Hansa Biopharma Q4 2023 Conference Call Transcript

Company Participants

Søren Tulstrup – Chief Executive Officer

Matt Shaulis – Chief Commercial Officer and U.S. President

Hitto Kaufmann – Chief Scientific Officer

Donato Spota – Chief Financial Officer

Conference Call Participants

Johan Unnerus – Redeye

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Operator

Hi, everyone, and welcome to the Hansa Biopharma Conference Call covering the Fourth Quarter and Full Year 2023 Earnings Results. Today's call is being recorded. For the first part of this call, all participants will be in a listen-only mode. Afterwards, there'll be a question-and-answer session. [Operator Instructions] Speakers, please begin.

Søren Tulstrup

Thank you, operator. Good afternoon, good morning, and welcome to the Hansa Biopharma conference call to review year-end results for 2023. I'm Søren Tulstrup, CEO of Hansa Biopharma. Joining me today is our Chief Commercial Officer and U.S. President, Matt Shaulis; our Chief Financial Officer, Donato Spota; and our Chief Scientific Officer, Hitto Kaufmann, who joined Hansa in December of last year. We're thrilled to welcome Hitto to the Hansa team at this pivotal time. With over 20 years of experience in research, development and advancement of science in both large pharma and small biotech organizations, Hitto is poised to lead the development of our scientific platform and advancement of our exciting pipeline of drug candidates. Hansa's Head of Investor Relations, Klaus Sindahl, is also with us.

Today, we'll discuss the progress we made during the last quarter of 2023 and review our near-term milestones. The presentation should take roughly 20 minutes, after which there will be an opportunity to ask questions during the Q&A session. Now please turn to Slide 2. Please allow me to draw your attention to the fact that we will be making forward-looking statements during this presentation, and you should therefore apply appropriate caution. Please turn to Slide 3, and an overview of Q4 highlights.

The fourth quarter of 2023 was a very eventful period for Hansa with strong commercial performance and continued solid progress across our pipeline development activities. In kidney transplantation, we continue to see good commercial progress in Europe as measured against our key launch metrics, including the implementation of treatment guidelines in both Italy and Germany, and continued growth in the number of clinics with

desensitization protocols in place. During the fourth quarter, we saw strong revenue generation with total revenue ending at SEK50 million for the quarter, including SEK43 million in product sales, which was supported by growth in key new markets such as the U.K., Germany and Spain.

In the U.S., we continue to enroll patients in the Phase 3 ConfIdeS trial in kidney transplantation to accelerate randomization with the goal of completing randomization in mid-2024, and a BLA submission in 2025 after a 12-month follow-up on kidney function measured through eGFR. In October of 2023, we announced positive data from our five-year follow-up study, confirming that patient and graft survival outcomes in highly sensitized patients, desensitized using Idefirix continue to mirror what's seen in the broader transplant base. The data also demonstrated graft survival of 82%, which is consistent with the outcome seen at three years post transplant.

Outside our core markets in Europe and the U.S., we continue to expand access to imlifidase for highly sensitized kidney transplant patients. In the beginning of this year, we announced a new commercial partnership with NewBridge Pharmaceuticals covering the Middle East and North Africa, also known as the MENA region. Matt will discuss the commercial progress in more detail during his section of the call. In early December 2023, Hansa announced plans to restructure the organization to better align with and focus on key clinical development and commercial priorities. The restructuring will result in approximately 20% to 25% reduction in the current workforce and translate into approximately SEK75 million to SEK85 million in annual savings when fully implemented.

While we firmly believe this initiative is necessary to help us deliver on our important mission, it was obviously a difficult decision to take as it impacts our most valuable asset, our people. We're grateful for the commitment and efforts of our colleagues who work tirelessly to advance potentially lifesaving medicines for people suffering from serious diseases and we remain committed to supporting those colleagues impacted by the restructuring. On the clinical development side, we are pleased with the continued progress we have achieved across our pipeline with positive readouts in several potential new indications for imlifidase, as well as a positive Phase 1 first-in-human trial of HNSA-5487, the lead candidate in our novel immunoglobulin cleaving enzymes for Repeat dosing program, also known as the NiceR program. We will cover HNSA-5487 in greater detail later during this presentation.

