853 advanced votes and voting instructions for the proposal, with naught against, [800 and -- 8,688] abstain. This general meeting against certain number of votes is considered to have adopted this resolution.

The next item is a determination of remuneration to the members of the Board, including the approval of the issuance for RSUs to the members of the Board. References made to the recommendation of the Nomination Committee, which is available on our company's web -- on our website and to Item 9 in the notice to this meeting regarding the authorization to the Board to increase its share capital in connection with the Board member remuneration.

The Nomination Committee has proposed to the general meeting to approve the remuneration to the Board, including the approval of issuance of restricted stock units, so-called RSUs, to members of the Board, in accordance with the recommendation of the Nomination Committee. The amounts are NOK 600,000 to the Chairman and NOK 330,000 to each of the members of the Board, plus remuneration for subcommittee work for the period from this Annual General Meeting and until next year's Annual General Meeting. Are there any objections to the proposal? Again, I'll stay quiet for about 10 seconds.

I have not heard any objections. We have received a total number of 20,791,038 advanced votes and voting instructions for the proposal, of which 336,885 are against and 11,688 abstain. This general meeting against set number of vote is considered to have adopted this resolution.

The next item on the agenda is the determination of remuneration to the members of the Nomination Committee. Again, reference is made to the recommendation of the Nomination Committee, which is available on our website.

The Nomination Committee has proposed for the general meeting to approve the remuneration to the members of the Nomination Committee in accordance with the recommendation of the Nomination Committee. The amounts are NOK 45,000 to the Chairman of the Committee and NOK 25,000 to each of its 2 members for the period from this Annual General Meeting and until next year's Annual General Meeting. Are there any objections to this proposal? And again, I'll wait about 10 seconds.

Again, I didn't hear any objections. So the following are the results. We have received a total number of 21,047,313 advanced votes and voting instructions for the proposal, of which 80,610 are against and 11,688 abstain. This general meeting against set number of votes is considered to have adopted this resolution.

The next item on the agenda is the resolution to issue freestanding warrants in connection with the PSU program. Since the end of 2017, the company has granted its employees about 2.5 million performance share units, so-called PSUs. Approximately 700,000 of those PSUs have already left. As employees have left or fasting conditions have not been met. Subject to all remaining vesting conditions being met, the remaining PSUs would give an approximate 1.8% dilution to the currently issued share capital.

In order to secure compliance of the company's obligations in the company's long-term equity incentive plan, the Board proposes that freestanding warrants are issued to the company's senior management and key employees who are allocated PSUs after the Board has been authorized to do so under Item 4 above.

The Board proposed that the general meeting passed the following resolutions:

#1, the company shall issue a minimum of 10,000 and a maximum of 1.5 million freestanding warrants.

#2, each independent subscription right shall, subject to the terms set out below, give the right to subscribe for 1 new share in the company with a nominal value of NOK 0.20. The freestanding warrants can be subscribed by employees, who have been awarded PSUs under the company's long-term equity incentive plan upon the decision by the Board during the period from the Ordinary General Meeting in 2021 to Annual General meeting 2022, the period. So basically from today to our AGM next year. The employees will have a right to subscribe for 1 freestanding warrant for each allocated PSU during that period.

Existing shareholders shall not have preferred rights to subscribe to freestanding warrants pursuant to the Norwegian Public Limited Companies Act, Section 11-13 CF Section 10-4 and Section 10-5.

Point #4, the subscription period for the freestanding warrant shall be from the 1st of February 2022 until the 30th of March 2022. The freestanding warrants have subscribed on a separate subscription form.

Item #5, no compensation shall be paid for the issuance of the freestanding warrants.

#6, the subscription price to be paid for the shares issued on the basis of the freestanding warrants shall be the par value of the shares, which is NOK 0.20 per share.

Item #7 or Point #7, the holder can only exercise the freestanding warrants to subscribe for shares the holder is entitled to subscribe pursuant to be PSUs allocated during the period. So that no free standing warrants can be exchanged for shares later than 5 years following the date of this general meeting.

Point #8. The holder of the freestanding warrants shall not have rights as shareholder with regard to capital increases, capital reductions or resolution to issues of subscription rights, dissolution, merger, demerger or reorganization, except with respect to shares that have been issued due and paid for by the freestanding warrant holder.

Upon changes in the company's share capital, such as a share split, the reverse split and other capital actions as provided for in the PSU agreement, the subscription rights, terms, the subscription price and/or the number of shares to be issued upon exercise shall be adjusted as set out in the PSU agreements.

Point #9, shares issued on the basis of freestanding warrants shall give rights to dividends declared following the date the shares are issued.

And Point #10, the final point, as part of the long-term equity incentive plan, the freestanding warrants cannot be transferred. The outstanding freestanding warrant will lapse if the conditions for exercising them are not met.

But the question to you, are there any objections to this proposal? Again, I'll keep some bit of silence.

Okay. I don't hear any objections. In total, we have received a number of 20,658,052 advanced votes and voting instructions for the proposal. 476,606 against and 4,953 abstain. This general meeting against set number of vote is considered to have adopted this resolution.

The next item on the agenda is the authorization to the Board to increase the share capital in connection with the exercise of RSUs. The Board has a need for an authorization to issue shares for the company to be able to fulfill its obligation under the company's RSU program for Board members, which is described on Page 95, in the company's annual report for the year 2020.

The Board proposes that the authorization may be used to increase the share capital with up to NOK 75,000. As the authorization shall be used in connection with issuance of shares to our RSU holders, the Board proposes that it's authorized to deviate from the shareholders' preferential rights subscribe for and be allotted new shares. The Board proposes that the general meeting pass the following resolutions:

#1, pursuant to Section 10-14 of the Norwegian Public Limited Companies Act, the Board is authorized to, in one or more occurrences, increase the company's share capital by up to NOK 75,000.

Resolution #2, the authorization may only be used to issue shares to members of the Board -- company's Board upon exercise of awarded RSUs.

And Resolution #3, the authorization is expanded for a period of 2 years from the date of this resolution.

Resolution #4, the shareholders' preferential right to the new shares pursuant to Section 10-4 of the Norwegian Public Limited Companies Act, may be deviated from.

Resolution 5, the authorization does not comprise share capital increases against contribution in kind, CF, Section 10-2 of the Norwegian Public Limited Companies Act.

Resolution 6, the authorization does not comprise share capital increase in connection with merger pursuant to Section 13-5 of the Norwegian Public Limited Companies Act.

And Resolution #7, this authorization replaces the authorization granted at the Annual General Meeting in 2020 for the same purpose from the date this new authorization is registered in the Norwegian register of business enterprises. A question to you, if there are any objections to this proposal.

I have not heard any objections. We have received a total of 20,780,881 advanced votes and voting instructions for the proposal, and 354,550 against and 4,180 abstain. This general meeting against set number of votes is considered to have adopted this resolution.

The next item on the agenda is the authorization by the Board to increase the share capital by up to 20% for other specified purposes.

To give the Board financial flexibility in connection with an acquisition or a similar transaction or to strengthen the company's equity in general, the Board proposed that it's given an authorization to issue shares for these purposes. In particular, Nordic Nanovector is in a late-stage development of its product candidate, Betalutin, and the company is preparing to be ready to build a commercial organization to launch Betalutin on one or several markets should the clinical data to be reported support and application for marketing authorization. It will be important to a Nordic Nanovector to be able to act in a flexible way to cover the need for financial resources in this important phase of our company's developments. It could be in the best interest of the company and our shareholders that placement of shares are directed at certain named individuals and/or enterprises. The Board's requested for that the authorization also encompasses the right for the Board to waive the shareholders' preemptive rights. Based on this, the Board proposes that general meeting pass the following resolutions.

Resolution #1, pursuant to Section 10-14 of Norwegian Public Limited Companies Act, the Board is granted an authorization to increase the company's share capital in one or more occurrences by up to NOK 3,810,749.

Resolution #2, the authorization may be used to strengthen the company's equity for general corporate purposes, including, but not limited to financing of acquisitions of other companies, businesses or assets, including of issuance of consideration shares in connection with the above mentioned transactions.

Resolution #3, the authorization is valid until the company's annual general meeting in 2022, but no longer June 30, 2022.

Resolution #4, the shareholders' preferential right to the new shares, pursuant to Section 10-4 of the Norwegian Public Limited Companies Act, may be deviated from.

And Resolution #5, the final resolution, the authorization comprises share capital increases against contribution in cash and in kind and the right to impose special obligations on the companies, et cetera, Section 10-2 of the Norwegian Public Limited Companies Act. The authorization covers resolutions on mergers as provided in Section 13-5 of the Norwegian Public Limited Companies Act.

Again, I ask the question now if there are any objections to this proposal?

I didn't hear any objections. We have received a total number of 18,666,014 advanced votes and voting instructions for the proposal, of which 2,450,660 are against and 22,930 abstain. This general meeting against set number of loads is considered to have adopted this resolution.

The next item on the agenda is the election of Board members. Reference is made to the recommendation of the Nomination Committee, which is available on our company's website. It is proposed for the general meeting to approve the following reelections.

First of all, Jan-Hendrik Egbert as Member and Chairman of the Board of Directors, which is me; secondly, Mr. Per Samuelsson as Board member; thirdly, Dr. Jean-Pierre Bizzari as Board member; also Dr. Rainer Boehm, as

Board member; Ms. Joanna Horobin as a Board member; Mrs. Karin Meyer as a Board member. And to approve the new election of Solveig Hellebust, as Board member for the period until next year's Annual General Meeting. Again, I ask the question, are there any objections to the proposal?

Again, I don't hear any objections. We have received a total number of 20,945,082 advanced votes and voting instructions for the proposal, of which 250,521 are against and 18,938 abstain. This general meeting against that number of votes is considered to have adopted this resolution. I want to thank you for your support again, and your vote in the Board.

I take the opportunity also to thank Mrs. Hilde Steineger for her valuable contribution, having served as our Board member since November 2014. And who has now, due to her increased workload, responsibilities and competing priorities, decided not to stand for election. We really appreciate all her help and support and energy she has dedicated to the company.

The next item on the agenda is the election of the members of the Nomination Committee. Again, references made to the recommendation of the Nomination Committee is available on the company's website. It's proposed for the general meeting to approve the reelection the following members: Mr. Johan Christenson as member and Chairman of the Nomination Committee; Dr. Egil Bodd as member of the Nomination Committee; and Mr. Pal Erik Robinson as a member of the Nomination Committee for the period until next year's Annual General Meeting. Again, I ask the question, are there any objections to this proposal?

I didn't hear any objections. We have received a total number of 21,116,516 advanced votes and voting instructions with the proposal, of which 157 against and 22,938 abstain. This general meeting against set number of votes is considered to have adopted the resolution.

We have now made it through the entire agenda. The Extraordinary General Meeting in Nordic Nanovector is hereby completed. I want to thank you for all your support over the past year and look forward to a very successful 2021. Thank you, and have a good day.

21.03.22. Nordic Nanovector ASA- Shareholder/Analyst Call. EGM

Presenter Speech

Jan Egberts (Executives)

Good morning, ladies and gentlemen. Welcome, dear shareholders. Welcome to the Extraordinary General Meeting of Nordic Nanovector ASA. My name is Jan Egberts, and I'm the Chairman of the Board.

With me here on the webcast is the interim CEO, Lars Nieba; and our CFO, Malene Brondberg; as well as the company's counsel, Fredrik Haavind. I assume that all shareholders and proxies present have been registered, and that our voting slips have been handed out. If someone still hasn't registered, ask you now to do this by the venue's entrance in the case you are there in person.

The company's PPS, Account Manager Nordea, is present and is assisting us to registered shareholders and proxies. A record of the shares that are represented in the general meeting shall be attached to the minutes. Nordea has finished the registration at 23,379,137 shares of a total of 95,268,734 shares are represented at today's general meeting. That means that approximately 24.54% of the company's shares are represented. It is suggested that I'll Chair the meeting as the Chairman of the Board of the company. For this reason, the general meeting will be coordinated in the English language, as my Norwegian language skills are fairly nonexistent.

The minutes of the general meeting shall be signed by the Chairperson and at least one other member elected by the general meeting amongst those present. I hereby suggest that Fredrik Haavind is elected to co-chair the minutes. I now open the floor to see if there are any other suggestions.

I don't think there are any suggestions. So Fredrik Haavind is hereby asked to co-sign the minutes.

The notice of the agenda have been sent to all shareholders with a known address. The information and the documents concerning the general meeting have been published on our company's website. Thus, the general meeting is convened in accordance with the articles of association and those rules that apply for listed companies. We, therefore, assume that no one has any objections to the notice. Are there any comments?

There do not seem to be any objections. So the general meeting is declared duly convened hereby.

We have, at this stage, completed the constitution of the general meeting and will now go ahead with the matters the agenda. The first matter on the agenda is authorization to the Board to increase the share capital related to the repair offering in the company. Again, the proposal has been published on the company's website.

The company has recently carried out a private placement. The purpose of the proposed Board authorization is to allow the company to carry out a repair offering, if appropriate. Such offering would allow existing shareholders where primarily minority shareholders who were unable to participate in the financing due to the minimum purchase requirement, and hence, have not been allocated shares in the private placement to participate in this private placement, well at the same terms and ensure equal treatment of all shareholders.

The Board has intended to complement the repair offering unless the trading price of the company's share over time is lower than the subscription price in the private placement. And the subsequent repair offering has become redundant, which is subject to the sole discretion of the company's Board of Directors. The repair offering will, if implemented, be directed towards the company's existing shareholders as of February 23, 2021, as registered, the Norwegian Central Securities Depository on February 25, 2021, were not allocated shares in the private placement.

The subscription amount for the shares issued in the repair offering will be the same as for the private placement, NOK 22.75. Are there any objections to the proposal?

We have received a total number of 23,324,570 advanced votes and voting instructions for the proposal and 54,567 against and abstain. This general meeting against set number of votes is considered to have adopted this resolution.

This is the end of the agenda. We have been through the entire agenda. Hence, this Extraordinary General Meeting in Nordic Nanovector is complete now. Thank you very much, and have a nice day.

