QURE Earnings Call Transcript

Date: 2025-11-10

Quarter: 3

Operator: Third Quarter 2025 Earnings Call. Good morning, and welcome to uniQure N.V.'s earnings call. All participants are in a listen-only mode. Please go ahead.
Chiara Russo: Good morning, and thank you for joining us for uniQure N.V.'s Third Quarter 2025 Earnings Call. Earlier this morning, uniQure N.V. released its financial results for 2025, and our press release is available on the Investors and Media section of our website at uniQure.com. Our 10-Q was also filed with the SEC earlier today. Joining me on the call this morning are Matthew Kapusta, Chief Executive Officer; Dr. Walid Abi-Saab, Chief Medical Officer; Kylie O'Keefe, Chief Customer and Strategy Officer; and Christian Klemt, Chief Financial Officer. After our formal remarks, we will open the call up for Q&A.; Before we begin, please know that we will be making forward-looking statements during this investor call. All statements other than statements of historical fact are forward-looking statements. They are based on management beliefs and assumptions and information available to management only as of the date of this conference call. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, the factors described in uniQure N.V.'s most recent SEC filings. Given these risks, you should not place undue reliance on these forward-looking statements, and we assume no obligation to update these statements even if new information becomes available in the future. Now let me introduce Matthew Kapusta, uniQure N.V.'s CEO.
Matthew Kapusta: Thanks, Chiara, and good morning, everyone. Thank you for joining today's third-quarter conference call. As you know, in the third quarter, we announced positive top-line data from our pivotal Phase 1/2 study of AMT-130 in Huntington's disease, the first gene therapy to demonstrate statistically significant slowing of disease progression in Huntington's disease. These groundbreaking results represent an important milestone not only for uniQure N.V. but also for patients and families who have long awaited a potential disease-modifying therapy. As previously disclosed, we met with the FDA in late October to review our data and discuss the potential submission of a BLA for AMT-130. Based on discussions at the meeting, we believe the FDA currently no longer agrees that the data from the Phase 1/2 studies of AMT-130 in comparison to an external control may be adequate to provide primary evidence in support of a BLA submission. Consequently, the timing of a BLA submission for AMT-130 is now uncertain. This feedback represents a notable shift from prior communications with the FDA during multiple Type B meetings over the past year. We plan to urgently engage with the FDA to discuss next steps, and we expect to receive the formal meeting minutes within the next 30 days. While the latest FDA feedback is certainly surprising and disappointing, we continue to strongly believe that AMT-130 has the potential to provide significant benefit to patients. We believe the data presented to date, widely recognized as the most compelling ever generated in Huntington's disease, provides substantial evidence of therapeutic effect. Every year, thousands of Americans die because of Huntington's disease, and thousands more are newly diagnosed. We believe AMT-130 has the potential to significantly slow disease progression and exemplifies the type of transformative innovation in rare diseases the FDA has pledged to support. We remain fully committed to our partners, investigators, and most importantly, to Huntington's patients and their families, and to working collaboratively with the FDA to bring this therapy to Huntington's patients in the U.S. as rapidly as possible. We will continue to act with urgency, transparency, and discipline as we work to deliver on the