In our AMR Phase 2 trial, imlifidase met the primary endpoint, as announced some time ago, demonstrating statistically significant faster and superior reduction in donor-specific antibodies observed among imlifidase patients within five days of treatment as compared to plasma exchange which is a cornerstone part of standard of care treatment. While we're encouraged to have met the primary endpoint, it is important to note that the secondary endpoints, which included a range of kidney function, measures and graft and patient survival were not met as the trial was neither designed nor sufficiently powered to show a statistically significant difference between the two arms, given the heterogeneity of patients, involving many patients with an additional cellular component of the immune rejection and given the small number of patients enrolled.

Patients with an acute AMR and without an additional cellular component of the immune rejection may be best positioned to benefit from a rapid and significant reduction in DSA, one of the main goals of any AMR treatment according to existing treatment guidelines. We aim to have a paper published on this topic in a peer-reviewed journal later this year. In our GBS

Phase 2 study, positive high-level data was announced in December 2023, demonstrating that imlifidase was safe and well tolerated when administered prior to standard of care, and that there was a rapid improvement in disease-related efficacy measures.

The results from this Phase 2 trial are very encouraging when compared to previously published data from studies with other therapies given the rapid improvement across several efficacy outcome measures observed in patients treated with imlifidase in combination with standard of care. Immunoglobulin G antibodies are thought to play an important role in GBS disease, and with its ability to rapidly cleave IgG, imlifidase could be a promising new option for holding this progressive and oftentimes highly debilitating disease. As previously guided, we expect further contextualized analysis of efficacy data to be announced this year.

Last, I am happy to report that the first clinical study with imlifidase in gene therapy was recently initiated by our partners at Sarepta Therapeutics. In this Phase 1b study, imlifidase is being investigated as a pretreatment to Elevidys, also known as SRP-9001, Sarepta's FDA-approved gene therapy in Duchenne Muscular Dystrophy. We expect the first patient to be dosed imminently.

Now please turn to Slide 4, and an overview of our strategic priorities. Hansa enters 2024 in a strong position to successfully execute on our key priorities. Our strategic priorities are anchored around our proprietary enzyme technology platform and with the goal of developing and commercializing immunomodulatory first-in-class or best-in-class treatments for organ transplants, rare IgG-mediated autoimmune diseases and gene therapy as well as exploring the potential application of our technology platform in oncology.

To deliver on this ambition, we have three key priorities. First, commercialize Idefirix in the first indication and markets, which includes successful launching Idefirix in Europe and securing FDA approval and launching the product in the U.S. Second, we are focused on expanding the Idefirix label and advancing ongoing imlifidase clinical programs across our franchises, including in the acute monophasic autoimmune diseases, anti-GBM and GBS. Third, we are very excited about the potential application of our enzyme platform to enable an improved AAV-based gene therapy and the potential ability of our next-generation enzyme, HNSA-5487, from the NiceR program to address significant unmet medical needs within a broader range of diseases, including not to be chronic autoimmune diseases.

We will cover these priorities in more detail throughout this presentation.

With this, I'll hand over to Matt to go through our commercial progress for the quarter. Matt?

Matt Shaulis

Thank you, Søren. Please turn to Slide 5. As Søren mentioned in his introduction, we saw strong commercial performance in the fourth quarter, with SEK43 million in product sales, which is our best quarter so far and is in line with the guidance set out early last year for sales to be backend loaded. Sales during the quarter were supported by growth in key new markets, including the UK, Germany and Spain. But we obviously are very pleased with our commercial performance and medical efforts supporting the growth and increase in treatment centers over time. I also have to reemphasize that as the base of centers grow, we'll continue to see volatility in sales from quarter-to-quarter as timing and the number of organs allocated as well as the rate of organ acceptance, is basically determined by factors that are out of our hands.