21.02.18. Nordic Nanovector ASA, Q4 2020 Earnings Call, Feb 18, 2021

Presenter Speech

Jan Egberts (Executives)

Good morning, ladies and gentlemen. Welcome to our Q4 and full year 2020 highlights and financials. My name is Jan Egberts, and I'm Chairman of the Board. And I'm here together with Lars Nieba, our interim CEO; Malene Brondberg, our CFO; and Marco Renoldi, our COO.

Over the past year, I've acted someone as an Executive Chairman, spent quite a bit of time with the company. Most of my colleague Board members have worked very intensely over the past year.

First of all, I want to acknowledge this had been a very difficult year and a somewhat disappointing year for all of you and all our shareholders since our stock price has not performed at all over the past year. Unfortunately, we had to spend that year focusing on a number of very important operational fixes, which, unfortunately, resulted that we had very little news to report. But I'm very pleased that I think today, we can report some very positive news to you, and I know you have been waiting for a long time with that.

In the next presentation that Lars and Malene and Marco will share with you, we'll show you that we have now more than doubled our recruitment rate from about roughly 12 patients during the first 3 quarters in 2020, so over the period of 9 months, 12 patients, to 14 patients over the most recent 3 months. So up over the first 3 quarters of last year, about 3 per quarter to 14 over the most recent 3 months, and that's a period from mid-November to mid-February. So a very significant improvement in our recruitment rate.

And this is all in spite of the fact that today, we're still in the middle of the second wave of the corona epidemic, which had a huge impact on our ability to run -- had a huge impact on the ability of running noncohort-related clinical studies. Really, hospitals were locked down and were closed for those kind of initiatives.

I'm also very pleased to report that we were able to reduce the number of required patients for submission due to the protocol changes that we have implemented during 2020. Now we only have 47 patients to go to completion of PARADIGME, so a significant reduction. We also expect that this recruitment rate will further improve to about 8 patients per month or so in the late spring, early summer of this year. And some of the further improvement in the recruitment rate to the 8 I just mentioned will come both from ongoing operational improvements but also from lessening of the corona impact after the second wave, which we expect will abate during the summer, but also more and more people getting vaccinated. So a further significant increase in our recruitment rate.

Just to refresh your memory, pretty much exactly 1 year ago, we embarked on a very major organizational refocusing. We appointed Lars as our interim CEO, Malene as our new CFO and later in the year, Christine as our Chief Medical Officer.

In addition, very early on last year, we made a number of very significant operational changes, significantly reduced operating costs, reduced our headcount by 25%, which really extended our runway. Unfortunately, in that process of reducing the headcount by 25%, we had to let go some of our excellent people.

In addition, we also revisited our clinical protocol. Based on the interim analysis that we conducted in the middle of the year and that were released in early August, the external independent safety monitoring team recommended that we should drop 1 of the 2 arms of our PARADIGME study. So until halfway last year, as you remember, we had 2 arms, and now we have only one arm.

And the reason for this is given the great safety profile, the Monitoring Board felt that we should take the best-performing arm and that because of the safety profile, we should be able to lift some of the restrictions we had on our clinical protocol. From that moment on, we were able to include patients with lower platelet counts but also patients who have had bone marrow transplantation.

These 2 facts, the lower platelet count and the patients that were coming included with bone marrow transplantation or have had bone marrow transplantation in the past, will increase the number of eligible patients we could potentially include in our clinical study by -- depending on the country, depending on the local practices in a different country, anywhere from about 30% to 70% more patients that could be included in the clinical study. So very important addition that would make more patients eligible for the clinical study.

After that decision, we also need to get approved by the local regulatory authorities. And as of this month, we just completed that entire process of getting all the local regulatory authorities to approve these protocol changes.

In addition, we -- with the help of Karin Meyer, one of our Board members, we implemented a significantly improved management of our CRO, our clinical research organization. We also implemented improved patient recruitment tools, in particular, in the U.S. So a number of additional measurements and decisions that really will help us improve our recruitment.

So in summary, I think we're very positive where we are. We have only 47 patients to go to complete the PARADIGME study. Our recruitment rate has increased from about 3 per quarter during the past year to 14 patients over the most recent 3 months, and that all in spite of the fact that we're still in the middle of a very significant second wave of corona. And like I mentioned earlier, we expect our recruitment rate to increase even further to around 8 patients per month in the late spring, early summer. In short, we reiterate and repeat our guidance of our key value inflection point or 3 months data readout in the latter part of this year.

Because of the nature of biotech and the fact that -- probably the question you will ask, why did it take so long? And because of the nature of biotech and the fact that Betalutin treats very sick patients, any change you'd like to make to a protocol like dropping one arm or broaden inclusion per care takes a long time to implement because you do need regulatory approval in each of the countries where you're operating the clinical study.

Again, we fully realize that 2020 has been a very difficult year for our shareholders, but we're really optimistic where we are and that we really have changed the corner now and can leave the phase where we need to implement all the required operational and organizational changes to fix our recruitment rate. And now we can focus on the more exciting phase of the submission and towards the market launch. We're not there -- we're not at the market submission yet, obviously, we need to complete the clinical study, but we definitely feel that the operational changes have now all been implemented.

And I really want to acknowledge all the hard work that has been done by the team, particularly Lars, our interim CEO; Malene, our CFO; Marco, our COO; Christine; and the rest of the management team. But also really with a lot of operational support from the Board, in particular, people like the Chair of our Clinical Strategy Committee, Jean-Pierre Bizzari, together with Joanna Horobin and Rainer Boehm. They have been very intimately involved in all the drafting of the protocol changes and some of the discussions with our regulatory authorities.

Also, Karin Meyer was very instrumental in the improved management of our CRO. And Hilde, ex-Chair of our Audit Committee, with Pier and myself have been very intimately involved in the financing.

I think that our new CMO, Christine Wilkinson, summarized at best a couple of weeks ago during a team meeting when she said, and I quote her, "We're beginning to see an encouraging improvement in the enrollment rate of PARADIGME. And based on the changes of the trial protocol and the initiatives that we are implementing to improve the execution of the trial," and this is where the important section is, "we now have clarity from the key regulators on the clinical data set that's expected as a basis for our filing. This clarity, in conjunction with the improving enrollment rate and the continuing recruitment initiatives, gives us confidence that we can meet our goal of having preliminary 3-month top line data in the second half of this year." So really, we feel very confident we're now on our track to submit -- to have the 3-month data by the end of this year. Again, this had been a true team effort working -- with management and the Board working hand in glove.

So that's kind of what I wanted to summarize, and I'd now like to hand over to Lars, who will take you through the rest of the presentation, and Malene and Marco.

Presenter Speech

Lars Nieba (Executives)

Thank you, Jan. From my side, good morning, everyone. And as Jan mentioned, let me go into -- in more detail through our Q4 update. I will start with the most important update on PARADIGME.

As Jan mentioned, we have made a significant improvement to our recruitment rate. So we have accelerated our recruitment rate from approximately 2 to 5 patients per month despite COVID. And also, we are expecting that

COVID is lessening. And assuming that, that happens, the rate can further increase to at least 7 patients on average per month in late spring.

Where did that improved rates come from? We have significantly improved the management of our CRO and also retained specialized firms to further improve our recruitment. We have converted our PARADIGME trial from a 2-arm into a single-arm trial. And we also introduced simplification in the execution for our clinicians.

We have very good, positive safety data set from the interim analysis, and that also allowed us to broaden our inclusion criteria. We are now able to include patients with lower platelet counts and autologous stem cell transplantation. That pool of eligible patients increase, depending by country, between 30% and 50%.

And the analysis of interim data showed that number of patients to complete PARADIGME can be reduced. So we were able to present that to the health authorities, and we can reduce the number of patients to 120. And that means we only have to have another 47 patients to go to finalize PARADIGME for the regulatory submission. With all of that, we reiterate our target to report preliminary 3-month top line data in the second half of this year.

Let me go in more detail through the highlights. We have now 73 patients enrolled as of yesterday. And to remind everyone, we had 59 patients as of November 18. That means we have 14 patients enrolled in the last 3 months with only 3 patients from August to November 2020. So there, you can see that all of our actions really come to [facilitation], and we are very confident that we can even go higher.

Our protocol amendments have now been implemented in all 24 countries. Last month, we're approving it -- last week. The final patients have been enrolled in our second cohort for Archer-1 and our second line Betalutin trial and also in the LYMRIT 37-05 phase where we are treating DLBCL patients. The preliminary data readout is expected in the first half of this year. Both trials now have been paused pending the analysis of data and the evaluation of further plans and development.

We also were able to publish in Journal of Nuclear Medicine the results of our preclinical studies demonstrating that Betalutin reverses tumor resistance to rituximab in non-Hodgkin lymphoma disease models. So all of that is really very, very positive, and we are on the right track.

Now reminding everyone what Betalutin is, going to Slide 7. Betalutin has a compelling, unique and differentiated value proposition for non-Hodgkin lymphoma patients. A short reminder, we have an anti-CD37 antibody. CD37 is highly expressed on B cells. We do have lutetium with a half-life of 7 days as a radioactive compound. And the mechanism of action of our antibody drug conjugate is internalization and cell death and, very important, the crossfire effect of lutetium, which gives us really very, very good results.

Now the key benefit, especially during the pandemic, we should not forget and our elderly patients. We only have a single-dose treatment, so none of our competitors have this. We have a durable response in elderly and heavily pretreated patients.

Our safety profile is very good. We have a predictable and manageable side effect burden. And very importantly, most treatments today are anti-CD20 treatment, and we do have an alternative target to CD20, which is suitable for rituximab refractory patients.

Now as we promised when I took over in February that we wanted to revise our clinical strategy and that we are focusing on PARADIGME, so that is what really happened over the last year. So we brought forward PARADIGME. And PARADIGME is our first-to-market in the trial, so the indication is third line relapsed/refractory follicular lymphoma. We are, of course, together with the data out of Archer-1 and LYMRIT 37-05, which I mentioned they are finalized and we are analyzing the data, we're looking at all of that data together to really realize the optimal strategy to advance in earlier lines. And since we do have also pretty good results in marginal zone lymphoma, we're also looking on the opportunity how to move ahead with marginal zone lymphoma.

Now going shortly to Part A. Sorry for everybody who has heard that several times, I think it's still a very impressive story. So what you can see here on the waterfall diagram is the amount of shrinkage of the tumor size. What you can see there in our 74 patients which we had in the 37-01 Part A trial that about 90% of the patients have a shrinkage or reducing in tumor size. And slightly other description is that we have an overall response rate of 67% and 24% of CR in rituximab refractory patients. As I mentioned, these are really the ones which are suffering most from not having any therapy available.

Our medium response rate for all responders is more than a year. And even more than 2.5 years, we do have for our complete responders. So that's a very impressive result with progression-free survival of around 9 months.

Now that is also important for how we position Betalutin in the market. As Jan mentioned, we are now preparing it. I would like to remind everyone our patient characteristics is that we have elderly patients. The median is 68 years old, and there is no huge difference between Part A and Part B. They've been heavily pretreated with advanced-stage disease. And that is also pretty similar between Part A and Part B. So overall, we have a very good safety data set and efficacy data set in that patient population. Betalutin was also very well tolerated. That is why we also can now treat patients with lower platelets and autologous stem cell transplantation.

Interim analysis, as mentioned by Jan, we had it in July last year. We had before a 2-arm trial with the lower dose and the higher dose. So the lower dose was the 15 MBq per kilogram Betalutin and the pretreatment of the cold antibody with 40 milligrams flat of lilotomab, and the higher dose arm was 20 MBq per kg and Betalutin and 100 mg per meter square lilotomab. So these were the 2 arms. And the Safety Review Committee looked at all of the data in very much detail and recommended to go ahead with the 40/15 arm. As mentioned, we have 73 patients enrolled as of yesterday. And the trial reduced to 120 patients with 47 patients to go. We have 95 sites opened in 24 countries.

We have promised that our #1 priority [indiscernible] is the improving of trial execution. Let me recap a little bit what we have done. So the protocol amendment, as we mentioned already, is now approved in all 24 countries. The broadening of the inclusion criteria has increased the pool size by 30% to 50% depending on the country. The decision to make PARADIGME a single-arm trial led to a reduction in patient numbers needed to complete PARADIGME for BLA filing. 47 patients are now needed to finalize it.

The site-specific action plan has been implemented. Senior leadership at NANO and our CRO are deeply involved in continuous monitoring of the site performance metrics, which are also increasing significantly. The CMO is hosting virtual meetings with trial investigators and the teams to promote PARADIGME. So Christine is very active here. She had more or less every PI on the call, and they are appreciating that very much.

The specialist firms we have appointed are there to focus on further improving our rate of recruitment, including targeted social media campaigns. The major focus currently is North America and then, particularly, the U.S.

There's also some other effects from our competitors. The 3 trials, our competitors have been finalized. And the bispecific -- one bispecific antibody trial is on clinical hold. So that also might give us a few different patients. And very important also here is the vaccination rollout is expected to reduce restrictions imposed by COVID-19. And as you know, our patients are, on average, 68 years old. They are in the group which needs to be protected. So from that point, it is very important for all patient population that the vaccination is going on very fast.

Our regulatory strategy to gain rapid approval. BLA filing with the FDA for accelerated approval based on PARADIGME data and initiation of confirmatory Phase III trial. So that is important. We will go ahead with our Phase IIb PARADIGME trial.

We do have orphan drug designation for third-line follicular lymphoma granted in the U.S. and in the EU. We do have fast track granted for both, for example, marginal zone. And in the U.K., we do have also the promising innovative medicine status. And of course, we are always exploring other routes to bring Betalutin faster to our patients.

Now coming to the positioning of Betalutin, going to Slide 16. What you can see here is what we mentioned before as well. And it's a unique product profile of Betalutin which positions us as the treatment of choice for elderly and frail patients, which are approximately 70% of all third-line follicular lymphoma patients. And if you progressed at a very early stage in the third line, you have great medicines like the stem cell transplantation, which I mentioned, or also the CAR-T, which goes to approval as they are looking with very promising results, very expensive. They do have high side effect, and only a very few patients are eligible for it.

We do have a competitor with tazemetostat, good results but only in a very minor collection of patients who do have a certain mutation, which corresponds to approximately 15% of the overall patients in follicular lymphoma. So overall, that means there is still a high unmet need. And with our safety profile with our single injection, we are very well positioned to serve these patient populations. And patients who have comorbidities that prevent the use of both chemotherapies or other therapies associated with a high side effect burden, they are very well

positioned for Betalutin. And what we have shown is a durable response with a very good safety profile and the single administration as mentioned. So really very well positioned for that.