promise of gene therapy to transform lives. I will now turn the call over to Walid.
Walid Abi-Saab: Thank you, Matthew. Good morning, and good afternoon, everyone. I would like to start by reiterating that the recent feedback from discussions at our pre-BLA meeting does not change our belief in our data. We continue to believe that AMT-130 represents the most compelling therapeutic dataset generated in Huntington's disease to date. The two highlights of the third quarter were the positive top-line data from our pivotal Phase 1/2 study of AMT-130 in Huntington's disease. Before I go on, I want to thank our employees, investigators, partners, and especially the patients and families who have been participating in the CHDI natural history studies and our clinical studies. It is thanks to their deep commitment and efforts that we have been able to achieve such progress. In September, we reported top-line data with the high dose of AMT-130 demonstrating a statistically significant 75% slowing of disease progression as measured by the composite Unified Huntington's Disease Rating Scale (cUHDRS) at three years compared to a propensity score-matched external control derived from the enroll-HD natural dataset, meeting the pivotal study's pre-specified primary endpoint. Equally important, patients treated with high-dose AMT-130 demonstrated a statistically significant 60% slowing of disease progression at three years as measured by the total functional capacity key secondary endpoint. Moreover, cerebrospinal fluid neurofilament light chain, a well-characterized and supported biomarker measuring neurodegeneration, was below baseline at 36 months in patients treated with high-dose AMT-130. The top-line data from the high dose were supported by consistent results in multiple sensitivity analyses demonstrating the robustness of these findings. We believe these results provide the first clinical evidence that gene therapy can potentially alter the course of Huntington's disease. In keeping with the spirit of full transparency for the scientific and medical community, we are working diligently on a comprehensive publication strategy, starting with publishing our full data results in a well-respected peer-reviewed medical journal. As Matthew noted earlier, we met with the FDA for a pre-BLA meeting in October, and based on discussions at the meeting, we believe that the FDA currently no longer agrees that data from the Phase 1/2 studies of AMT-130 in comparison to an external control may be adequate to provide primary evidence in support of a BLA submission. This feedback was unexpected. We believe AMT-130 has the potential to significantly slow disease progression. We plan to urgently interact with the FDA and are fully committed to working with the agency to find an expedited path forward. Turning now to AMT-260 for mesial temporal lobe epilepsy. In May, we announced initial data from the first three patients with five months of follow-up. At that time, we observed a promising reduction in seizure frequency over the first five months of follow-up with no serious adverse events. This data generated enthusiasm among investigators and potential patients. We have now activated 17 recruiting sites in the United States and completed enrollment of the first three patients in the first cohort. Following a favorable review by the independent data monitoring committee, recruitment has now expanded to mesial temporal epilepsy in the dominant hemisphere and the initiation of a second cohort at a higher dose per the protocol. We expect to provide updated data from the study in 2026. Moving to Fabry disease, in September, we also reported encouraging results from the ongoing Phase 1/2a trial of AMT-191, which were presented at the International Congress of Inborn Errors of Metabolism in Kyoto. Across the patients treated in the first cohort, we observed supraphysiological alpha-galactosidase A enzyme activity. The lower patient successfully withdrew from enzyme replacement therapy while maintaining stable plasma lyso-Gb3 levels through the July 24, 2025, data cutoff date. These results, together with a manageable safety and tolerability profile, reinforce the potential of AMT-191 to be a one-time dose gene therapy for Fabry disease. Enrollment in the second lower dose cohort has been completed, with a third cohort currently enrolling. We expect to update data in 2026. I will now touch on some additional pipeline updates. We have voluntarily paused enrollment in the Phase 1/2 episode 1 trial of AMT-162 for SOD1 ALS based on the recommendation of the independent data monitoring committee following a September 2025 review of the preliminary data related to the safety and efficacy of AMT-162 in the context of a dose-limiting toxicity that was observed in one patient in the second cohort. This event resulted in a serious adverse event determined to be related to AMT-162. At this time, we will continue to collect and evaluate data from the patients treated with AMT-162. To summarize, the third quarter marked an important milestone for AMT-130. The positive top-line data from our pivotal Phase 1/2 study. Recent feedback from the FDA has introduced uncertainty into the path forward, but we believe in our data and we are

focused on working with the agency to define the next steps. Now I will turn the call over to Kylie to discuss our recent patient advocacy work. Kylie?

Kylie O'Keefe: Thank you, Walid. As both Matthew and Walid have said, our commitment to the HD community remains unwavering. Following our September data announcement, we experienced a groundswell of hope and support from patients, patient advocacy groups, clinicians, and scientists alike. We understand and deeply appreciate the concern and disappointment expressed by the community following our announcement last week regarding the pre-BLA meeting with the FDA. We are reminded, however, that every step of this journey, including moments like this, reflects the seriousness of our mission and the importance of getting this right for HD patients. During this period, commercial and medical teams continue to thoughtfully plan and execute with discipline and focus. Our primary focus continues to be on stakeholder engagement and education, including treatment centers of excellence, payers, and patient advocacy, to best position us to be fully prepared for a strong and informed potential launch of AMT-130. Concurrently, as we have a focus on building the foundational strategy for the U.S. market for a potential launch of AMT-130, we are also looking to additional potential markets outside of the U.S., such as the EU and the UK. Feedback we are receiving from the physician and patient community reinforces both the high level of unmet need and the enthusiasm for the potential of AMT-130. Their support continues to motivate our team, and we remain committed to maintaining open communication and collaborating with the community as we plan next steps. We believe deeply in our science, the data we have generated to date, and the impact the therapy could have for HD patients. Now I will turn the call over to Christian for a financial update. Christian?