As you may recall from our recent conference call, we're committed to creating paradigm shifts in kidney transplantation, resulting in significantly better patient outcomes. We're launching a transformative product as well as enabling the treatment of cross-match positive patients who previously had no viable options to enable transplantation. With this novel therapy for paving the way forward to change the desensitization treatment ecosystem in transplantation, requiring significant changes in both transplant protocols and organ allocation assessments.

The ability to identify the right patient and then manage his or her immunological complexity is a huge leap in modernizing transplantation care for highly sensitized patients. Entering successful early experiences in key early adopter clinics is highly critical for the long-term market uptick of this innovative product.

So, ultimately, we must win the acceptance battle both for treatment of the patient type and the subsequent adoption of the product. We measure our progress using a set of key launch metrics, which we have previously introduced. These metrics will directly or indirectly impact future adoption and sales of Idefirix, as a new transformative therapy. We'll revisit these on a regular basis to demonstrate our progress. These metrics include market building and market access activities, patient identification, and transplant center readiness and use.

First, market building activities, such as implementation of new treatment guidelines will support the long-term uptake of Idefirix. During the fourth quarter, we saw Idefirix-specific guidelines being implemented on a national level, on new key markets such as Germany and Italy, taking the total number of countries with approved guidelines up to seven, compared to no countries a year ago. These guidelines provide a new clinical practice framework for healthcare professionals, on a management pathway for highly sensitized patients. And our medical teams are supporting further country-level guideline development in additional European countries.

Second, securing market access is another key component for Idefirix launch in Europe. For the last 12 months, we have secured pricing and reimbursement in five markets, Slovenia being the latest addition on top of such important markets, Spain, Italy, Belgium and the Czech Republic, increasing the number of countries with full market access to a total of 14, including all the top five in volume. In addition, HTA processes continue to run in several other markets such as Portugal and Switzerland.

Third, let's look at patient identification. Following the conditional market authorization in Europe, Hansa is running a mandatory post-approval study in Europe in parallel with the commercialization. We've now completed approximately 56% of the post-approval study, which is more than a factor of three times compared to a year ago. Post-approval study is set to complete treatment in 50 patients by the end of 2025. The post-approval study helps clinicians generate valuable experience in treating and managing patients as we build the foundation for Idefirix to become a new standard of care in desensitization. While in the short term, the study may affect commercial sales and patient uptake, long term, the experiences from the study will positively impact sales growth.

Ongoing patient identification through organ allocation systems, such as Eurotransplant, is another critical factor. Its increased access to organs is critical to equitable care for highly sensitized patients.

On that note, we are pleased to say that the first patient has been treated in Eurotransplant's new desensitization program following increased patient identification and selection, during the fourth quarter for both the first and second wave of patient assessment took place for treatment of new Desensitization Program. New pilot program, under the Acceptable Mismatch Program is intended to transform desensitization across eight European member countries including Germany, the Benelux and select Eastern European countries.

Fourth, scaling up the base of transplant centers with clinical experience is a key commercial metric, and while uptake will remain volatile from quarter-to-quarter, even with a growing base with the unpredictability of organ allocation to highly sensitized patients on waiting lists. We're pleased with the continued progress in establishing new centers that use Idefirix. Today, approximately 50 clinics qualify as Idefirix ready to treat patients. We're very pleased that this number has doubled in the past year.

More importantly, the number of clinics that have treated patients commercially or through our post-approval study has grown to more than 23 centers, which compares to 10 centers a year ago across these clinical studies and commercial activities. Similarly, during the fourth quarter of 2022, we had four centers with repeat usage, and we now have grown that to 14 centers with repeat usage by the end of the fourth quarter of 2023.

More recently, we've seen orders from new key markets such as the UK, Spain and Germany, and therefore expect additional clinics to generate experience in the coming periods. Very early indications from January show that we are off to a good start first quarter 2024 sales, this will of course be subject to underlying volatility as the quarter progresses.