And that is also the feedback we are getting more and more from our customers. There is -- the efficacy observed in 37-01 is seen as a major strength. Our response rate and the median duration of response in complete responders is very compelling to HemOncs. And the combination of potential benefit is what sets Betalutin apart: the onetime treatment, the durable efficacy, the manageable and benign safety profile and the simplicity for patients and physicians. But HemOncs view elderly and frail patients, which are majority of the patients with follicular lymphoma with comorbidities, including patients with refractory to rituximab, as the ideal Betalutin patients.

With that, I will hand over to you, Malene.

Presenter Speech

Malene Brondberg (Executives)

Thank you very much. Let's take a look at the financials. And so as you can see, we have still a good control over the finances. We spent NOK 107 million in the last quarter, which is compared to NOK 139 million last year. And of course, we see here some of the effects of the reductions we did in, unfortunately, staff, but other things as well earlier in 2020.

As you can see also, and then we will continue to -- of course, to look for further savings. When that said, we do not, of course, want to jeopardize the study. We do want to complete on time. So it is most important now to spend the money on the right thing, which means, of course, clinical and also our CMC activities.

On the next slide here, you can just see that the cash run rate, which is now extended into Q3 2021, so this year, and it gave us in the end of the year a cash position of NOK 294 million. As we will continue, as I said, to look for savings, so we can push it as fast we can. And as I said, NOK 294 million in the bank at the end of the quarter, which is, of course, a result of the financing round that we did in December.

With that, Lars, I will hand it back to you.

Presenter Speech

Lars Nieba (Executives)

Thank you, Malene. So we are 100% focused on delivering on our PARADIGME trial. We are highly confident in the potential of Betalutin to fulfill the important unmet clinical needs. The goal is to complete PARADIGME, and we are targeting our preliminary 3-month top line data in the second half of the year. We have reduced the trial size and it means we only have to have 47 patients to go to complete PARADIGME for BLA filing.

We have significantly improved the rate of patient recruitment into PARADIGME despite the second wave of the corona pandemic. So our inclusion criteria has been broadened. We have shown that we have a very good safety profile. And we are even going further with additional initiatives to further enhance the rate of recruitment.

Our promising clinical efficacy and safety data seen from a onetime administration in relapsed/refractory in non-Hodgkin lymphoma. And very important to mention is Betalutin is 100% owned asset. We are targeting a total NHL opportunity to approximately USD 26 billion by 2026. So -- and of course, we are actively pursuing flexible regional commercialization strategies to maximize our value.

So with that, I only need to remind everybody on the next dates from the financial calendar. The AGM will take place on the 15th of April. You will hear our Q1 results end of May, on the 26th, and the first half -- the half year results on the 27th of August.

So with that, we are open for questions.

Answer

Unknown Executive (Executives)

Yes. We do have quite a lot of questions here, but many of them are similar. So I'm trying to address the main questions here now.

First question is about financing. And we have a couple of questions here related to the future financing plan referring to in the Q3 report, you said something about the extended cash runway could be done with different tools. And how will the company work looking forward to secure the financial situation from Q3 2021 and forward?

Answer

Lars Nieba (Executives)

Jan, will you take that question?

Answer

Jan Egberts (Executives)

Yes. As we mentioned during our previous quarterly, we do need to raise some money during the first half of this year. And we clearly want to raise money beyond what we consider the key value inflection point, which is the 3-month data readout later this year. So management, together with the Board, are evaluating various options we will hear more about in the nearby future. But it's clearly a recognition which we mentioned during the previous quarter release that we need to raise money at some stage during the first half of this year.

Answer

Unknown Executive (Executives)

Thank you, Jan. We do have a lot of questions about the PARADIGME study, of course. And some of them have been addressed and answered during the presentation, but some of them are also new.

So first one, what is the impact of COVID-19 on follow-up visits and data collection for PARADIGME?

Answer

Lars Nieba (Executives)

A very good question. So what we are doing is, as mentioned, we have really a very good interaction with our CRO and also with our investigators in the hospitals. So the overall processes are now in that way, that we always have somebody in the hospital who can take care of that. Wherever a visit is possible, of course, we are doing visits. But when not, we have implemented procedures that are corona conform and that we can get all of the data and more of the visits made, as mentioned in the protocol.

Answer

Unknown Executive (Executives)

Thank you, Lars. The second question about PARADIGME is on recruitment. Can you indicate anything on the geographical split of where most patients have been recruited from so far?

Answer

Lars Nieba (Executives)

So far, as we mentioned before, our best recruiting countries have been historically in the U.K. and France. What we are seeing now is that wherever the corona pandemic is going down, we do see a huge impact on -- the patients are coming back. So from that point, we are expecting as soon as the corona is going down that also all of the other countries will come back.

Answer

Unknown Executive (Executives)

Thank you. And there is also a question about the split between the 40/15 dose and the 100/20 dose among the 37 patients that have been recruited so far.

Answer

Lars Nieba (Executives)

The 37 patients? 73 patients.

Answer

Unknown Executive (Executives)

Sorry, the 73 patients.

Answer

Lars Nieba (Executives)

Yes, of course. There was a split because we have -- until the interim analysis we went ahead with the 2 arms, we have done the interim analysis at 47 patients. And as soon as we got the approval for the single arm, we are focused on the single -- on the 40/15 trial. And the patients which have been dosed with 100/20 are, of course, counting to the overall patient number of the 120.

Answer

Unknown Executive (Executives)

Thank you. Another question is do you see any safety issues with regards to -- sorry, that question disappeared right now. Do you see any safety issues with regards to the patients treated under the new protocol?

Answer

Lars Nieba (Executives)

No. We don't see anything there yet, but we need to be careful here because we, of course, need to wait for the 3-month data of the patients. And as mentioned, the protocol has been approved in all 24 countries, and we have patients coming in under the new protocol. What we have not reached yet, the 3-month data set.

Answer

Jan Egberts (Executives)

But we have not had any material adverse changes, and that would have been reported. Just to be clear, there are no material adverse changes at all. It's a very safe -- it has a very strong safety profile of the compound. Obviously, there are patients with comorbidity, which means they have multiple other diseases, so we're dealing with very sick patients. But we have not seen any indication of any problems with the compound itself.

Answer

Unknown Executive (Executives)

Okay. Next question is could you comment further on the target for the 3-month top line data in second half of 2021 with respect to when you then would need to be fully recruited and what rate of enrollment would be reached -- required to reach this?

Answer

Lars Nieba (Executives)

What we mentioned, we are very confident that we can reach our preliminary 3-month top line data this year. And as mentioned in the presentation, we are very confident that we can increase our rate of recruitment to at least 7 patients per month.

Answer

Unknown Executive (Executives)

Thank you. There is another question about MZL and whether it's possible to provide an update regarding MZL.

Answer

Lars Nieba (Executives)

Yes. The update is that, of course, we are working together with our Clinical Strategy Committee with the Board on how can we move ahead. And as Jan mentioned in his introduction, that is also a strategic question, so we are looking on where do we position the company best. And we have very good results in marginal zone. We are working on a clinical protocol there. And as soon as we know more, we will inform you.

Answer

Unknown Executive (Executives)

Thank you. Could you also say something about alpha 37, how that is going?

Answer

Lars Nieba (Executives)

Also that one, it was only one in the presentation yet, put our research activities on hold. So we are looking as soon as we do have a clear path forward there that we might want to go ahead or -- but yes, as mentioned before, we focus everything on PARADIGME. And with that, we have put it on hold.

Answer

Unknown Executive (Executives)

Thank you. We do also have some questions about regulatory approval and market access. And there's a question about where we do stand when it comes to the fast tracks.

Answer

Lars Nieba (Executives)

So fast track, it's a regulatory status. So as soon as we have submitted them, the FDA is agreeing to handle that with a fast track pathway. So from that point, we are still having, of course, fast track. But since we haven't submitted yet, there is no fast track pathway yet. We expect, as soon as we have the data, that we are reaching out to the health authorities so that we can have the submission in 2022.

Answer

Unknown Executive (Executives)

And you mentioned both FDA interactions and internal review provides you confidence that 120 patients is enough for a filing for accelerated approval. The question is did the FDA approval that 120 patients number? And what color can you give on what gives you confidence?

Answer

Lars Nieba (Executives)

As we mentioned before, we have regular interactions with the health authorities. And we did get very good feedback and interactions with the health authorities. And that is why we are absolutely confident that the 120 patients is good for submission, of course, depending on the clinical data.

Answer

Unknown Executive (Executives)

Thank you. And another question is, is there a minimum amount of U.S. patients specifically that you need to recruit to support an FDA filing?

Answer

Lars Nieba (Executives)

There is no specific requirement for U.S. patients, so there's no rule or any law or something like that in the FDA regulations. It is more that there is, of course, an expectation that you have to have some U.S. patients as we have seen with our competing trials. And we are in a good range there that we are confident that we reach sufficient U.S. patients to meet the expectations of the FDA.

Answer

Jan Egberts (Executives)

Yes. The other thing to keep in mind is that the FDA now accepting also patients from countries that kind of have a mutual recognition. So it's not just the United States but also some other Anglo Saxon countries.

Answer

Unknown Executive (Executives)

Thank you. The next question is, can you file in Europe based on PARADIGME? Or is that unlikely?

Answer

Lars Nieba (Executives)

Marco, in that case, I need to hand over to you. I think you have looked into that in very much detail on our European approach.

Answer

Marco Renoldi (Executives)

I think, in general, European regulatory authorities have been a bit more [vigilant] in terms of approving products based on Phase IIb trials. But most recently, drugs that have demonstrated a strong clinical advantage over available therapies have been able to obtain conditional approval. So our first priority is, of course, filing with the FDA, but we will explore all options to support a filing with the EMA authorities as well with the current trial. I hope that satisfies the question.

Answer

Unknown Executive (Executives)

Thank you, Marco. We are going to raise the last question here. And after that, there might still be some questions that have not been answered yet, but the more detailed questions will be handled via e-mail in order to not go in too much detail here.

So the last question is about partnerships. The usual questions, are there any big pharma companies that are interested in making a deal with you? Or have you been contacted by big pharma? Are you thinking about such cooperations?

Answer

Lars Nieba (Executives)

Sure. We are always thinking is our duty to the company, so we are always investigating different business development opportunities. And as usual, we will revert to you and to market with updates if and when any of these discussions materialize.

Answer

Unknown Executive (Executives)

Thank you, Lars. That concludes the Q&A session. And as I said, there might be some questions that have not been answered yet of the more detailed kind, and we are going to respond to those by e-mail. Thank you.

Answer

Lars Nieba (Executives)

Thank you, [Carrie]. Thank you, everyone. With that, I think we can conclude session. Jan, anything from you, final words?

Answer

Jan Egberts (Executives)

Again, I want to thank everybody. I want to acknowledge that last year has been a very difficult year for our shareholders, but I really think the company has now turned the corner, and we're now really at the phase moving forward towards the submission of Betalutin and going to the market. So I think we are entering a very exciting phase, and both Board and management are very optimistic about the future. So I want to thank you all for your support over the past year. Again, I acknowledge it was not an easy year, but I think we're going to the finish line now.

20.11.19. Nordic Nanovector ASA, Q3 2020 Earnings Call, Nov 19, 2020

Presenter Speech

Lars Nieba (Executives)

Good morning, everyone, and welcome to the Q3 presentation from Nordic Nanovector. My name is Lars Nieba, I'm the interim CEO of Nordic Nanovector. I have with me today our Chairman, Jan Egberts; our CFO, Malene Brondberg; and our COO, Marco Renoldi.

Let me directly start with our Q3 highlights. As a lot of you might have read already, we have a positive outcome from our PARADIGME interim analysis. The Independent Review Committee who looked on the data recommended to focus on a single arm and investigating our 40/15 dosing regimen. We have approval of the protocol amendments to PARADIGME proceeding as planned and completed in best recruiting countries. To remind everybody, it was designed to enlarge our eligible patient population and to increase the rate of enrollment.

Our pivotal Phase IIb PARADIGME trial with Betalutin is progressing in third-line follicular lymphoma. We do have 59 patients enrolled as of the 18th of November 2020. I would like to add here that our activities, which we have pursued and where we'll come later to has increased awareness at the sites. We do have also 3 patients now in screening.

Nevertheless, COVID-19 continues to have a negative impact on our recruitment as we are seeing currently the second wave in a lot of countries being even more severe than the first wave.

We are very pleased with our private placement that we successfully completed in September, raising around NOK 231 million. We have done a lot of activities to extend our cash runway into Q3 2021.

We have appointed a very experienced Chief Medical Officer, Dr. Christine Wilkinson Blanc. She has more than 25 years experience in clinical development with a focus on oncology and hematology.

As you might have read this morning already, we also have successfully enrolled into Archer-1, our Phase I safety trial of Betalutin in second-line follicular lymphoma. So the final 2 patients are enrolled. We expect preliminary data readout in the first half of 2021. As promised in April, we will pause the trial pending the analysis of the data and the evaluation of the plan for further development.

Another highlight, which happened also after Q3 is our publication in Journal of Nuclear Medicine. So the result of the preclinical study demonstrated that Betalutin reverses tumor resistance to rituximab in non-Hodgkin lymphoma disease models. That is a very, very important message and it really adds evidence supporting the potential of Betalutin and rituximab in combination in non-Hodgkin lymphoma.

We are doing everything for PARADIGME. So we have focused all of our activities on PARADIGME. That is what we have mentioned before as well. And our core focus is the third-line relapse/refractory in follicular lymphoma. And we, of course, have other opportunities for PARADIGME like marginal zone, which we are still evaluating. Together with the results we have now in Archer-1, we are evaluating the optimal strategy to advance into earlier lines.

We are also very confident that we can finalize the enrollment of our DLBCL study still this year with, of course, all other clinical -- preclinical and research activities, as mentioned before.

Now in more detail to the interim analysis. The recommendation of the Independent Review Committee is to focus on our 40/15 dosing arm that followed a comprehensive review of the interim data. And the outcome is that both arms are well tolerated. That demonstrated our manageable safety profile and our activity with respect to complete responses, partial responses and stable diseases. The 40/15 arm has demonstrated a more consistent and favorable clinical response across all subgroups, which we have looked into.