Christian Klemt: Thank you, Kylie. I will now share financial highlights of the third quarter of 2025. Please refer to the earnings press release issued this morning and our quarterly filing with the SEC for additional detail. Revenue for the three months ended September 30, 2025, was $3.7 million compared to $2.3 million in the same period in 2024, an increase of $1.4 million. The increase in revenue resulted from a $1.5 million increase in license revenues and a decrease of $100,000 from collaboration revenues. Cost manufacturing revenues were nil for the three months ended September 30, 2025, compared to $800,000 for the same period in 2024. Following the divestment of the Lexington facility in July 2024, the cost of contract manufacturing revenues is recorded net of revenue within other expenses. Research and development expenses were $34.4 million for the three months ended September 30, 2025, compared to $30.6 million during the same period in 2024. The $3.8 million increase was driven by an increase of $10.1 million in direct research and development expenses, of which $6.6 million related to preparation for the BLA submission of AMT-130, offset by a decrease of $3.4 million in severance costs and a $3 million decrease in costs related to disposables, facilities, and other expenses. Selling, general, and administrative expenses were $19.4 million for the three months ended September 30, 2025, compared to $11.6 million during the same period in 2024. The $7.8 million increase was primarily related to a $2.4 million increase in employee-related expenses and a $4.9 million increase in professional fees, including $3 million in credit repair to support the preparation of a potential commercialization of AMT-130 in the United States. Cash, cash equivalents, and investment securities totaled $649.2 million as of September 30, 2025, compared to $376.5 million as of December 31, 2024. The increase is primarily related to the net proceeds of $404.2 million from our public offerings this year. With this strong balance sheet, we believe uniQure N.V. is well-positioned to meet its clinical and operational priorities. We expect cash, cash equivalents, and investment securities will be sufficient to fund operations into 2029. I will now turn the call back over to Matthew.

Matthew Kapusta: Thank you, Christian. As you have heard today, 2025 was a pivotal year for uniQure N.V., and we continue to have strong conviction in both the compelling dataset and therapeutic potential for AMT-130. Our focus now is on working with the FDA to clarify next steps and determine the most expeditious path to bring AMT-130 to patients in the U.S. In parallel, we will plan to advance discussions with other regulatory agencies, including those in the European Union and the United Kingdom. As we move forward, we do so with confidence in our science, clarity in our mission, and a deep determination to make a meaningful difference for patients and families affected by Huntington's disease. Before we open up for questions, I would like to note that because we have not yet received the final meeting minutes from our pre-BLA meeting with the FDA, and out of respect for the agency and our shared goal of AMT-130 for patients with Huntington's disease, we will strictly limit our