Please turn to Slide 6. With regard to our pivotal U.S. ConfIdeS trial in kidney transplantation, we'll continue to enroll additional patients as previously guided. The ConfIdeS study is set up to evaluate imlifidase as a potential disruptive therapy for highly sensitized patients waiting for a deceased donor kidney through a U.S. Kidney Allocation System. Approximately 2,500 highly sensitized patients in the U.S. with a CPRA score of 99.9% and above fit into this category are not transplanted today despite prioritization points on the waitlist.

Total of 64 highly sensitized patients will be randomized in the trial and as of today, we have enrolled 104 patients versus 87 patients in Q3 last year. We've randomized 40/64 targeted patients, equivalent to approximately two-thirds of the study randomization. As previously guided randomization is expected to be completed by mid-2024 with a BLA submission expected 2025 under the accelerated approval path.

Please turn to Slide 7. Early January of this year, Hansa Biopharma and new NewBridge Pharmaceuticals announced the formation of a new commercial partnership covering the Middle East and North Africa region. MENA region will be the third outside of Europe where Idefirix is commercialized, with the goal of enabling kidney transplantation and highly sensitized kidney transplantation.

New collaboration is rooted in the existing European conditional marketing authorization for Idefirix, intending applications for marketing authorization in the respective MENA markets. New collaboration follows our stated strategy to expand access to Idefirix for local partners

beyond our core markets, allowing us to build off the existing European conditional marketing authorization for our transformative desensitization therapy for highly sensitized kidney transplant.

2022 approximately 1,500 kidney transplantations were performed in the Middle East alone, with most transplantations carried out with organs from living donors. In the Middle East, it's estimated that 10% to 15% of kidney transplant candidates are considered highly sensitized. Our clinics in this region are known for having high comprehensive experience with desensitization through local protocols like in Saudi Arabia.

Potential approval and market access in MENA could lead to a meaningful commercial opportunity for Hansa outside of our core – as we expand access to our transformative innovation in kidney transplantation care for patients and clinicians.

With this update, I will hand over to Hitto to discuss HNSA-5487 second generation lead enzyme candidate and the progress with the rest of our pipeline.

Hitto Kaufmann

Thank you, Matt. Please turn to Slide 8. Back in October last year, we were pleased to report encouraging high level data from the first in-human trial HNSA-5487, the lead candidate from our NICE program, focused on developing next generation IgG cleaving enzymes.

Let me first start with the left hand side of this slide. Importantly, this compound is engineered to offer low preexisting immunity and full activity across all IgG subclasses while allowing to distinctly different redosing regimen, short interval redosing and long interval redosing. This would open the potential for a broad range of indication.

First, we see potential for HNSA-5487 in short interval redosing regimen. To extend the IgG low period, allowing very efficient clearance of Fc-fragments created following the first dose. This would be beneficial, for example in acute clinical phases of several autoimmune diseases.

Additionally, we see potential for HNSA-5487 to address unmet need in autoimmune diseases by improving long-term disease control in combination with humoral inhibitors targeting B cells or plasma cells.

Furthermore, this novel drug candidate could play a key role in enabling AAV based gene therapy redosing and extending treatment regimes in systemic oncolytic virus therapy.

Please turn to Slide 9. As mentioned, the potential for short-term and long-term interval dosing is something we continue to explore, so that we can better understand the role of HNSA-5487 and several indications and how this powerful new drug candidate and the broader NiceR program could benefit patients with diseases where prolonged IgG free window is needed and the repeat dosing would be beneficial.

Just a few quick words on the NICE-01 study, which was designed as a double blind, randomized, placebo-controlled trial evaluating safety PK and PD of single ascending doses of HNSA-5487 and 36 healthy volunteers. Results demonstrated that the molecule was safe and well tolerated with fast and complete depletion of immunoglobulin G antibodies observed at increasing doses in all subjects. Pharmacokinetics were in line with expectations

and pharmacodynamics expressed through efficacy on IgG cleavage showed a fast and complete cleavage of IgG to F(ab')2 and Fc-fragments with increasing doses.

