CLOSER LOOK

MEMORANDUM

Diamyd Medical announces interim analysis results from ongoing phase 3 DIAGNODE-3 trial of precision T1D treatment – March 30, 2026

Interim analysis demonstrates "results that were unexpected" and "not aligned with prior retrospective or prospective data"; webcast highlights topics related to potential next steps

Diamyd Medical just announced pre-specified interim analysis results on the ongoing phase 3 DIAGNODE-3 trial (n=330) of retogatein, an antigen-specific immunomodulatory precision therapy for the treatment and prevention of T1D. As background, retogatein is a GAD65 protein-containing molecule for people with detectable GAD65 antibodies and the HLA DR3-DQ2 haplotype, which affects about 40% of people with T1D. The analysis, which included 174 out of 321 participants of the trial, demonstrated "results that were unexpected" and "not aligned with prior retrospective or prospective data." In the interim dataset, retogatein did not show an effect on C-peptide, neither in the overall population nor pre-specified subgroups, including those identified as "super responders."

The company held a conference webcast this morning, during which Dr. Ulf Hannelius (Diamyd Medical CEO) and Dr. Mark Atkinson (Diamyd Medical Board Member; University of Florida) commented on potential next steps for the DIAGNODE-3 trial, speculation about the absence of efficacy, and overall impressions of the trial. Following this webcast, our team also spoke with Dr. Atkinson to gain further insight into the prespecified interim analysis results.

We are very sorry to see the events unfold as they have and we would bit be surprised about further twists or turned ahead. Although Diamyd Medical hasn't yet stated specific timing for next steps, we salute the timing with today's call, which could not have been easy to achieve. We of course will discuss further updates on the interim analysis and on the next steps for progressing the DIAGNODE-3 trial as the company shares them.

Table of Contents

Dr. Hannelius and Dr. Atkinson share reactions on the negative outcomes of the DIAGNODE-3 trial

During the webcast, Dr. Hannelius said the company expected three potential outcomes for the DIAGNODE-3 trial: (i) statistically significant results; (ii) not statistically significant results but not meeting futility criteria[1]; or (iii) not statistically significant results and meeting futility criteria. The DIAGNODE-3 trial demonstrated results falling into the third category, meeting the low-threshold futility analysis, which Dr. Hannelius called "very, very surprising." Given that the trial met the futility criteria, future steps are unclear.

While the company has only seen "very little" of the data so far, it was "quite surprising" not to see statistical significance, even across subgroups identified as the "super responders." During Q&A, Dr. Hannelius said at this point in time, it's also difficult to understand whether the placebo group simply performed unusually well. Nevertheless, Dr. Hannelius expressed hope that the company will continue developing retogatein and develop a treatment that can truly improve patients' lives.

Dr. Atkinson said that the company is taking necessary steps to evaluate trial results, including the potential for placebo effects and treatment degradation. He expressed confidence in the many divisions of the company currently at work to address these uncertainties, including an scientific advisory board composed of three dcotors from the US, one from Sweden, and one from Great Britain, as well as the Board of Directors.

Speculations on the ongoing DIAGNODE-3 trial and future outlook of the trial

Dr. Hannelius said the company has not yet decided to discontinue the trial because it first needs to complete the previously mentioned steps to ensure the negative results aren't due to the trial procedure. However, if the trial does continue, the futility analysis indicates that the likelihood of the results changing by the full trial readout in 2027 is "very low." He emphasized that the purpose of a futility analysis is to check early on, and if there's no chance of seeing differing results, the company shouldn't continue, saying, "It's just a waste of patients' and the clinic's time and shareholders' money."

In the meantime, the company has communicated the interim results to trial centers. Dr. Hannelius assured the utmost priority of patient safety and emphasized that all the information will be communicated to regulatory authorities appropriately.

Further findings expected as analyses progress

Reflecting on the results of the DIAGNODE-3 trial, Dr. Hannelius shared potential next steps the company plans to take. Upon receiving the results, the company has already begun investigating logistics for the trial, including observations on the trial procedures. The company then plans to investigate the underlying data and re-analyze results, including immunology and glycemic data. On the expected timeline, Dr. Hannelius said these procedures can take "a few weeks". He said different steps will require different timelines, but the initial steps should be "quite fast and informative."

Dr. Hannelius also shared his perspectives on unblinding data[2] and its potential impact on the trial readout. He said the trial results must be unblinded in a "very controlled manner" because there's a high likelihood of "destroying" the trial integrity and introducing bias. With proper regulation, Dr. Hannelius said, there will be careful observation that informs necessary decisions based on the data.

Diamyd Medical plans to continue core operations during the period of comprehensive assessment

The company plans to continue core operations during the period of comprehensive assessment of the interim results. In parallel with the clinical trial, Diamyd Medical continues processing the Good Manufacturing Practice (GMP) certification for the production of GAD, which Dr. Hannelius described as a "very important, central molecule for T1D." He said that even if the company decides to discontinue the DIAGNODE-3 trial, the demand for GAD will remain high. Regardless of the assessment of the interim results, Dr. Hannelius sees the company having other opportunities for internal manufacturing or for external customers.