responses about that meeting to the information disclosed in our November 3, 2025, press release. We appreciate your understanding and are happy to address other questions you may have. Operator, please go ahead and open the call.
Operator: Thank you. In the interest of time, we ask that analysts please limit themselves to one question. Thank you. Our first question today comes from Joe Schwartz from Leerink Partners. Please go ahead. Your line is open.
Joseph Thome: Great. Thanks very much for taking my question. So the treatment effect you have reported out to three years is quite large. So I am wondering, to what extent have you stress-tested the results in order to see what a very conservative rendition of the results would look like? For example, could you remind us how you constructed the external control arm to consider whether there were any potential sources of bias?
Matthew Kapusta: Hey. Thanks, Joe. Walid, do you want to answer that one?
Walid Abi-Saab: Hey, guys. Can you hear me?
Operator: Yep.
Walid Abi-Saab: You can? I am sorry. I was not sure if I am muted or not.
Matthew Kapusta: Yes. We can.
Walid Abi-Saab: Yeah. Thank you. Alright. Thanks for the questions. So actually, what we have done is essentially follow a rigorous way to do the propensity score matching with enroll-HD. I think enroll-HD lends itself to provide fairly robust data because of the size of it. You get very good matches. And what we have done in discussion with the FDA is prepare a series of sensitivity testing evaluating propensity score matching using different types of matching with propensity score weighting. We have also looked at a smaller number of variables, which was part of an SAP that we have proposed much earlier in the process during the RMAT application. We looked at regional differences. We looked at comorbidities based on medication and so on and so forth. And last but not least, we compared to a track and predict sensitivity analysis again as part of the pre-agreed types of sensitivity analysis with the agency, and across a variety of these analyses, the results were very consistent, demonstrating the robustness of these findings. And that is why we have really strong confidence in the results that we have seen. But regardless, if you also look at the numerical change from baseline in our patient population and compare it to a number of data that is being published by a number of studies that are run in that space in comparable patients, you see that the magnitude of the change from baseline at three years is very small compared to what one would expect in placebo or untreated subjects.
Operator: Our next question comes from Uy Ear from Mizuho. Please go ahead. Your line is open.
Uy Ear: Hey guys. Thanks for taking the question. Maybe just help us understand a little bit about what happened in AMT-162. Could you kind of remind us what the vector was and whether it was similar to the other pipeline studies, and along with that, what was the dose difference between the first cohort and the second cohort? Thanks.
Walid Abi-Saab: Yeah. Thanks for the question. We have not quite disclosed all of the data about the dose so far, but with this product, we have seen previously in a compassionate use that there was a case of dorsal root ganglia toxicity. It is a known adverse event, particularly for this route of administration. And we knew and we were monitoring very carefully with this. Unfortunately, we have seen that at the middle dose, which I can tell you is about threefold higher than the low dose. And as a result, we backed down. But now we are monitoring the data to see over time how this will evolve, and we will have a discussion with the FDA and the IDMC to determine the next steps for this program. We should be able to come back in the first half of next year with some answers on this. And just to be clear, Uy, this is a totally different capsid than what we use in our other programs and a different mode of administration.
Operator: Our next question comes from Salveen Richter from Goldman Sachs. Please go ahead. Your line is open.
Lydia Erdman: Hi. Good morning. This is Lydia on for Salveen. Thanks so much for taking our question. Could you just talk to what details you hope to learn from the final meeting here in the next 30 days? Thanks so much.
Matthew Kapusta: Yeah. I think what I would say is we do not want to speculate on what will be in the minutes. We assume that they will reflect mostly the conversation that we had in Washington, D.C. But

