

Question-and-Answer Session

Operator

[Operator Instructions] Our first question comes from the line of Ted Tenthoff from Piper Jaffray. Your line is open.

Ted Tenthoff

Great, thank you very much for the thorough update and exciting to see the continued progress. One quick question if I may with respect to the new peritoneal dialysis study. This is the first of the targeted studies that you're initiating. So tell us what the plan is with the ongoing Phase I at intermediate and to high dose and will this PD study start at low dose and cut escalators on how many patients should we see in that?

Mike Cola

Ted, I'm going to let Garry take that for you.

Garry Neil

Peritoneal dialysis patients usually require much lower doses of equal of dialysis patients so we're starting at the low end of the spectrum and we're going to advance the dose using a very similar protocol according to their response.

So, but I think that we all expect that we're not likely to see requirement for dosing as high as

what will be necessary for the hemodialysis patient, but again if you look at what the data that Mike showed you can see that the patients were treating there have very, very high EPO requirements.

Ted Tenthoff

Thanks a lot excellent.

Garry Neil

Right. And we're going to continue on the intermediate dose so as usual this is a type of gene therapy you have to go slow initially evaluating each patient, we do that for the first three patients and then once we're satisfied then we have adequate safety and we're in the right range that we can enroll the next three patient faster than that. And make a decision on whether or not to make sense to go to the highest dose that we have planned.

Ted Tenthoff

Excellent. And when should we get that decision?

Garry Neil

Well, we're doing very well with our enrollment right now. So I think we'll be making that decision probably sometime in the next quarter or two.

Ted Tenthoff

Great. Thank you very much, guys.

Operator

Your next question comes from the line of Brian Marckx with Zacks Investment. Your line is open.

Brian Marckx

Good morning, guys, and congratulations on all the progress. How many of the mid dose patients have been enrolled? And when do you expect full enrollment for the mid dose?

Mike Cola

We've got two enrolled and we expect to be able to enroll all of the patients in that – by the end of the next quarter.

Brian Marckx

Okay. And that will be six patients as well?

Mike Cola

Yes.

Brian Marckx

Okay. And you expect the high dose will begin enrollment this year as well?

Mike Cola

Yes, if we do it. I think as Ted just said - or as we just talked above with Ted, we'll evaluate the results of the intermediate dose and then decide whether or not we need to proceed to the higher dose.

Brian Marckx

Okay. And regarding CHOP, it sounds like the entire focuses is orphan and rare indications, but is it possible as you go through the iterations of potential candidates that you look at non-orphan indications?

John Leaman

It's absolutely, possible, but our deal with them is specifically rare and orphan related to Center for Applied Genomics. I think when you look at the slides that Garry laid out you have these extreme phenotypes with underlying genetic mutation. Many times those mutations are found outside of the extreme phenotype in other syndromic diseases.

So I think our idea is very specifically go after the very narrow patient population and then extend out to where the gene leads us in other sub population. Not unlike the way cancer development has been done in the last 10, 15 years.

Brian Marckx

Do you have a general timeline on when you hope to identify the initial candidates?

John Leaman

Yes, we've been telling folks mid-year. There is a number of candidates I think Garry laid out the criteria that we're using and we're prioritizing based on these criteria. I think it's a little different for us than we expected when we started the relationship.

There are near term clinically, more clinically relevant opportunities than we expected and there is also the potential to repurpose existing products. I can't call them drugs because some of these things have been shelved. Again, we really didn't have or want to decide it to when we signed the deal pack.

Brian Marckx

Okay, all right, great. Thanks guys.

John Leaman

Thank you, Brian.

Operator

[Operator Instructions] You have a follow-up question from the line of Ted Tenthoff with Piper Jaffray. Your line is now open.

Ted Tenthoff

Great. Thank you very much. So my second question has to do with CHOP, and I really get the sense and I appreciate the way you kind of characterized that you guys maybe just found an entire goldmine in terms of just the number of opportunities that you're going to be able to go and pursue. I mean I think this is a transformable really, really exciting in terms of providing this discovery engine for you guys.

So Garry, I guess maybe kind of adding a little bit more to the discussion from your side. Have you prioritize these opportunities more specifically? And ultimately, how do you pursue them all? I mean, is this something how about partnering start to feed into the larger strategy here as you consider all of these exciting targets that are going to start to merge?

Garry Neil

Great questions, Ted. So the prioritization process as we've said I'm really looking for a strong phenotype well characterize as an initial program because we have the best change of identifying a mechanism and showing that we can intervene. Some of the diseases that we see down there may be pretty severe malformation struck hold disease that sort of thing where a drug intervention isn't likely to help.