The 100/20 arm is already discontinued. However, the dosed patients will be further monitored and be in the remainder of the trial.

We are evaluating options to reduce the patient number required for completing PARADIGME based on a single-arm design, meaning the 40/15 dosing arm.

Now coming to COVID. The impact of the COVID-19 pandemic has negatively affected recruitment into all non-COVID clinical trials, particularly those involving vulnerable patients. Our patient population is approximately 70 years old and is counted with a high-risk for COVID-19. The restrictions of movement during lockdowns prevent a follow-up with its data collection on existing patients and dosing of newly enrolled patients. The recent emergence of the second wave had led to restrictions that may outweigh the actions we have taken. It's getting more difficult to screen and enroll patients. So I can only speak to Switzerland. Currently, there, we have seen that there's a lot of reprioritization in hospitals. Our ICUs are fully blocked, and I think that's the same in U.K. and in other countries in the world. Health care staff or patients being affected by the virus or supplies due to restrictions of movement. These uncertainty around lockdowns and continued restrictions in Q4 and into 2021 may lead to further delays to complete enrollment.

Still would like to highlight that we are fully focused on improving the trial execution. As mentioned before, we -- the approval of the protocol amendments to PARADIGME is proceeding as planned and is completed in best recruiting countries. This will significantly enlarge our eligible patient population allowing inclusion of follicular lymphoma patients who have had autologous stem cell transplantation, which is frequently used for treating second-line follicular lymphoma in a variety of countries. We also have included patients with a lower platelet count at baseline.

The enrollment continues under the existing protocol until amendments are approved. And as mentioned, we have patients in screening. That is a very good signal.

We have enhanced our relationship with our CRO and our interactions with our study investigators. We have implemented improved patient referral networks. But not only that, we are really speaking with the investigators more or less every day. And we have made an evaluation of the sites. We are doing targeted solutions for the individual sites to support our investigators to be able to still have our patients. All of these actions are expected to improve the rate of patient enrollment.

We're still targeting the 3-month data outcome readout in the second half of 2021 with all actions we have taken.

Let me move on to other opportunities, which we have in non-Hodgkin lymphoma, and that is our Archer-1. So we are very pleased to see that the patient enrollment into base safety cohorts is now completed.

To remind everybody, our patients in follicular lymphoma had more than 1 prior regimen.

Our primary objective of that study is to evaluate the safety and tolerability of Betalutin in combination with rituximab. And our secondary objective is to evaluate the primary anti-tumor activity of combination treatment. What you can see here is the trial design, and we are now really at the very right side. So we will review the data from the first 2 cohorts and plan -- and pause the trial to evaluate how to progress further. So the final 2 patients have been enrolled, and the preliminary data readout is expected in the first half of 2021.

Now coming to Betalutin in general and why non-Hodgkin lymphoma, and in particular, follicular lymphoma, is a very good indication for Betalutin.

Non-Hodgkin's lymphoma, there's a lot out there but there is still a need for new treatment options. You need to know that around half of the indolent non-Hodgkin's lymphoma patients are treated with rituximab-containing regimen, either refractory or develop resistance within 5 years. These relapse/refractory patients may not tolerate chemotherapy because of their age and their comorbidities.

In addition, most of the regimens are CD20 regimens, but there is a need for an alternative target to CD20, and of course, a chemo-free regimen with gentle side effect profile.

What you can see here is a 5-year progression-free survival of these patients. So if you're a first-line, you have a chance of around 60% to have a progression-free survival. Now if you unfortunately progressed into second-line, you decrease -- the chance of the 5-year progression-free survival decreases to only 36%. And then if you're progressing further into third-line, your chance of surviving 5 years is only 26%. That is true for follicular lymphoma, marginal zone and DLBCL. So from that, what you can see is there is a high unmet need in follicular lymphoma.

Now Betalutin. We have compelling and a unique differentiated value proposition for non-Hodgkin lymphoma patients. Our antibody is an anti-CD37 antibody and it is a targeted radioimmunotherapy. We do have lutetium-

177, which is a low beta-emitter with a half-life of around 7 days. Now the mechanism of action is not only the internalization and the cell death, we also have a crossfire effect, which targets [indiscernible] the antibody and that gives a very, very powerful tool.

Our key benefits are the single dose treatment; we have shown in our Phase IIa durable responses in elderly and heavily pretreated non-Hodgkin lymphoma patients; have shown a predictable and manageable side effect burden; and anti-CD37 is an alternative target to CD20, which is suitable for rituximab refractory patients.

That positions us very uniquely. And the Betalutin profile is positioned as a treatment of choice for around 70% of the third-line follicular lymphoma patients who are elderly and frail. What you can see here is that if you're young and fit, meaning if you unfortunately have progressed into third-line follicular lymphoma at a very young age, then you do have a wide variety of possibilities with CAR-T, with stem cell transplantation or with bispecific antibodies. All of them do have pretty significant side effects. If you're progressing, you can go on to immunotherapy [indiscernible] or the rituximab-lenalidomide. Also there, it is an anti-CD20 treatment and it is chemotherapy, so it is not without any side effects.

Now coming to the patients we are targeting. What is there? There is not a lot. So you do have Zevalin, 20 years old, rarely used.

You do have the PI3 kinase inhibitors, started with a great hope, and what we have seen is that the side effects of the PI3 kinase inhibitors are very severe and they are rarely used.

The recently approved compound is tazemetostat. Great results in about 15% of the patients because you do need to have a certain mutation, then it works great. The other 85% of the population were wild type, who do not have said mutation, can be treated with tazemetostat, but the overall response is pretty poor.

And of course, you can give rituximab. However, rituximab in rituximab-refractory patients is not working very well.

Recently, meaning last week, we have seen the first results of the second generation PI3 kinase inhibitors, in particular, umbralisib. The result of umbralisib are in the same range as the first-generation PI3 kinase inhibitors, around a little below 40% ORR and the single-digit CR rates, and you still have significant side effects. So there might be a slight improvement, but not a huge.

With the profile we have, Betalutin is ideally positioned to treat these huge amount of patients at more than 70% or around 70% of follicular lymphoma patients who are elderly and frail. These patients do have co-morbidities that prevent chemotherapy or targeted therapies with a high side effect burden. And we have shown that we can deliver durable responses with a gentler safety profile in a single administration.

So Nordic Nanovector is well positioned to expand awareness to the benefits of radiopharmaceuticals. I would like to highlight here the growing interest in radiopharmaceuticals where we are well positioned. Novartis confirms the commitment to build on its late-stage radioligand portfolio and they are going further with Lutathera in Phase III. They do have also metastatic castration-resistant prostate cancer also with 177-lutetium.

We have seen the IPO of Fusion Pharmaceuticals in Canada, which was a huge success. In addition, they announced a collaboration with AstraZeneca to commercialize next-generation radiopharmaceuticals.

POINT Biopharma, also in Canada, have a Series A financing. And RayzeBio from San Francisco has also raised a Series A financing.

We are very pleased to see all of that because that really helps us also to create the awareness of radiopharmaceuticals with health care providers, with payers and so on and so forth and policymakers, of course. So all of that, I think, is a very, very good signal that there is a growing interest in radiopharmaceuticals.

With that, Malene, I hand over to you. Shall I drive the slides further?

Presenter Speech

Malene Brondberg (Executives)

Yes, please. If we can go to the next slide. So yes. So good morning from London, from the U.K., where we also got a national lockdown where everything is basically closed, and of course, the hospitals are struggling. Unfortunately, here, the rate is still going up, as Lars also alluded to.

If we look at the quarter here, we can see that we had NOK 88 million in spending. We did say that we will see some of the restructuring to come through in the second half. We have seen some of that. You can see approximately NOK 6 million of that was in the quarter.

We are, as we've said previously, continuing to focus on the -- on PARADIGME and to take as many costs in -- or put as many costs towards PARADIGME spending the right way.

Next slide, Lars, please. So here, you could just see, as you know, we had the financing round, which gave us NOK 230 million in the gross. And here, you can see we had in the end of the quarter NOK 381 million in the bank. As we have said before, we expect that we have cash into the Q3 in 2021. And again, as I said, we will, of course, focus on spending the money on PARADIGME.

With that, Lars, I will hand it back to you.

Presenter Speech

Lars Nieba (Executives)

Thank you, Malene. We are focusing on PARADIGME. So our goal is to complete PARADIGME as quickly as possible. And I would like to highlight again the recommendation from the IRC, the Independent Review Committee, on the interim analysis has provided clarity on advancing PARADIGME. And it has confirmed our manageable safety profile.

We have approval of the amendment and it's proceeding as planned to complete in best-recruiting countries.

We have enhanced our partnership with our CRO to implement other initiatives to speed up enrollment.

We are targeting a readout of the 3-month top line data in the second half of 2021.

And I would like to reiterate, we are absolutely confident and we have high confidence on the potential of Betalutin to fulfill important unmet needs in non-Hodgkin lymphoma.

That I would like to close and only give you a short overview about our financial calendar. So our Q4 and our full year results will be in February next year, Q1 in May and Q2 in August. A 2-week quiet period takes place ahead of the full year and the quarterly results.

And of course, if you have any questions, please send to ir@nanovector.com (sic) [ir@nordicnanovector.com]. It will go directly to our CFO, Malene.

So Malene, with that, I hand over to you again for -- to see if there's any questions.

So first of all, thanks, everybody, for listening to us. And that, we open the Q&A.

Answer

Malene Brondberg (Executives)

Yes. Thank you very much. The first question we got -- we got a lot here, but we will try to go through all of them. And if there are some of them we don't have time for, please come back on the IR e-mail.

But the first one here is when do you foresee a speedup in recruitment of PARADIGME to happen as you've only had 3 patients since the last update.

Answer

Lars Nieba (Executives)

It's a very good question. So as mentioned, we are doing a lot. We are seeing that patients are coming back. We do have patients in screening, which is a very good signal. We are going further there. We are doing a lot of PR. We are bringing Betalutin back to the top of the investigators in all of our sites.

So with that, we expect that there is a pickup as soon as we do have the -- we have now the protocol amendment approved in a variety of countries. With all of that, we expect at beginning of the year, we do see a pickup in recruitment.

Answer

Jan Egberts (Executives)

Yes. This is Jan Egberts, I'm the Chairman. I'd like to add to that. So there are 2 factors at play here. On the one hand, what Lars was already alluding to, we have modified the protocol as more patients are eligible today, significantly more patients than there were in the past. That's really helping us.

Secondly, where the collaboration with our CRO is significantly improved.

On the other hand, we cannot deny the COVID. It is very -- a lot of hospitals are closed down or locked down and they're not focusing very much in these kind of patients.

So there are 2 opposing forces. We do expect and hope for every region, not just for the company, but for everybody also on the call that COVID will get better as we get a vaccine introduced. But COVID continues to be a problem, we cannot deny that.

So 2 things on the opposite: on the positive side, better inclusion criteria, better collaboration with all the clinical sites; on the other hand, still being affected by COVID.

Answer

Malene Brondberg (Executives)

Thank you for that. Then in the Q3 report, the CEO, "You mentioned the possibility to reduce the patient sample." Is this related to only selecting 1 dose for the remainder of the trial?

Answer

Lars Nieba (Executives)

Yes. As mentioned in the presentation, what we just said, we are evaluating options to reduce the patient number required for completing PARADIGME based on the single-arm design. So what that means is we have changed the trial to a single-arm design. Beforehand, we had a comparison between the 2 arms.

And what we are doing is we, of course, need to work on statistical analysis and everything to understand what does it now mean for us. And as soon as we have that, we need to discuss that with the health authorities. And that is where we are saying there is a possibility that we might be able to reduce the number of patients. But I will not promise anything.

Answer

Malene Brondberg (Executives)

Yes. Okay. We do have a lot of questions about the 130, whether that's still the aim, to enroll 130 patients. okay. And do you have more comments or...

Answer

Lars Nieba (Executives)

No, no. I only want to say currently, yes, we have a -- there is the current protocol to see 130 patients. That remains unchanged.

Answer

Jan Egberts (Executives)

Yes. But the current protocol is 2 arms. And if you go to 1 arm, we would have more patients in that single arm. So that's a key issue.

When you do a clinical study, you need to focus on 2 things. One is efficacy, does the product work; the other hand is the safety. So we're really talking about the efficacy side of the compound here. And there's a feeling that we might be able -- we cannot guarantee it, we might be able to reduce the number of patients in the sample.

Answer

Malene Brondberg (Executives)

Thank you. Very clear. And how many and which countries have the protocol amendment been implemented?

Answer

Lars Nieba (Executives)

We are implementing the protocol in all 24 countries.

Answer

Jan Egberts (Executives)

No. He means where has it been accepted, I think.

Answer

Malene Brondberg (Executives)

Yes.

Answer

Lars Nieba (Executives)

I will need to come up with that later. I think -- it's changing on a daily basis since the health authorities are approving currently more or less on a daily basis. And we do have a 2-step approach. One is the health authorities, one is the ethic approvals and the ethic committees are even more than the health authorities. So I really need to follow up with ICON to have. It's not only countries, it's also sites. So I can answer that question perhaps on the web, Malene.

Answer

Jan Egberts (Executives)

Yes. But just to -- also a number of countries is not a terribly relevant number because the very -- some countries generate a lot of patients and some countries relatively few. But we're pursuing very aggressively in all countries. And obviously, we are dependent on the health authorities and -- but we're making good progress there.

Answer

Malene Brondberg (Executives)

Leading on to the next question. Why have not all countries accepted the protocol amendments for PARADIGME at this late stage?

Answer

Lars Nieba (Executives)

That depends also on the state of the health authorities. We have submitted all of our protocols and now we are waiting on the feedback from the health authorities. So the health authorities, I only can speculate, and they're

probably also overwhelmed by COVID. And so from that point, it's very difficult for me to judge on the speed of the health authorities.

We have done everything we can at the highest speed we can to submit everything, and now we are waiting for the feedback of the health authorities. But of course, we are following up with them also on a very regular basis.

Answer

Malene Brondberg (Executives)

Yes, thank you. You state very generally that you have improved your patient referral network. In which countries does this improvement apply? And what does this improvement consist of?