Long-awaited results from the phase 3 DIAGNODE-3 trial of retogatein in T1D

Diamyd Medical has long pursued retogatein, first targeting the treatment for the broader T1D population and eventually focusing on the specific group with T1D and HLA DR3-DQ2 haplotype, transforming it into a precision treatment. The company has positioned the DIAGNODE-3 trial as pivotal, with the primary objective of evaluating the efficacy and safety of retogatein as a precision therapy for people with detectable GAD65 antibodies and the HLA DR3-DQ2 haplotype, which affects about 40% of people with T1D.

In previous earnings calls, including its most recent one in 4Q25, Diamyd Medical has reiterated its expected results by the end of this month. Management said the interim analysis would mark a key milestone as the company prepares for the next phases in regulatory, manufacturing, and pre-commercial operations. Management also emphasized that the readout would include results from approximately 170 individuals who had completed their 15-month visit, with C-peptide as the primary endpoint. Of note, in December 2025, the FDA accepted the company's proposal to change the primary efficacy timepoint from 24 to 15 months.

Dr. Atkinson reinforced that the DIAGNODE-3 trial is pivotal, as C-peptide as a clinical endpoint helps evaluate

whether retogatein could preserve or improve natural insulin production in people with T1D. Dr. Atkinson said he's particularly interested in observing the loss of C-peptide in the placebo and treatment groups compared with previous trials of retogatein. He said, "That could be one explanation of the variance." Importantly, Dr. Atkinson said to our team, "We will leave no stone unturned in determining the reason for these results."

Close Concerns' Questions

1. When does Diamyd Medical expect to share updates on the interim results and on the next steps for progressing the DIAGNODE-3 trial?
2. How does the company think the change in primary timepoint from 24 to 15 months could have impacted expected results?
3. Do these results impact the ongoing phase 2 DiaPrecise trial (n=16) in people with stage 1 and stage 2 T1D?

Diamyd Medical Webcast Q&A

Q: **Is it possible to skip phase 3 and go directly to phase 4? How quickly could phase three be redone?**

A (Dr. Ulf Hannelius, CEO): Phase 4 is usually considered something that you do post approval, so you are approved, and then you continue with long-term follow-ups, for example, phase four studies, real-world evidence studies, and these kinds of things. In this case, it would mean we would use the company's existing data to seek potential approval now and continue afterwards. I mean, these are always something that needs to be really discussed with the authorities. The point here was that this phase 3 should serve as the evidence supporting approval. Assuming that and with this outcome, if this holds, obviously, I think the regulators want to get some kind of confirmatory data. Yeah, I mean, it would be a difficult case to just use this, plus all the previous support rationale, to get approval; you need to do something like a second phase 3. In this case, maybe easier said than done right now. Thinking we're sitting here, we need to obviously do all the analysis first before we go there. But I mean, that's the next step.

A (**Dr. Mark Atkinson (Diamyd Medical Board Member): I** cannot emphasize how much effort went into this precision medicine-based trial. In other words, that this was really a first-in-class effort would, in terms of T1D, using an antigen or a molecule associated with the disease, be glad to get. But in people who had undergone genetic screening, previous studies using diamond showed that only a subgroup of those with T1D benefited, and they benefited extremely well. And so in this trial, it was precision medicine. And our hope was that, again, this would add to the beneficial outcome. And again, this is something we'll just be exploring moving forward.

Q: Is there any significant site variability observed that could explain it? What about the average versus the median effect? Are there significant outliers present in the data?

A (Dr. Ulf Hannelius, CEO): Again, we've seen very little of the data so far, and not everyone has seen it, so we've seen like summarized data so far on the main, like the, let's say, full population and the pre-specified subgroups. And there, as we said in the press release, we don't see any effects across the board in any subgroup, which is just by statistical chance. Also quite surprising that you don't even by chance see statistical significance anywhere. There are not all of these. I mean, once you have all the raw data, if you go that far and unblind, you can start to really explore different subgroups. But there's been, like, a certain pre-specified, on a regional level, and before, like, the super potential super responder group that you also mentioned. So, a subgroup within this group of individuals, on a genetic basis, that previous data has shown may benefit extra. Well and again we see we see nothing across the board and all these things are obviously why we are so surprised and we need to really understand get to one of this might very well be the true so we shouldn't like again speculating become conspiratorial but the most important thing is to understand this because again like Mark was alluding to the likelihood that all the previous data from several different trials, both retrospective analysis, prospective trials, stage three, type one, which you are doing now, but also early stage T1D in adults. And that all of that would just be the child's findings. I find that very highly unlikely.

Q: You state that you see no effect at all, presumably compared to the placebo group. Have you examined whether the placebo group performed unusually well, for example, compared with what is typically seen in placebo groups?