Ted Tenthoff

Yes.

Garry Neil

So we tend to set those aside and focus on the ones where metabolically or mechanistically we can intervene with a gene therapy, a drug or protein something like that and have a good chance of benefiting the patient. And then, we're looking for things that we can measure in the

short term that would allow us - would give us comfort that we're seeing at pharmacodynamic, in fact, allow us to be able to assess the dose and also to assess the feasibility for using our target system we're trying a different type of an approach.

And then, you also way into that the size of the opportunity, the competitive landscape and all of that goes into it. So I think it's hard to be formulate, but we have these criteria that we use and that we're applying right now. And I think it's going - the things that we're able to select - we're going to be able to select pretty well.

And then, from there we go into designing a translational type of program that gives us the shortest path and what we're doing right now we're also sitting down with the conditions who are treating these patients. And talking to them about this and talking about the - this from the perspective of the patients or in some cases foundation of patient efficacy groups because we know that we're going to need their help in designing the overall program.

Mike Cola

And just the couple of things on the relationship itself again enrollment were all of four months into it. I do think the other side of what we're discovering is that the characterization of mechanism is there and that there may be molecules to actually treat some of these diseases just because they've been shelved because they were studying in the wrong patient population doesn't mean that they can't be very good drugs that are actually relevant to this type of mutation as Garry said. Many of these drugs sell because they're not setting the right patient population.

If you look at the productivity of the group or working with them – it is off the charts in the last 7.5, 8 years it had over 400 publications with most people don't realize that there is a 150 to 200 discoveries on rare and orphan diseases a year and many of them actually come out of this group. So some of these things are actually new and novo, they are not in the NORD's catalogue, they are actually novo mutation, novo patient population.

Given all of that, there is tremendous volume that we're working through in backlog. It is a little bit overwhelming in times, but to your last point about partnering and some of these things actually have natural owners that would be a fit and I think as we are out talking to other

potential partners basically on the biopharma side.

There has been a lot of interest for – how do we leverage this relationship. The Garry's point, we can't chase every single one of these targets, but there is certainly people interested in very specific areas that would naturally be wanting to invest in these types of diseases. We're just starting those discussions now.

Ted Tenthoff

Really, really exciting. Keep up the great work guys.

Garry Neil

Thanks.

Ted Tenthoff

Thank you.

Mike Cola

Thank you, Ted.

Operator

[Operator Instructions] Our next question comes from the line of Mike King with JMP Securities. Your line is now open.

Mike King

Hi, good morning, guys. Thanks for taking the question. Can you hear me okay?

Mike Cola

Yeah, you're very crystal clear.

Mike King

Great. Sorry, I'm on the road. I may have missed some of the things I'm about to ask about, but I want to ask you regarding the hypo-responders. How should we think about that physiology versus either peritoneal or the transplant patient population. In terms of the biologic feedback and how that's going to influence the way you think about dosing with the micro-organ, et cetera? And there are any special considerations that we need to think about with regard to that population versus the others?

Mike Cola

Mike, I'll let Garry take this.

Garry Neil

The way we should think about this biologically is - you want to have a much more physiologic type of response to maximize the output of the erythron which is the part of the marrow that produces red blood cells. And probably the least physiologic way you could possibly think of treating with Depo would be to give very large doses intervenes intermittently which stimulates the acute leading paradigm versus giving it more like the running the body naturally does more or less continuously at very low dose.

And so as we've seen, we are able to achieve more stable hemoglobin production, we're going to show those results at the ASGC team meeting in New Orleans in May versus intermittent EPO injection at a much lower overall exposure.

So there is some hope that people that need very high doses of IV needs much very much lower doses can have the better response with continuous. But I think the other way that we should think about it, and the way that we are thinking about it is this these high intermittent doses again stimulating more acute bleeding can be associated in some patients with very severe hypertension possibly related to some of the other cardiovascular events.

And so as part of our program and looking at peritoneal dialysis and other patients, is to see now whether or not we can have less of an impact on blood pressure in these patients.

So you can imagine that some of the patients who are getting very high doses might also be suffering some side effects as a consequence of that specifically hypertension and other cardiovascular events.

So that's something we want to explore, we've talked to the agency little bit about that and see whether or not we can provide some benefit there to some of these patients who have those types of risk.

Mike King

Sure. I mean I would agree that something resembling normal physiology is desirable whenever possible I'm just wondering do these patients have such damage marrow whatever original blast

failure or anything like that, that accounts for the type of responsiveness that may make them less responsive to a micro-organ. What you think that once you restore normal EPO levels that it will come right back?