Answer

Lars Nieba (Executives)

What we are working on, let me start with the second part of that question, is we have chosen many academic sites for the clinical trial, as usual. And what we have done is follicular lymphoma patients -- follicular lymphoma is a very slow-growing cancer. And they are very often also at these sites which are not academic centers.

And what we have done now is that we have worked together with the academic centers and with the referral sites to really also have patients which are not identified at the academic sites that they have referred to the academic site. But we really have a good network of clinics and investigators who do refer eligible patients to our principal investigators. We have done that in a variety of countries, mainly our best recruiting countries, which is also France, which is the U.K., we have started also in the U.S. with that.

Marco, do you want to add anything since you are very close to that with the MSLs?

Answer

Marco Renoldi (Executives)

No, I think you've covered it very well. I would add new countries where we are increasing our efforts to generate these networks, also thanks to the increased collaboration with our CRO and those are Italy, Israel, Turkey and Spain. So the number of countries where we are maximizing the referral pathway is growing and that will have an impact.

Answer

Malene Brondberg (Executives)

Thank you very much. So how robust do you consider the guided data readout on PARADIGME today compared to when you made it in the Q2 presentation?

Answer

Lars Nieba (Executives)

We are still very much behind, say, that we get the 3-month top line data in the second half of 2021. So we are equally convinced as in Q2. We are doing a lot of effort to increase the speed of enrollment and we are very confident that, that will work and thus we are very confident. However, as Jan and I mentioned, we, unfortunately, have no crystal ball for COVID. And still, we are very confident that, that is possible.

Answer

Malene Brondberg (Executives)

Okay, thank you. And then we jump to other topics of funding, which I think the first question here is actually to me. Thank you for that. Why isn't the company focused more to get a better shareholder base with strong investors, U.S.-based, for instance?

I can say the way that we actually work with the shareholders and target shareholders is that we actually have a list where we identify. So we know exactly for instance, in the U.S., which are the top investors in health care and in biotech. We also scan who, for instance, was in on the -- on Endocyte in AAA so we know the big investors. And that's the way we work.

So we do actually work very targeted, not just the U.S., but the U.K. and we got a whole set of data and list and we follow them up all the time. And we know exactly who we met the last years and who we would like to meet going forward, of course. So we are trying to do everything that we can to expand the shareholder base.

Then someone also -- then the second part of the question also, have you thought about NASDAQ?

And here, I will say, yes, that is, of course, an option. But I'll leave it up to Jan to elaborate maybe a little bit more on that because that's a board thing.

Answer

Jan Egberts (Executives)

Thank you. Yes, I lived for about 30 years in the U.S. just came back only a couple of years ago to The Netherlands, my home country. U.S. -- as a foreign company getting traction in the U.S. takes a long time and it particularly takes a lot of personal meetings with investors. And unfortunately, because of COVID, significant travel reduction, that has not been possible. So those tend to be very long ongoing dialogues. But in our most recent financing, we had a significantly larger representation of non-Nordic investors than we had previously.

With respect to the question about NASDAQ listing or any other listing. Yes, we're continuing to reviewing it, but there are no imminent plans at this moment to change the main board, but that could very well change in the future. But at this moment, there are no imminent plans.

Answer

Malene Brondberg (Executives)

Perfect. Thank you very much for that. And then you mentioned raising funds through a partner deal in both the press release related to the private placement in September and in the podcast with Radio Forsk (sic) [RADFORSK] in August. Lars addressed it's not just a deal, but the right deal. Could you elaborate on what the right deal is, not just in terms of saying creating shareholder value? Maybe, Jan, you would start with this.

Answer

Jan Egberts (Executives)

Shareholder value is probably one of the key drivers. So to actually -- yes, I'm not sure I'm answering the question.

I mean we have not finalized our go-to-market strategy. We're really focusing on the clinical study at the moment, but it doesn't mean we haven't thought about it. I think the emergent thinking is that we probably need different types of partnership in different parts of the world.

And let me just talk about the 2 extremes. Like Nordic countries, that's probably an area we could easily do ourselves. If you talk about places like China and the Far East, we almost certainly cannot do it on our own. And there in between, there are a lot of other countries where different strategies might be pursued.

That hasn't been finalized yet. And so that's where we are. There are ongoing discussions, but that's probably the best I can say at this moment.

Answer

Malene Brondberg (Executives)

Thank you. I don't know -- Lars, I don't know if you have anything further to add or Marco?

Answer

Lars Nieba (Executives)

Yes. I would leave it up to Marco since Marco is also heading up our business development and it's our daily job to really look for our partners. But Marco, please.

Answer

Marco Renoldi (Executives)

Yes. No. Thank you. I think Jan covered it very well. We cannot deny that we are in dialogue with all players who are present in the hematology space, players who appreciate the value the radiopharmaceuticals can bring to the treatment of cancer.

But all of these dialogues have 1 goal in mind, which is to put Betalutin of Nordic Nanovector on their radar screen and explore at the appropriate point in time the best option as highlighted. I don't think I would add more than that.

Answer

Malene Brondberg (Executives)

Thank you for that. Then we jump to the next question and I think, Jan, this is for you. Many shareholders would agree that it's now critical that the Board appoints a permanent CEO. When will a permanent CEO be appointed?

Answer

Jan Egberts (Executives)

Yes. I cannot say anything about that.

Answer

Malene Brondberg (Executives)

Yes. Then we're going back to some of the clinical. What is the status of LYMRIT 37-05? And when will the company communicate the current results and plans forward?

Answer

Lars Nieba (Executives)

So LYMRIT 37-05, it's DLBCL, yes. It's DLBCL. So as soon as we have finalized our enrollment, we will communicate that we have finalized the enrollment. And as mentioned before, we are confident and that we can do -- finalize the enrollment still this year.

Answer

Malene Brondberg (Executives)

Thank you. Has the Alpha37 IND been submitted? And if not, why not?

Answer

Lars Nieba (Executives)

No. It has not yet been submitted. We are working very closely with our partner, Orano Med, as you know. And due to COVID, we couldn't easily travel between the sites and so we had a little bit of a delay. So we are working together on the current planning with Orano Med and when exactly to submit the IND, but we are in final stages of the preclinical work.

Answer

Malene Brondberg (Executives)

Okay. Then we just have a few follow-up questions here. Please clarify in which countries have the protocol amendments been approved at this point. Surely, you must know this.

Answer

Lars Nieba (Executives)

I mentioned that before, yes, I will answer that question afterwards because it's, as mentioned, the health authority and the ethics approval of the different sites. And I don't have it on my hand yet.

Answer

Malene Brondberg (Executives)

Yes. And we jump, too, on the Archer-1. So Bayer's copanlisib is already approved for FL in the U.S. under the Accelerated Approval Program. According to Bayer in October 2020, good results from their combination study with rituximab, CHRONOS-3, is soon due to be presented at a scientific congress and subsequently they will discuss the data from CHRONOS-3 with health authorities worldwide. Given these developments in the market, what are the merits and justification of pausing Archer?

Answer

Lars Nieba (Executives)

Okay. We are -- we want to look into -- we have finalized now the cohorts. We will look on to the data and then decide upon how to move ahead into second-line follicular lymphoma. We had very good results, as you know, in our first cohort, which had 100% ORR and 3 out of 3 CRs, which is a fantastic result.

However, if you are looking into the space of follicular lymphoma second-line, you also need to think about is combination the right strategy to go or a single agent is the right strategy to go. That is why we would like to compare the data and we want to have a look in that how is the best positioning of Betalutin.

And you also need to take into account here that the recruitment for Archer-1 was not the fastest one. So we are not only looking into the results, we also would like to understand why the recruitment was slower than expected.

Marco, you are our expert from the market positioning point of view. Would you like to add anything?

Answer

Marco Renoldi (Executives)

No. Once again, I think you covered it very well. So we are not undermining the excellent results we have achieved in the first cohort of Archer-1, and we hope to be able to soon deliver the results of the second. And we believe that combination could be an excellent treatment opportunity for patients. I think we need to consider what is the fastest way to come to a second label, to an expanded label in second-line. That's the key decision we have to take. It's not about dismissing the combination with rituximab, it's about deciding the best clinical and regulatory strategy. And this is a discussion that we need to finalize. So I hope that clarifies.

Answer

Malene Brondberg (Executives)

Thank you. Yes. And then just a last question on that one. Have the first 3 patients from the first cohort treated with the 10/40 dose in Archer-1 trial now all relapsed?

Answer

Lars Nieba (Executives)

I must admit I'm not sure when the follow-up scans are due. Marco, I think they are not due yet, isn't it?

Answer

Marco Renoldi (Executives)

We will communicate the results, the updated mature data from both cohorts when we are ready to communicate the data from the second cohort. So we normally do the data cleaning at one point in time. So please expect that response in first half of 2021.

Answer

Malene Brondberg (Executives)

Thank you for that. And then just last 2 questions here. Can you disclose the median duration of response data from LYMRIT 37-01 with the 20/100 patients excluded from the patient population? You promised to look into that at the Q2 presentation.

Answer

Lars Nieba (Executives)

That one's a Part A data question. We have looked into more detail into the LYMRIT 37-01 - Part A data. We are -- when I recall it correctly, that was questioned in Q2, and yes, we are looking into all of the scans. We have follow-up scans and we are following up there in dividing the 40/15 and the 100/20. We are still working on it.

Answer

Malene Brondberg (Executives)

Yes. Thank you. And then the last question, I guess, that's for me. What was the net proceed from the late private placement?

And I know the prospectus is not a popular document, but you can actually see all the details in that and it was roughly always NOK 15.7 million that you can deduct. So we are in roughly NOK 215 million. But you can find much more on that in the prospectus for those who are interested in that.

Let me just see, I actually just got a follow-up here. Given that other drugs have been approved based on the Phase II trial in the third-line FL indications have included around 100 patients, can you really lower the size of the patient trial of the -- PARADIGME trial, given that you said earlier before the protocol amendment was approved that there was a 50-50 split between the 2 doses. Will not the number of patients in the 40/15 dose be too few in order to actually to get the drug approved if you reduce the number of patients in the trial from 130 patients. Sorry, it was very long this question.

Answer

Lars Nieba (Executives)

Yes. It's a very good question. That is why I said we are working on the statistical analysis of the new protocol synopsis to say what is the right powering of the trial to have significance in our efficacy and have a large enough safety database. That is exactly where we are looking in.

However, as you have rightly mentioned, others have done around 100 patients to get -- to submit for accelerated approval. So -- and we are at 130 since there is some room, as pointed out also by Jan and myself, that we can reduce the number of patients. We are confident that there is a possibility. We are -- as said, we can't promise it.

Answer

Malene Brondberg (Executives)

Thank you very much. And then the absolutely last question. Are the PARADIGME interim data available to Nordic Nanovector?

Answer

Lars Nieba (Executives)

The PARADIGME interim analysis data from the IRC, these data are available to Nordic Nanovector. There's a few people in the company who have direct access and that is, of course, our Chief Medical Officer.

Answer

Malene Brondberg (Executives)

Thank you. And then I said it was the last question, but that's -- there is one more, but this one is actually for me.

It's saying that the NOK 88 million cash burn, yes, this quarter. And what is the prediction for the next quarter.

The next quarter, if you look at the historic Q4, that is where we have a lot of costs. So we should expect it to go back up just because there is some seasonality in the cost there. So it's hard to say exactly where we are going to land, but you should look at what we had last year and then maybe a little bit lower. That's my best comment right now on that.

Otherwise, that concludes the Q&A session. Lars, I will hand it back to you.

Answer

Lars Nieba (Executives)

Thank you, Malene, and thank you to all of our shareholders for the really good questions. I hope we could answer most of them to your satisfaction.

And with that, I would like to thank you and looking forward meeting you next time. Jan, anything to add?

Answer

Jan Egberts (Executives)

No. Also I'd like to agree and hoping we can see each other in person soon again because this is obviously not the optimal way. So I hope everybody stays healthy and a very early best wishes for the holidays and the new year. And hope everybody stays healthy and prosperous.

Answer

Malene Brondberg (Executives)

Thank you very much.

Answer

Lars Nieba (Executives)

Thank you.

Presenter Speech

20.10.21. Nordic Nanovector ASA, AGM

Presenter Speech

Jan Egberts (Executives)

Good morning, dear shareholders. Welcome to the Ordinary General Meeting in Nordic Nanovector ASA. My name is Jan Egberts, and I'm the Chairman of the Board. With me is the CEO, Lars Nieba; and the CFO, Malene Brondberg; as well as the company's Counsel, Fredrik Haavind. We assume that all shareholders and proxies present are registered and that the voting slips have been handed out. If someone still hasn't registered, ask if this is done now by the entrance.

The account PPS, Account Manager Nordea is present and is assisting us to register shareholders and proxies. Unfortunately, I'm not on location since I'm living in the Netherlands. So I call in remotely, and I need to ask the people on the premises to take care of these activities.

The presentation of the record of shareholders -- a record of shareholders that are represented in the general meeting shall be attached to the minutes. Nordea has finished the registration, and I understand that 18,430,483 shares of a total of 78,319,612 share are represented at today's general meeting. That means that approximately 23.2% of the company's shares are represented. It suggested that I'll Chair the general meeting as the Chairman of the Board of the company. For this reason, the general meeting will be conducted in English, as you probably have already noticed.

The minutes of the general meeting shall be signed by the Chairperson and at least one other person elected by the general meeting amongst those present. I hereby suggest that [Cristina Harber] is elected to co-sign the minutes. I want to see if there are any other suggestions.

It sounds like there are no other suggestions. So hereby, Cristina is asked to co-sign the minutes with me.

The notice and the agenda are sent to all shareholders with a known address. The information and documents concerning the general meeting are published on the company's website. Thus, the general meeting is convened in accordance with articles of association and those rules that apply for listed companies in Norway. We, therefore, assume that no one has any objections to the notice. I want to see if there are any comments.

It sounds like there are not. So hereby -- the general meeting is hereby duly convened. We have, at this stage, completed the construction of the general meeting and will now go ahead with the matters on the agenda.