most importantly, we hope it will give a sense of the concerns that the FDA has and give us an outline for how to address concerns in a subsequent meeting with the FDA.
Operator: Our next question comes from Joseph Thome from TD Cowen. Please go ahead. Your line is open.
Joseph Thome: I guess, are you able to kind of confirm that prior meeting minutes documents did confirm the ability to file for accelerated approval based on the cUHDRS? Maybe the meeting minutes from the RMAT meeting in 2024. Was that officially documented in what they sent to you? And maybe how much detail do they go into in these meeting minute documents around the definition of the statistical analysis plan and the external comparator? Thank you.
Matthew Kapusta: Yes. I can confirm that in our November 2024 multidisciplinary meeting with the FDA and the written comments that we received, the FDA stated that the data from the Phase 1/2 study in comparison to an external control may serve as the primary basis of a BLA submission. They also confirmed that the composite UHDRS would be considered an acceptable intermediate clinical endpoint to support accelerated approval. In that particular meeting, they did not get into specifics on the statistical analysis plan but had recommended that we pre-specify a stats plan, and that was discussed in detail as well as the natural history protocol in our April 2025 meeting with the FDA.
Operator: Our next question comes from Luca Issi from RBC Capital Markets. Please go ahead. Your line is open.
Luca Issi: Oh, great. Yeah. Thanks so much for taking my question. Maybe, Matthew, again, I appreciate the situation is still fluid here, but can you just talk about what needs to happen from here over the next few weeks in order for you to invest capital in Huntington's? I guess what I am trying to ask here is where do you draw the line between continuing to fight this versus just giving up? Any color there would be much appreciated.
Matthew Kapusta: Yeah. I would not characterize this as a fight. I think that we are 100% committed to continuing to collaborate and partner with the FDA to determine an expedited path to submit a BLA. I think we strongly believe that AMT-130 can meaningfully benefit patients. I think we feel that we have what is considered to be the most compelling dataset in the field of Huntington's, with three years of clinical outcomes data showing a meaningful slowing of disease progression. And we think that if there are concerns or issues, they ought to be addressed in a proper review. And so, we will continue to work with the FDA to address any concerns they have, with the hope of having an expeditious submission of a BLA in the near future. That is the pathway that we are going to be focused on. And we are committed; we believe we have a drug that works. We have a patient group that has an urgent need, and we are committed to doing everything we can to bring this to them as quickly as possible.
Operator: Our next question comes from Yanan Zhu from Wells Fargo. Please go ahead. Your line is open.
Yanan Zhu: Great. Thanks for taking our questions. Just first, a quick clarification for the ALS program. Is it intrathecal delivery? And if so, is the AE the dorsal root ganglion AE previously known to this route? Then maybe just on the Huntington's program, just wondering, can you characterize how motivated or mobilized the patient and doctor community is on this issue and how that could help move the issue along? Thank you.
Matthew Kapusta: Okay. Walid, do you want to answer the first one, and then I will kick it to Kylie to do the second?
Walid Abi-Saab: Thanks, Matthew. Yeah. On the first question, the answer is yes to both. So intrathecal delivery, and it is dorsal root ganglia toxicity, which, again, as I said, unfortunately, is associated with this mode of administration, and we knew this was a risk. So over to you, Kylie.
Kylie O'Keefe: Thanks, Walid. Yeah. As I just said, the patient and physician community is very motivated. They have a huge unmet medical need and are collaboratively working together to look at how to move this forward. I think one of the things that is important is we received a big expression of hope and excitement coming out of the data, and then to have this disappointment a few weeks later is a bit of an emotional roller coaster for the community. I think that they are working together to look forward and say, how do we bring this therapy to patients?
Operator: Our next question comes from Patrick Trucchio from H.C. Wainwright. Please go ahead. Your line is open.

Arabella: Hi. This is Arabella on for Patrick. I was just wondering if you could clarify if you have received any EMA or MHRA preliminary feedback on accepting the same dataset external control for AMT-130 as primary evidence, and could you see ex-U.S. submission proceeding ahead of FDA approval?
Walid Abi-Saab: Sure. So we have not yet engaged in the UK or EMA with MHRA or EMA. That is the plan to go next. We are prioritizing the FDA. But I will say that we are committed to working with the FDA also to continue to find a path forward and also with other regulatory agencies, and we will advance as quickly as possible on all these fronts to bring this therapy to patients as quickly as possible.
Operator: Any additional questions, please press star followed by one. Next question comes from Paul Matteis from Stifel. Please go ahead. Your line is open.
Paul Matteis: Great. Thanks for fitting me in. As it relates to the meeting, again, answer whatever you are comfortable with. But, you know, given that your dialogue here, I guess, as I understand it, has been with a relatively similar group of people across the spring meeting and then last November last year. When they came out and told you that they did not think this path was no longer supportive of a BLA, did you ask them why and what exactly had changed? And then just separately, can you clarify for us what specific data have you shared with the FDA at this point, and have they seen more data from this three-year analysis than we have? Thank you so much.
Matthew Kapusta: Yeah, Paul. You know, unfortunately, we are not going to be able to comment on the details of this specific meeting. But, you know, we do hope for clarity once we do receive minutes. And to the extent that there are material updates, we will endeavor to update investors and analysts. So I think that is the answer to your first question. And then the second question, yeah, on the data, no. The data that was submitted to the FDA was consistent with the data that was shared publicly a number of weeks ago. Obviously, there is some additional data like sensitivity analyses that have not been presented, but there was no new follow-up or additional data that was provided to the agency.
Operator: We have no further questions. This will conclude today's question and answer session and today's call. You may now disconnect.