Garry Neil

Right well that is something that we have to study and we are studying that I think there is - it's a solid hypothesis that we can test and as far as the patients that we're treating right now, Mike showed you that lot of them are getting 20,000 units a week, getting fairly high doses. Those people their marrow is perfectly capable of responding to pretty low concentrations of EPO and we give to them that way.

Mike Cola

Mike we have people that are really on the - I will say the upper edge, I'm sorry the lower edge what we think as the high dose and they are responding well.

I mean you asked a very good question this is not a simple disease or situation, you have nutritional status, iron stores and inflammation that impact the ability to produce red blood cells and what learning - this is truly a novel experiment we're learning about how this works together at true physiologic levels and I think this is more of an autologous transplant than an injection of recombinant EPO.

Garry Neil

Okay. And then I just wonder if I could just drill down a bit more on MDS. Can you say specifically what Israel authorities want to see for your outlook there?

Mike Cola

The regulatory question really was would they allow us to do these studies under our existing IMPD which is their equivalent of an IND. And we initially thought that we would be covered under this because it's EPO it is a same product, the IRV, the DMOH review it.

So we're going to go through that process with them and we're not expecting anything out of the ordinary here but it's just an extra step that we have to take.

Mike King

Okay. So no additional data science like that, the clinical data that keeps generated?

Mike Cola

No, they haven't requested anything at this point, we have been able to answer all the questions but we will be meeting with DMOH and we will be discussing it with them and we don't anticipate that we're going to need anything more than we're able to provide, we have human data, human safety data and the investigators seem to be comfortable with that but we'll work with them and will do whatever they require.

Mike King

Okay. Just a quick question on CHOP again not ask you to reveal all your secrets but this is far as the way we should think about these targeted disease areas. Are they monogenic disease, are they sort of classic enzyme replacement diseases, none of the above, all of the above.

Mike Cola

It's in all of the above.

Garry Neil

The best way to answer the question to me is to look at the 400 publications, not than anybody needs to do that but you name an area they have a discovery in that area although it's - everything from complex networks of genetic mutations sound through monogenic mendelian diseases.

So I think for us we realized we need to be flexible in our solutions to these problems and we love our technology, we can TARGT platform that's great, so we're going to have to run our portfolio of capability to actually treat some of these diseases.

So, luckily there is a lot of shelved molecules out there and, the stop that we think it bring immediately able to treat these patients - in anyway most of the patients we are talking about have building out recourse [indiscernible].

John Leaman

And we have a lot of capabilities related to, the recombinant protein and molecular biology, which is core to our main technology platform so we can bring that the bear as well.

Mike King

Right. So it's - Mike, you said at couple times about shelved programs, can you say whether the programs are shelved because lack of a suitable delivery vehicle or inability to manufacture again this had and all the above kind of answer.

Mike Cola

Yes, I think there all the above but again we're looking for programs obviously that have clean safety profiles, that have, some known effect but where they were studied in a very diversification population and heterogeneous population and so the company got back a very weak signal on the efficacy side.

There is something that's down on the efficacy side is of great interest to us, as in fact we can stratify the patients as Garry laid out in his approach here. We stratify the patients with the genetic biomarker, we're going to get a much higher response again as you look through cancer diagnostics and developments, and the way its really has gone in the last ten years or so.

We identify the patient that the drug is going to work in based on a biomarker and its been hard to translate that into other therapeutic areas but I think we have real shy here as Garry has said, the tools are there, data is there, CHOP –

The other thing is that we made, the patient's there, they're accessible, they're definitely called back so that's really the approach.

Mike King

Okay. And then finally just real quick on GLP-2 any update there?

Garry Neil

We continue to progress as you know we had interest from NPS and we're in discussions with them. We do think we have a better approach to delivering either Gattex or native GLP-2 and we can't discuss other conversations that obviously there is a natural owner for our GLP-2 product. We'll continue to pursue partnership.

Mike King

Okay. Thanks for taking my question.

Mike Cola

Actually it was more than one Mike.

Operator

I'm not showing any further questions at this time. I would now like to turn the call back to Brian Piper for any further remarks.

Brian Piper

Okay, thank you Abigail. I think that will conclude today's call. We appreciate everyone taking the time this morning to listen in, and with that we'll conclude the call. Thank you folks, we appreciate your time.

Operator

Ladies and gentlemen, thank you for participating in today's conference. It does conclude today's program. You may all disconnect. Everyone have a great day.

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