The first matter on the agenda is the authorization to the Board to increase the share capital related to a repair offering in the company. The proposal has been published on the company's website. As you know, the company has recently carried out a prior placement. The purpose of the proposed Board authorization is to allow the company to carry out a repair offering, if appropriate. Such offering would allow existing shareholders who have not been allocated shares in the private placement to participate at the same price and ensure equal treatment. The Board have intended to implement the repair offering, unless the trading prior to the company shares over time is lower than the subscription price in the private placement and the subsequent repair offering hence become redundant, which is subject to the sole discretion of the Board of Directors. As you probably know, the stock price has traded below the pricing. So this section does apply to us.

Based on the trading following the completion of the prior placement, there has been good liquidity in the company's share at a price below the private placement price. Hence, it is likely that a repair offering will not be implemented. The repair offering will, if implemented, be directed towards the company's existing shareholders as of September 23 of this year, as registered in the Norwegian Central Securities Depository on September 21. We will not allocate shares in the private placement. The subscription amount for the shares issued in the repair offering will be the same as for the private placement. Are there any objectives to this proposal?

It sounds like there are not. We have received a total of 17,348,827 advanced floats and voting structures for the proposal. 94,033 against and abstain of 250. This general meeting against set number of shares is considered to have adapted this resolution relating to Board authorization to acquire its own shares.

The next matter on the agenda is Board authorization to increase the share capital of the company by up to 20%. The Board's authorization from the Annual General Meeting to implement a share capital increase by 20% in the company have been used in full -- in connection with the private placement recently carried out by the company.

The proposals are published -- have been published on the company's website. The purpose of the authorization is to allow the Board, if required, to ensure financing for further development of the company, and/or to carry out acquisitions by issuing shares as consideration. The authorization entails that the Board shall be authorized to execute one or more share capital increases by issuing in total 15,878,125 shares with a nominal value of NOK 0.20. The total amount by which a share capital may be increased is set to NOK 3,175,625. It is proposed that the authorization is valid until the Ordinary General Meeting in 2020 (sic) [2021], however, at the latest, until June 30, 2020 (sic) [June 30, 2021].

Are there any comments or questions to the proposal?

Sounds like there are not. We've received a total number of 16,179,961 advanced votes and voting instruction for the proposal. 1,191,136 against and 72,013 abstained. This general meeting against set number of votes is considered to have adapted the resolution regarding Board authorization to increase the share capital.

We have now been through the agenda, and I want to thank you all for your attention and your support, and hence, the Extraordinary General Meeting in Nordic Nanovector has been completed. Thank you very much again. Have a good day.

20.08.27. Nordic Nanovector ASA, Q2 2020 Earnings Call, Aug 27, 2020

Presenter Speech

Lars Nieba (Executives)

Thanks Christine. Good morning, everyone, to our Q2 call from Nordic Nanovector. I'm Lars Nieba, the interim CEO of Nordic Nanovector. I have the Chairman, Jan Egberts with me on the phone; and in the room in Oslo, I have our CFO, Malene Brondberg. I would like to -- I would like to apologize Marco Renoldi. He had a death in the family, and therefore, cannot join us for the Q&A today.

I will now start with the slides. And we go to Slide #2. I would like to remind everybody on forward-looking statements.

And now to Slide #3. I would like to start with the Q2 highlights, which we had this year. We completed our strategic review and as you know, and which we already mentioned, we are focusing everything on PARADIGME and extended our cash runway into 2021. Our PARADIGME trial in third-line follicular lymphoma has enrolled 56 patients. The enrollment is still affected by COVID-19. I would like to point out that we are recruiting, which really speaks for Betalutin and its onetime injection where patients only need to be onetime at the hospitals.

Of course, negative effects is due to the lockdown, which we have still in several countries. We maintain our targets to recruit 130 patients.

Another very positive news for us is that we had our protocol amendment and that we can enlarge our eligible patient population. And really by that, looking forward to increase our rate of enrollment.

There is a background noise, sorry.

Decision base was, of course, on FDA review. Betalutin also granted fast track and Orphan Drug Designation for marginal zone lymphoma this year.

Going to Slide #4. The very important event we had that was in July, August was the interim analysis. First of all, I really would like to thank my whole team here that we managed it despite COVID to be very much in time of the interim analysis. It was a very comprehensive overview of the data, which we had by an independent review committee. And the recommendation of the independent review committee was to focus on the 40/15 dosing arm.

I would like to point out that both arms were active and on efficacy measures based on complete response, partial response and stable disease. The 40/15 arm has demonstrated consistency across all subgroups.

With that, the recommendation of the IRC was to discontinue with the 100/20 arm. Of course, the so far dosed patients will stay in the trial and will be monitored further.

As mentioned before, we will still target to recruit 130 patients, which is due to the fact that we also have to have a solid safety database.

We have a clear plan to implement the protocol amendment. And in other words, we have submitted the protocol amendment to the health authorities. And we are, of course, waiting now for the feedback of the 24 health authorities. And other initiatives have been started to increase patient enrollment.

We target our 3-month top line data in the second half of 2021. And of course, this paves the way for the planned regulatory filing with Betalutin. It is really a pleasure for me to welcome Christine onboard at Nordic Nanovector and on my leadership team. Christine Wilkinson Blanc has been appointed as Chief Medical Officer. She is really experienced with more than 25 years' experience in the field. So she worked also on -- not only on -- in oncology and hematology, but she was also experienced in radioimmunotherapy.

Let us go to Slide #5. As said, our strategic review was really to look on to everything, to look under each zone, and we decided to really focus on advancing PARADIGME.

On Slide 6, we have our revised clinical development strategy. Our core focus is the third-line follicular lymphoma on PARADIGME. I would also like to point out that we are working on an optimal strategy in earlier

lines. And as mentioned before, we got positive feedback for marginal zone, the fast track and the Orphan Drug Designation. And of course, we had very promising responses from LYMRIT 37-01. Also here, we are working on opportunities on how to go further with marginal zone.

As you know, we have 2 other clinical trials ongoing. And as mentioned before, we pause after completing the ongoing cohorts. The first one is Archer-1, which is in second-line follicular lymphoma together with rituximab, and we have seen very good initial efficacy. But we still see that the recruitment is very slow and very challenging.

Together with what I said before that we are looking for the optimal strategy, we need to consider the future positioning and the optimal strategy in second-line follicular lymphoma.

We are also working on DLBCL. We do have a single-agent trial, LYMRIT 37-05, ongoing. Also here, the recruitment is very slow. We are very close to finalizing our cohort. So the good news here is that we are only missing one additional patient. So we recruited the patient in the last few weeks here. And DLBCL, of course, remains a very important indication as we -- after the finalization of the cohort, we need to evaluate the optimal development strategy here. All other preclinical and research initiatives have been paused.

Slide 7. What does it mean focusing on PARADIGME? You see here the layout of our clinical trial. As I mentioned already, the 130 patients. And I would like to remind everybody that it is a difficult-to-treat patient population in third line, typically more than 70 years old, pretty fragile and have very often serious comorbidities. The primary endpoint is our ORR. And we do have several secondary endpoints.

When you're looking on the trial layouts, you can see that we have 2 arms. And after the interim analysis, we now continue with the 15/40 arm; and to recruit the final amount of patients, and we discontinue the 20/100 arm. As mentioned, we have 56 patients, and we are active in 24 countries for enrollment.

Slide #8. The most important part in focusing on PARADIGME is, of course, the trial execution. We are also convinced that by simplifying the protocol now to only 1 arm, that also will have a positive impact on our trial. So that means increasing the rate of enrollment. In addition, I already mentioned the protocol amendment which has now been submitted. And that also will significantly enlarge the patient population. So it will allow to include stem cell patients, the stem cell transplant patients, which, in several countries, like U.K., Italy, Turkey and others, is really a treatment of choice for most of the follicular lymphoma patients.

We estimate that the approval of the protocol amendment will take 2 to 3 months. We already reminded our PIs, of course, that the enrollment can continue under the existing protocol. But we do have the protocol and we also informed all of the principal investigators that they should go on with the 40/15 arm, and we received very positive feedback on that. And hence, working relationship with our CRO is equally important, especially in times of COVID, where we have to have the interactions with our study investigators. And we are also working together with them on better patient referral networks so that we have really dedicated hospitals for the treatment. And as mentioned, we are targeting the 3-month data readout in the second half of 2021.

Going to Slide #9. Of course, COVID is still on everybody's mind. Otherwise, Jan and I would have been in Norway today. So you see that we still have some travel restrictions. And we have seen improvements in quite a bunch of countries. I mean in the last few weeks, we have also seen that the improvement can go back. So the negative impact due to COVID continues, already to impact patient recruitment during Q3, what you have seen.

Nevertheless, as mentioned, we are recruiting, which is very, very positive. There are other companies who are more or less at 0. And the target population is a high-risk group. So restriction of movement during lockdown prevented, of course, all our visits and data collection and dosing of newly patients. Nevertheless, we are working very hard to overcome that. We have people on the ground in the countries who really can help the patients, who can help the hospitals.

During the past 2 months, we have seen some easing of the COVID lockdown. And wherever that happens, of course, our trial, but probably also other clinical trials have been restarting. And we expect a better enrollment rate due to the protocol amendment and the other initiatives and, of course, only 1 arm when that is implemented.

Slide #10. Betalutin really has the potential to address the unmet need in follicular lymphoma.

On Slide 11. I know that a few of you, or a majority of you have seen that slide, but I still would like to go through. There is really a high unmet need in -- especially in third-line follicular lymphoma. What you can see here is the 5-year progression-free survival, and especially in third line, which is a red line down there, is that we only had 26% 5-year progression-free survival.

The other part, which is equally important is that especially relapsed/refractory patients may not tolerate chemotherapy because of their age and the comorbidities. There is a high need of an alternative target to CD20 and of course, chemo-free regimens with a gentler side effect profile.

Slide #12. We are convinced that Betalutin offer that. Betalutin has a compelling, unique and differentiated value proposition. You know how we -- how it is built up. It's an anti-CD37 target. It's a radioimmunotherapy. And we are using the lutetium-177 as the beta-emitter with a half-life of close to 7 days.

Our mechanism of action is internalization and cell death and, of course, a crossfire effect around the target cells. All of that is in a single dose treatment with a promising and durable response, which we have shown in our Part A. And that is very important for elderly and heavily pretreated NHL patients. I already mentioned the side effect. I cannot stress it is more at really, really a very good data profile. And for all of the elderly patients, that is very important.

And of course, it's an alternative target for CD20 and starts well suited for NHL patients to become refractory to any rituximab-based treatments.

On Slide 13, I would like to show you how we position ourselves. And that is the third-line follicular lymphoma. So on front base, follicular lymphoma can start really at young patients in the age of 50, not -- likely not a very good demand. Most of the patients affected by third-line follicular lymphoma are in the age of 65 and above. For the young and fit patients, there are certain possibilities. I already mentioned the stem cell transplantation, but they're also coming new target and new therapies like CAR-T and other, which you have heard about it.

Betalutin with a very strong and good side effect profile, we position ourselves really for the majority of the patients, and these are the elderly patients and the fragile patients. I would like to point out here that these patients, as mentioned before, have comorbidities and cannot go for therapies like chemotherapies. But also like the PI3 kinase inhibitors, what you can see here as a single agent, have a pretty high side effect.

Other therapies, which are just new on the market is tazemetostat. Tazemetostat only targets about 15% of the elderly patients because you need to have a certain mutation. Duvelisib itself is not used anymore to a large extent. And of course, if you are on rituximab refractory, and the rituximab therapy is not extremely effective. So from that point, we are convinced that our positioning here is very good. And what we have seen so far makes us very proud of that we have very good results in that patient population.

We already mentioned also that we have done a cost saving initiative and our corporate reorganization.

I'm going to Slide #15 now. What have we achieved? We have changed the management team, myself as the interim CEO; Malene as the CFO; and Christine as our CMO. We have reduced our head count by approximately 20%. And we have cost savings of approximately NOK 35 million in connection with that restructuring on an annual basis. And we have Jan on the phone, and we have also increased involvement of our Board of Directors.

With that, Malene, I would like to hand over to you to guide us through our financial results.

Presenter Speech

Malene Brondberg (Executives)

Thank you very much, Lars, and good morning from sunny Oslo. So here, we have first the quarterly spending, as you can see. And we are fully aware, of course, that it's the shareholders' money that we're spending. So we're trying to spend them as careful as possible. You can see the Q2 result came in more or less on par with Q2 last year. And we announced earlier in the -- or in May, and that we were going through some restructurings, which will impact the cost savings of NOK 35 million, and we will see them start to materialize in the second half of 2020.

So if we go to the next slide. Here, we could just see the cash runway. And as we've said early on, we are confident that we can get into the next year. And right now, or the end of June, the cash position was NOK 246 million.

If we look at the next slide, just a reminder about the financial calendar. We will come back to the precise date for February and for May. But this is just a reminder that the next result is the 19th of November.

With that, I will hand it back to you, Lars.

Presenter Speech

Lars Nieba (Executives)

Thanks, Malene. And the only thing that I can do, so I can really sum everything up. So what you have seen is what we promised, we delivered, so we are focused on PARADIGME and our goal is to complete PARADIGME as quickly as possible despite COVID-19. You have seen all of the activities which we are really doing. We target our 3-month top line data readout in the second half of 2021. We are very pleased with the recommendation from the IRC on the interim analysis, and that really has provided clarity on how to advance PARADIGME.

The protocol amendment, I mentioned, is already submitted and will be implemented throughout all 24 countries. We are also working very closely with our CRO to implement that, but also to implement other initiatives to speed up enrollment. And we are absolutely convinced of our confidence for the potential of Betalutin to really fulfill the important unmet needs in non-Hodgkin's lymphoma.

With that, I open up the floor for questions.

Answer

Malene Brondberg (Executives)

Thank you very much. I think we will start with questions here in the audience, we don't have many audience today, but we do have a few. So thank you for showing up.

Do we have any questions from the audience? Otherwise, we'll go straight to the web. Thank you.

Answer

Unknown Executive (Executives)

Yes, looks like we go straight to the web then. We're going to start with some clinical questions and there are quite some of them. The first one is, going forward, will you allow inclusion of FL patients who have had SCT treatments? Has this population been given Betalutin before?