A (Dr. Ulf Hannelius, CEO): And again, we've seen some table summarized table information. So we don't really have

all of that data. I mean, based on what we see, nothing stands out dramatically. But we can't really answer all of these questions right now.

Q: Have you verified that there has been no degradation of the product?

A (Dr. Ulf Hannelius, CEO): I mean, all of these things are things that we need to look into, but we got these results late Friday evening. So we've had the before, and now we just start digging into all of these potential hypotheses. We need to do it in the right manner again, from an integrity perspective, so we don't compromise the trial too early.

Q: We have talked about whether the study will continue or not. We will see. But could you have it analyzed by an external party, for example?

A (Dr. Ulf Hannelius, CEO): I mean, it's again, we do it in steps, but that's on a clear thing to do as well to if we go come that far, then it makes sense to have an external party doing like just a sort of a second opinion using the same statistical models to make sure that we get the same, same outcome.

Q: I don't know if you can answer this, but there are a lot of similar questions like this about the trading halt in the stock. Can you comment on that?

A (Dr. Ulf Hannelius, CEO): That's not our decision. I mean, it's that the stock market has its own rules and algorithm around that, and we as a company, I think, shouldn't get involved in that. I think that can only make things worse if we try to somehow influence those kinds of decisions

Q: The dialogue with regulatory authorities, such as the FDA, is progressing now that the interim results were not as expected.

A (Dr. Ulf Hannelius, CEO): Obviously, with patient safety first, all the clinics will be informed or are informed about this. We need to make sure that patient safety is it's always on the top and then this will be communicated to in the right manner to regulators as well. I mean, they need to be informed as well, about how the decision is made, and how the company is moving forward with the trial.So all of that is ongoing.

***A (*Dr. Mark Atkinson (Diamyd Medical Board Member):** Yeah, I find it both interesting and assuring that your audience is a smart one with these questions, because as you might imagine, when the news came to us, like Friday afternoon, my time here in Florida afternoon, those questions that you've been asking over the last few minutes, we were asking ourselves those many, if not all of those same questions on Friday and Saturday and even yesterday, having meetings. And you people can be assured that with time, things like the placebo effect, these will all be evaluated.

Q: Is there any alternative strategy to avoid a company failure, like buying a new molecule and starting to study it?

A (Dr. Ulf Hannelius, CEO): So again, there will be many other companies, many parallel activity streams. Now, one obviously has to get to the bottom of these results again, doing it the right way. As we also mentioned in the press release, our core activities at the company will continue, including manufacturing at our biologics facility. I mean, we have manufacturing, and a GMP certification is ongoing; it's very likely we will get the GMP certificate to produce for clinical studies. GAD is a very important central molecule in type one diabetes. So that's important. That's close is ongoing because I know there's a lot of support from other stakeholders in our technology and in the antigen-specific approach. Obviously, we need to look at it from a cash perspective, and there will be a prioritization right now internally. So, for activities that aren't core, we shouldn't focus on them; we should focus on the ones I just mentioned, and then on strategic options… That's always something to look at especially now because we don't really know what the investigation around the phase three results, what the turnout will be. But again, the focus is now really on understanding phase 3. But parallel activities will be ongoing.

Q: Given the interim results, have you received any concrete feedback or signals from your US investors or partners regarding their willingness to continue supporting the program?

A (Dr. Ulf Hannelius, CEO): We've had this data for only a few days right now. So we will have discussions, everyone, and obviously, with these new investors, which we are, I mean, obviously, we have been on such a roller coaster ride here.

Q: What would you like to say to investors, patients and families who have followed the development for a long

time? Why should they continue to have confidence in your research and your work?

A (Dr. Ulf Hannelius, CEO): We are as disappointed as everyone else right now based on what we've seen here. I think that I mostly understand the shareholder perspective. Obviously, personally, I've put quite a lot of investment into this. Obviously, a huge amount of time. I think almost all patients are, I think it's important. There's a lot of hope there. I really hope that we can continue this. I mean, we get to the bottom of what we are seeing now, and we can continue development, because in the end, that's what we want to try to come up with something that can improve patients' lives.

***A (*Dr. Mark Atkinson (Diamyd Medical Board Member):** I'll say that you should find hope in the many divisions of Diamyd that are still going to be working hard at the production division that you mentioned that still keep pushing forward on manufacturing Diamyd Medical's an external scientific advisory board, including three people from the United States, one from Sweden and one from Great Britain. They are eminent scholars in diabetes, and they will be looking at this data, the management division that I'm sure will continue to work and evaluate it, and then, finally, the board of directors. That, again, is one of the primary objectives: protecting investors. So everybody will be part of a team on this effort moving forward.

--by Esther Min, Monica Oxenreiter, and Kelly Close

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[1] Futility monitoring refers to the assessment of the results of an ongoing trial to determine if the trial is unlikely to meet its objectives.

[2] Unblinding refers to the process by which the sponsor of the trial gets access to the trial results.