Answer

Lars Nieba (Executives)

So honestly, I must say, I'm not sure about that inclusion criteria. I'm very sorry, I will follow-up that question, and I will provide you with a feedback on that one. Then I will reach out Christine and ask her about the SCT patients. I'm not 100% sure that is why I don't want to answer that question directly. If that is okay with the person who has had that question.

Answer

Unknown Executive (Executives)

We will make sure to follow-up. And that goes for a follow-up question related to whether such patients who had SCT were included in LYMRIT and whether you can comment on effects in this subpopulation. So we'll get back to that as well.

Next question is about the amendments to the protocol of PARADIGME. Can the new criteria take effect in each country as it is approved there? Or will the old protocol be used everywhere until the last country has approved the amendment?

Answer

Lars Nieba (Executives)

No. The first one. So as soon as we got approval in the country, we can directly switch to the new protocol version.

Answer

Unknown Executive (Executives)

Thank you. Have you screened relapse SCT patients that are just waiting for the protocol amendments to be approved in their respective countries? And can you, in that case, eventually say something about how many are waiting to be treated by Betalutin?

Answer

Lars Nieba (Executives)

No. Since we are currently not allowed by protocol to take any patient into screening, we have not screened the patients. What we have seen is we have screen failures due to former autologous stem cell transplantation. And what we also have seen, which is the far more important piece because there were only a very few because they shouldn't have been included, what we have seen more is really the feedback from our principal investigators across a wide variety of countries where they ask us to really include these patients and because there are quite a few patients out there with stem cell transplantation.

Answer

Unknown Executive (Executives)

And with the amended criteria to include previous SCT-treated patients, do you have a conservative percentage estimate on how much larger the patient population that is available for screening, giving -- given, sorry, that SCT treatment is the majority of our FL patients?

Answer

Lars Nieba (Executives)

A very good question here. That is not that easy to say in general because in all -- I mentioned about 6, 7 countries, where we do have the majority of the stem cell patients being treated, all the FL patients being treated with stem cell transplantation, other countries might have a different rates there. So we have done an epidemiology, and we, of course, asked our KOLs but it is far too early to give any percentage of how much manageable patients will be increasing. We are only very confident that it will increase significantly.

Answer

Unknown Executive (Executives)

And the next question is, are there other amendments that are not mentioned to the public?

Answer

Lars Nieba (Executives)

I mentioned also -- you mentioned also lower platelets. So one of the points is we have been conservative in the start of the clinical trial of PARADIGME and that we have some certain threshold of platelets. As you know, it's a radioactive compound, and it can have an effect on platelets. And we have seen that we have a very safe compound. And for that, we got allowance to also lower the platelets. So that also will have a positive effect on our eligible patient population.

And the other activities which we are doing are more operational excellence activities, so to really increase the speed of the clinical trials.

Answer

Unknown Executive (Executives)

The next question is about the time line. And it is asked whether the time line of 2 to 3 months is counted from June or August when it comes to the amendments.

Answer

Lars Nieba (Executives)

The 2 to 3 months that counted from the day where the health authority have received the new version of the protocol. And you have between 60 and 90 days of work at the health authorities and depending, of course, on their question and the back and forth with us, that might vary a little bit, but we are very confident bringing that after 3 months, we have the majority of the country approved.

Answer

Unknown Executive (Executives)

Thank you. Do you recruit patients in Norway?

Answer

Lars Nieba (Executives)

Yes. We recruit patients in Norway.

Answer

Unknown Executive (Executives)

And the next question is regarding enrollment cost, whether it is possible to swap from a fixed cost than to pay per enrolled patient?

Answer

Lars Nieba (Executives)

Can you repeat the question I might not have gotten it? So that we are only paying for patients who have been enrolled. Is that the question? Or what is the question exactly?

Answer

Unknown Executive (Executives)

Yes. The question is whether it's possible to swap from a fixed cost payment to a payment per enrolled patient.

Answer

Lars Nieba (Executives)

Okay. It's an interesting question. It's a little bit like what we are currently discussing also in public with Novartis with CAR-T, so that they're only paying if the drug is already working. Usually, if you have a CRO and you're at a site, you're paying for the site setup. And then the principal investigator is also -- are looking for its patients. So the CRO has a fixed cost, and that is also how our contract is made. And since we have the contract, it is not possible to really pay by patient.

But in principle, I think it is an interesting idea to follow-up.

Answer

Unknown Executive (Executives)

Thank you. Your CRO, ICON, are self-situating themselves as the best off-site treatment company in the world. And the question is, can patients be treated with Betalutin in their own homes due to COVID-19 risk in the hospitals?

Answer

Lars Nieba (Executives)

It is an infusion, so you have to go to into any -- into a specialized office where it needs to be treated. And the other part, as you know, it is a radioactive compound. So you have to have a radiopharmacy in your own house, who is registered as a radiopharmacy because otherwise, you can't do the right dose. So from that point, not at home.

Answer

Unknown Executive (Executives)

Thank you. And is it automatic that the FDA will accept one dose going forward in PARADIGME?

Answer

Lars Nieba (Executives)

We, of course, have the protocol now where we have one dose written. And from the protocol itself, it was written by an independent review committee. Committee can make that decision. So we have not. It was certain, I would say we have very good argument why they should accept it. Let's wait for their details.

Answer

Unknown Executive (Executives)

Thank you. Then the next question, can we expect NANO to be part of the ASH conference in 2020?

Answer

Lars Nieba (Executives)

Malene, will you take that question?

Answer

Malene Brondberg (Executives)

Yes. Well, it's difficult, as you know, with the COVID situation. And so far, what we've seen this year is that we have seen that most conferences have actually gone on the web. And that's a totally different way of going to a conference, of course. And how it's going to be is, I think, still a little bit up in the air but most likely on the web. So -- but we are still talking about that.

Answer

Unknown Executive (Executives)

Thank you, Malene. Then a couple of Archer-related questions. Because of those situ recommendation in PARADIGME, will the Archer-1 follow the same dosage in the future? And are you disappointed that the 20/100 dosage was not recommended?

Answer

Lars Nieba (Executives)

First going to Archer. No, we have an ongoing protocol in Archer, and we will go on with the current dose regimen, which we have in Archer-1. And as mentioned before, as soon as we have finalized the current cohort, we will look on the data and we will look where to see, what is the best dosing and the best combination and so on and so forth in second-line follicular lymphoma. So if we have 2 very good treatment schedule and then, of course, we would need to work also with our principal investigators to go ahead. We definitely go only with one dose into a Phase III trial.

Am I disappointed with 100/20? Honestly, no, not at all. I think it was extremely good that we have 2 doses competing to each other. And that gives us now the confidence that we have chosen the right dose.

Answer

Unknown Executive (Executives)

And could you please provide us with the status on the recruitment in Archer-1? How many patients are recruited and how many are left to finalize the study?

Answer

Lars Nieba (Executives)

We're still missing 2 patients.

Answer

Unknown Executive (Executives)

And why is this so extremely time-consuming to recruit the last patients for Archer-1 given the 100% CR in the first 3 40/10 patients?

Answer

Lars Nieba (Executives)

I think during COVID, one, now it has been very difficult to really get patients into the hospitals, we have -- since it's only a very small study, we have opened up 6 sites. And in all countries in the 6 sites, COVID has really given us hard times. And our major investigator of course is in the Oslo University Hospital, and he is still recruiting. And we have screening -- screened patients there. So we are very confident that we will finalize the cohort in the next few months.

Answer

Unknown Executive (Executives)

Thank you. Then a couple of Alpha37 questions. In June, you said that Alpha37 research with Orano Med would be paused only after reaching IND submission. Has this been achieved? And if not, will you give updates on this going forward?

Answer

Lars Nieba (Executives)

Yes, we are working together with Orano Med, and we are working on the IND submission. So that is what we mentioned. So we -- due to COVID, we had also a few different countries in the list that we couldn't enter also. So we have a few weeks now where we still have to work on the IND.

Answer

Unknown Executive (Executives)

Thank you. And in November '19, you issued a press release being awarded on a nondilutive grant of NOK 12 million for a NANO yield project, aimed to optimize the production yield of the antibody NNV003 in partnership with SINTEF. Can you give an update on this project?

Answer

Lars Nieba (Executives)

Can we also put that project on hold? So we first need to understand how we are moving forward with all the projects in early research. And as mentioned during our review, of the strategy, we have said that we want to focus on PARADIGME and PARADIGME is the most important asset of the company.

Answer

Unknown Executive (Executives)

Thank you. We still have some more clinical questions here. Did you apply for a total patient number reduction when the 20/100 arm was canceled in the recent protocol amendment?

Answer

Lars Nieba (Executives)

The recent protocol amendment was for all of the changes in inclusion criteria. So from that point, the protocol can change untouched from the amount of patients.

Answer

Unknown Executive (Executives)

Thank you. Are you expecting to include MZL as part of PARADIGME? And how do you expect this to affect the total number of patients to be recruited?

Answer

Lars Nieba (Executives)

For the marginal zone patient, we are now working on what is the right dose and what is the right way of running a clinical trial there. There is, of course, a possibility that it can be part of PARADIGME. The advantage there would be that they have supply, and the size for follicular lymphoma and for marginal zone are pretty similar. The advantages of running it are low. And the inclusion/exclusion criteria are, of course, slightly different and the other one is it is different patients, so it has nothing to do with each other.

So the amount of patients for follicular lymphoma and for marginal zone are independent of each other. But we are still working on the best way forward and the right way forward. We are currently focusing, as mentioned, on PARADIGME, on the third-line follicular lymphoma to bring everyone forward. And as soon as we have worked on the synopsis of the protocol, yes, we will, of course, inform the public how to move ahead in marginal zone. We are very confident that, that is a very important indication. You can see that since we have received fast track and ODD. So I think there is a wish outside, and we have interviewed, Malene, I think 60 principal investigators and one feedback on marginal zone, and we received very positive feedback on that. So that is why, I think, it's also on us to really work on a very good protocol that we can get the recruitment of marginal zone very fast.

Answer

Unknown Executive (Executives)

Thank you, Lars. Can you say something about the mDOR from LYMRIT for 2 dosages, 15/40 and 20/100? Was there a difference between the 2 dosages?

Answer

Lars Nieba (Executives)

mDOR, I must say, it warrants -- is that standing for?

Answer

Unknown Executive (Executives)

I am not sure.

Answer

Lars Nieba (Executives)

Then let's -- let me clarify that afterwards and then we can give you a feedback on that.

Answer

Unknown Executive (Executives)

We can give a written feedback on this one.

Answer

Lars Nieba (Executives)

Yes.

Answer

Unknown Executive (Executives)

And the next question is, can you give us the DOR data from the LYMRIT 37-01 study, if you exclude the 20/100 patients from the results?

Answer

Lars Nieba (Executives)

That's a very interesting question. We do have the mDOR data published. We have -- since the majority of the patients were treated with 40/15, I think, it might be a little difficult to really go with respect to be in there. Let me work on that, but I know that we have also worked with our main investigator, Dr. Kolstad, here and we are also working on some new data and some more mature data on that one.

Answer

Unknown Executive (Executives)

Thank you. Then we have quite some questions about share capital issue. And all these questions actually ask the same. Let me guess, yes. When are you going to go to the market and raise new capital? And how are you going to do it? And how much are you going to get?

Answer

Malene Brondberg (Executives)

All interesting questions, I must say. Well, as I said, we are -- of course, it's the shareholders' money we are spending. So we are trying to spend them in the best way and try to get as much as possible out of them. Which is why we've initiated a lot of projects internally where we review a lot of things. And then one of the outcomes, as you can see, is that we have the NOK 35 million when we will gradually come through in the second half.

When that is said, and I said previously, we are confident we will get into next year. That said, of course, we do and we are a biotech company and always looking for, of course, financing. So we will, of course, have to look at that. And we will, again, of course, try to find a -- look for the best timing. Right now, no decision has been made. But of course, we will, of course, are looking into this and we're looking into this all the time. It's not a new topic, as you can put it like that. But we're also, at the same time, going through the best way to spend the money.

And as Lars said, we are focusing on PARADIGME. And then, of course, we are trying to complete the Archer and the DLBCL cohort as quick as possible, get them analyzed because, of course, we're also spending money there, and yes. So it's -- there's a lot of work going on. It's a good process.

Answer

Unknown Executive (Executives)

Thank you, Malene. There's also a question related to a sale of the company. When will Nordic Nanovector be sold?

Answer

Lars Nieba (Executives)

Jan, will you take that?

Answer

Jan Egberts (Executives)

No. I mean I guess no one want to take that. I want to answer also the previous question. Yes, no decision has been made about any financing or the timing thereof. So I just want to be clear about that. I really -- we are pursuing a strategy to bring the product to the market. And we haven't finally decided how we're going to do that. We are not currently "for sale". But we understand that we are a venture, we're backed by our shareholders, and they are interested in maximizing value. But just absolutely no intent at this moment to sell the company.

Answer

Unknown Executive (Executives)

Thank you, Jan. A follow-up question is, do you talk to any big pharma company about any partnership or license agreements?

Answer

Jan Egberts (Executives)

Yes, it's all in the same category. I don't think we disclosed about ongoing discussions. But obviously, large companies are interested with what we're doing, and then we have ongoing dialogue with any and every company that could be interested in this technology. It's a very small community. We know all the major players. So we're in continuous dialogue. But we have not decided anything about how we're going to commercialize this product once we get our approvals.

Answer

Lars Nieba (Executives)

Yes. And let me also really reemphasize what Jan just said. I think the key objective is really, as I mentioned before, to bring that onto the market and to maximize the shareholder value and exploring opportunities, of course, is part of the job, as Jan mentioned. So I think from that point. That's all.

Answer

Unknown Executive (Executives)

Thank you. And that concludes the questions for now from the webcast. And to the extent that there are questions that have not been answered here, we are going to go carefully through the questions from the web and make sure that every question is responded to by e-mail later on. Thank you.

Answer

Lars Nieba (Executives)

Yes. Thank you, also, from my side. It was a pleasure to talk to you and getting such a lot of very interesting questions. So then with that, I would like to conclude. Jan, any final words?

Answer

Jan Egberts (Executives)

No, fine. Thank you very much. Thank you all for your attention and support. We appreciate it, and we know what needs to be done. So we're continuing our execution. I think it does really what the primary objective is right now is execution and then including the improvement motivations. And obviously, with our expanded inclusion criteria, we think we're much better positioned than we were 6 months ago. So I appreciate your patience. I know it has been a long and difficult ride, but I think we're really moving in the right direction now.

Answer

Unknown Executive (Executives)

Okay. Thank you very much. I think that concludes our quarterly results. Thank you for coming.

20.05.26. Nordic Nanovector ASA, Q1 2020 Earnings Call, May 26, 2020

Presenter Speech

Lars Nieba (Executives)

Good morning, everyone. I would like to welcome you to the audiocast for Nordic Nanovector's Q1 Results. I'm Lars Nieba, the interim CEO of Nordic Nanovector and, as mentioned by the speaker, we have Jan Egberts with us, our Chairman; Malene Brondberg, our new CFO; and Marco Renoldi, our COO.

Let me first go to the next slide, which is the forward-looking statement. As usual, we do have that. And on the next slide, I would like to introduce our management team with a lot of international experience. We do have Dominic Smethurst, our Chief Medical Officer; Marco, who most of you probably know, our Chief Operating Officer; Rosemarie Corrigan, our Chief Quality Officer; our new CFO, Malene Brondberg; Jostein Dahle, our Co-Founder and Chief Scientific Officer; and Gabriele Elbl, our Vice President for Global Regulatory Affairs.

On the next slide, I would like to guide you through our Q1 highlights. As you've probably read in February, I was appointed as the Interim Chief Executive Officer. In March, we appointed Dominic Smethurst as our Chief Medical Officer. Our update on our PARADIGME trial and in third line follicular lymphoma with Betalutin, whatever we have there as our Q1 highlights. That is also why we are on the audiocast. COVID-19 not only had an impact on all of the countries with lockdowns, it also had a negative impact on our PARADIGME trial during the first half of 2020. We have now 51 patients enrolled as of yesterday. We have started -- initiated a strategic review with focus on advancing PARADIGME and extending our cash runway into 2021.

Next slide. What happened until today? We have completed our strategic review. Clinical development strategy has been revised, and cost-saving initiatives have been implemented. An FDA meeting sought to discuss PARADIGME protocol amendments designed to enlarge eligible patient population and increase the rate of enrollment. As stated here, [Betalutin and] PARADIGME time lines are under review. We have reduced our head count by approximately 20%. The cost savings in connection with the restructuring is approximately NOK 35 million on an annual basis. We received very good news in the EU that Betalutin is recommended for Orphan Drug Designation for marginal zone lymphoma.

Next slide, please. I would guide you in a little bit more detail through our strategic review and on our focus of PARADIGME.

Next slide, please. What is our revised clinical development strategy to capture the significant value from Betalutin in non-Hodgkin lymphoma? As mentioned, our core focus is PARADIGME. It is a single-agent Betalutin trial in third line relapsed/refractory follicular lymphoma. We are targeting that indication as first-to-market. We evaluate the optimal strategy to advance into earlier lines. We evaluate the opportunity to investigate in relapsed/refractory marginal zone that is based on, as most of you know, the promising response in LYMRIT 37-01 trial; we received the Orphan Drug Designation that is reflecting an unmet need; there is also a possibility to augment patient flow into PARADIGME by leveraging the existing infrastructure.

We also looked into our other trials in our strategic review. So under review is currently Archer-1. We remind everyone that is Betalutin with rituximab in second-line relapsed/refractory follicular lymphoma. It presented very good initial efficacy. However, the recruitment in our eyes is too slow. We need to consider here the future positioning and the optimal strategy in second-line follicular lymphoma.

For LYMRIT 37-05, there, we are using Betalutin as a single agent in the DLBCL. So here, the recruitment has been slow, and we all know that DLBCL remains -- is and remains an important indication. So here we need to evaluate the optimal development strategy. Our goal with a revised clinical development strategy is to develop a differentiated target product profile for Betalutin to meet requirements of non-Hodgkin's lymphoma patients, KOLs, regulatory and reimbursement agencies.

Next slide, please. So in more detail on our revised development plan. As mentioned, we focus exclusively on PARADIGME. We pause enrollment of patients into Archer-1 and LYMRIT 37-05 following the completion of the current cohorts. We then will start evaluating the results. We also pause all preclinical and research initiatives, our ongoing partnership with Orano Med on Alpha37 only after IND submission. A formal meeting request has been filed to the U.S. FDA. There, we seek expansion of inclusion criteria to increase the pool of

eligible patients. Overall, we aim to improve execution of PARADIGME. We also have aligned the CMC activities with the clinical timelines. We target top line PARADIGME data in 2021 and, of course, subsequently submit BLA in the U.S. based on results, if positive.

Next slide, please. As a reminder, we are focusing on PARADIGME, and all of our resources are prioritized towards PARADIGME. What is PARADIGME? It is a clinical trial where we are looking for 130 third line refractory follicular lymphoma patients. Primary endpoint is the overall response rate. Secondary end points are duration of response, progression-free survival, overall survival and quality of life. We do currently have 51 patients enrolled. We have 95 sites in 24 countries open for enrollment.

Next slide. How do we improve trial execution? Actions have been taken. We have enhanced our working relationship with CRO and also far more interactions with our study investigators. In addition, we have implemented patient referral networks in several countries. Nevertheless, the COVID-19 impacted us. So impact of actions blunted by COVID-19 really has an adverse effect on PARADIGME. You need to remember our target patient population is at high risk. On average, they are more than 70 years old and are fragile. That restricted movement has prevented follow-up with it and data collection of existing patients and dosing of newly enrolled patients. A lot of hospitals, as you know, have been closed and focused their -- or their trials only on COVID-19, and the resources they have also only on COVID-19. What we are seeing now is the easing of COVID-19 lockdown enable cancer clinical trials to restart. We remain in close contact with our investigators. We do see an increased enthusiasm for trial and potential of Betalutin.

Next slide, please. Improving the PARADIGME protocol. So as mentioned, after a meeting with the FDA, the briefing book is submitted, and we seek expansion of inclusion criteria to increase the pool of eligible patients. The PARADIGME protocol amendments to be filed after the review of the feedback. So we expect the FDA response in late Q2 or early Q3. Following the FDA response, we estimate 2 months -- 2 to 3 months to gain approval for the protocol amendments with regulators in all 24 countries. We are working very closely with our CRO to really maximize the enrollment once the new protocol is approved.

Going into a little bit more detail on Slide 12 for our cost-saving initiatives and the corporate reorganization.

Next slide, please. Cost-saving initiatives implemented. What kind of initiatives we have implemented? We have reduced our head count by approximately 20%. We have consolidated our number of leadership functions. We have ongoing focus on our core clinical and CMC activities. The spending on CMC is aligned with the progress in PARADIGME. Our members of the Board of Directors will voluntarily reduce their fee by 20% for the Board year 2019/2020. The financial impact of these changes will materialize gradually. The Q2 results will reflect costs associated with these organizational changes. My colleagues and I on the leadership team will continue to seek further efficiencies.

Next slide, please. Overall, the organizational changes have affected about 30% of our team. You have seen our new leadership team. Myself and Dom have been appointed in Q1. And as mentioned, Malene Brondberg, our new CFO, has just been appointed, and the role is expanding. So she has the oversight of both finance, HR, and IR and communications. We focus further on organizational efficiencies. We have consolidated certain staff functions, we have expanded roles of certain key individuals, and we have moved talented people into new functional roles. In addition, also Jan, our Chairman, increased his involvement and also other members of the Board. Jan and I will very closely work together. And also our Clinical Strategy Committee is involved in the revised clinical strategy.

Next slide, please. Now coming to the financial results for our Q1. So Malene, please, walk us through...

Presenter Speech

Malene Brondberg (Executives)

Thank you very much. If you look at Slide 16, which is called Investing in Betalutin, you can actually see the development quarter-over-quarter. And as you can see, in Q1 last year, we had NOK 90 million in spend; this year, we had NOK 126 million. And that is, as you remember, maybe from last year when we did the funding rounds, we said we will spend more money on clinical or focus more on clinical and CMC, and that's what this is really a result of.

If you turn to the next slide, you can see the cash runway extended into 2021. And here, we have a net cash from operating activities of minus NOK 116 million. In the end of the quarter, we have a cash position of NOK 384 million. And as Lars alluded to also is that we have executed a restructuring plan, which, on a yearly basis, will provide savings of approximately NOK 35 million. And we are working on several initiatives to extend our cash runway into 2021. And we will see in Q2 that we will still have an effect of -- Q2 in line with -- more or less with Q1. And we will see some of those savings coming through in the second half.

Next slide, please. Lars, back to you.

Presenter Speech

Lars Nieba (Executives)

Thank you, Malene. Let me summarize. So we are really focused on PARADIGME. We continue to target our readout of top line data for PARADIGME in 2021. Our -- current COVID-19 situation has prompted a review of enrollment time lines for PARADIGME, which previously was guided for H2 2020. We expect to provide an update on time lines for PARADIGME once we have received all relevant regulatory feedback from the FDA and we have more clarity on the impact of COVID-19. Again, we reconfirm the top line data in 2021, despite the headwinds of COVID-19, that we are waiting for the FDA meeting to discuss the proposed protocol amendments. As mentioned, we seek, of course, approval for the protocol amendments from all of the local health authorities in all 24 countries. In addition, we evaluate the opportunity and clinical trial development strategy in third line relapsed/refractory marginal zone lymphoma. And of course, we will submit the BLA in the U.S. based on the results, if positive.

Overall, we really can confirm that our confidence in potential of Betalutin to fulfill important unmet needs in non-Hodgkin's lymphoma remains unchanged.

With that, Malene, would you like to guide us through the financial calendar?

Presenter Speech

Malene Brondberg (Executives)

Yes, I can do. The next upcoming event is our AGM, and that is on the 10th of June. And then we follow on with the Q2 results on the 27th of August and then on the 19th of November is the Q3.

Presenter Speech

Lars Nieba (Executives)

So with that, I would like to thank everybody. And we will open the floor for questions.

Question and Answer Operator Message

Operator (Operator)

[Operator Instructions]

Answer

Unknown Executive (Executives)

We do have a few questions already. And the first one goes to the Chair of the Board. There's a question about, can you make a comment to the process to get a permanent CEO and a permanent CMO?

Answer

Jan Egberts (Executives)

Thank you. Yes, there -- I would say that our current primary focus is on implementing the programs we announced earlier in the year, the restructuring program, that's our #1 priority. Yes, there's an ongoing search going on, but our primary focus right now is on implementation of all the changes we have announced, including

the cost reduction, the Type C meeting that Lars was talking about and the other changes. And actually, I'm quite pleased with the way things have been going on and how we work together with the management team. So again, the #1 priority is implementing the changes we announced earlier in the year.

Answer

Unknown Executive (Executives)

Thank you. The next question is related to the recruitment of Archer. How do you explain the horrific recruitment of Archer, which data has shown 3x CR in the first arm? And is it 3 or 6 patients in the ongoing arm? Has cut-off on recruitment taken place? And are we only awaiting the evaluation?

Answer

Jan Egberts (Executives)

Thank you. For Archer-1, we have currently recruited -- there is an echo. Now I think it's better. Yes, for Archer-1, we are in the second cohort. We have recruited 5 patients. One of them was not eligible. And we have to find 2 additional patients to close the final -- the current cohort for Archer-1. So in total, we will have some 6 patients to evaluate the data in Archer-1.

Answer

Unknown Executive (Executives)

Thank you. And there's a follow-up question on this one. Has the request for a Type C meeting been sent? And when do you expect to hold the meeting?

Answer

Jan Egberts (Executives)

Yes. As mentioned, we have submitted the briefing book to the FDA. And we have asked for a written feedback, but as you know, the process currently is a bit unpredictable as the FDA is also partly locked down under the COVID-19. So we hope and expect to receive the answers from the FDA in June and then from all of the other -- subsequently from all of the other health authorities in Q3 this year.

Answer

Unknown Executive (Executives)

Then I have a couple of questions about the progression or status on the interim data readout. This was an important reflection point according to the company update on the 1st of April, so hence the question.

Answer

Lars Nieba (Executives)

Absolutely. So the interim analysis -- we are on track with the interim analysis. We are evaluating the data, and we expect the final outcome of the interim analysis around -- during August. And so that will only give us a slight delay despite the headwinds of COVID. Here, I would really like to thank our clinical team. They have worked very hard to get all patients follow-up despite the hard time with COVID-19, and that hard work really seemed to have paid off, as I mentioned, as we expect to be ready during August.

Answer

Unknown Executive (Executives)

Thank you. The next question is, if all the changes to inclusion criteria that you have discussed with the FDA are accepted, how much will the available patients in third-line FL increase?

Answer

Lars Nieba (Executives)

We have asked for the feedback from the FDA with all of the different inclusion criteria which we have asked for. It's a little too early to answer that question. We will come back to you as soon as we do have all of the feedback from the FDA.

Answer

Unknown Executive (Executives)

Thank you. And there's a question for Malene. Did I understand you right that operating costs in Q2 are expected to be in line with the costs seen in Q1 and that the savings should start to come through in the second half? And does the operating costs in Q2 also include all the one-off costs expected for the organizational changes?

Answer

Malene Brondberg (Executives)

Yes, that is correct that we received the Q2 more or less in line with the Q1. And as you know, it takes time when you make changes. So we will see them -- it's also correct, we will see them go down the cost in the second half, and all of them are included in the first half.

Answer

Unknown Executive (Executives)

Thank you, Malene. The last question we have now is if interim is [paused] with both arms continuing, how will this affect your ability to include MZL in PARADIGME?

Answer

Lars Nieba (Executives)

A very good question. Also there, as mentioned, we need to wait for the feedback from the FDA and the health authorities. There are several possibilities, including marginal zone, which we will first discuss internally, and then of course, also with our Clinical Strategy Committee and then with the health authorities. So we do see several ways forward for this very important indication.

Answer

Unknown Executive (Executives)

Thank you. That was all the questions we had. So that concludes the Q&A session.

Question and Answer Operator Message

Operator (Operator)

Thank you very much for attending. Please go ahead.

Answer

Lars Nieba (Executives)

I only wanted to thank everybody for attending and looking forward. Have a good day.

Answer

Malene Brondberg (Executives)

Thank you. Have a good day.

Answer

Jan Egberts (Executives)

Thank you. Have a good day. Goodbye.