The trial also included exploratory endpoints focused on achieving a deeper understanding of the immunogenicity profile, which follow-up on all subjects for 12 months and this part is currently ongoing. As part of the ongoing Phase 1 study we are evaluating different dosing levels that potentially can increase and extend efficacy. This analysis will give us key input which will be helpful in determining the future clinical development program, including selection of first indication to 2024.

With this, I will hand back to Søren to go through the latest progress on our pipeline. Please turn to Slide 10.

Søren Tulstrup

Thank you, Hitto. And please turn to Slide 10, as Hitto said, as we discussed in the beginning of this call, we're happy to report that the first clinical study with imlifidase in gene therapy was recently initiated by our partners at Sarepta Therapeutics. In this Phase 1b study, imlifidase is being investigated as a pretreatment to Sarepta's FDA approved gene therapy elevators in Duchenne Muscular Dystrophy. The first patient is expected to be dosed imminently and with a high level data readout coming later this year.

In our Phase 2 program, investigating imlifidase in antibody mediated rejection episodes. The full data was announced at the end of last year. We will now pursue a potential publication in a peer reviewed journal as rapid and significant reduction in donor specific antibodies is one of the main goals of any AMR treatment according to existing treatment guidance.

In our Guillain-Barré Syndrome Phase 2 program, Hansa presented positive high level data in December of last year, demonstrating that imlifidase was safe and well tolerated when administered prior to standard of care and that rapid improvement in disease related efficacy measures was observed in imlifidase treated patients.

As previously communicated, further analysis will contextualize efficacy data and is expected to be announced later this year. In the investigate initiated Phase 2 trial in ANCA-associated vasculitis, three patients are currently involved out of a target of ten patients with severe ANCA-associated vasculitis and acute respiratory distress syndrome due to pulmonary hemorrhage. Patients will be treated with imlifidase on top of standard of care consisting of standard immunosuppression as per center protocol and intensive support care.

This study is carried out at Charité - Universitätsmedizin Berlin. In anti-GBM, we have recently seen an accelerated uptake in patient enrollment in our pivotal global Phase 3 study with a talking of patients since we announced our Q3 report.

In addition, the number of active sites continues to expand now 34 sites, which is up from 25 sites at the end of third quarter of last year. In total, 18 patients have now been enrolled out of a target of 50 patients across centers in the U.S., UK and EU, confirming that we are on track to complete enrollment in 2025 as previously guided.

The primary objective of the study is to assess the superior efficacy of imlifidase in combination with standard of care versus standard of care alone, consisting of a combination of immunosuppressives, steroids and plasma exchange with a six month follow-up on renal function. Last our post-approval study continues to track according to plan. As Matt pointed out in his comments, with 28 patients enrolled equating to 56% completion, the study is set to complete in 50 patients by the end of 2025.

With this overview, I'll now hand over the call to Donato, who will walk us through a review of financials for the fourth quarter and full year 2023. Donato?

Donato Spota

Thank you, sir. Please turn to Slide 11, total revenue for the fourth quarter of 2023 amounted to SEK50.4 million, including SEK43.3 million in product sales and approximately SEK7 million in contract revenue, mainly from the agreement with Sarepta. For the full year of 2023, total revenue was SEK134.1 million, including approximately SEK104 million in product sales.

Product sales came in back end loaded as guided. With Q4 sales, more than doubling over Q4 four 2022 and almost tripling over Q3 2023

The increase in sales is mainly driven by contributions from new markets such as the UK, Spain and Germany.

While we are very pleased with strong revenue generation in the fourth quarter, we still like to emphasize that quarter-on-quarter volatility is expected to remain high in the periods to come, given the dependency on organ supply and allocation to highly sensitized patients.

Having said that, we start seeing a base being built with increased demand across a number of markets. As Matt mentioned, early signs from January indicated that we're off to a good start in the Q1.

Please turn to Slide 12. Total SG&A expenses for the fourth quarter of 2023 amounted to SEK106 million, compared to approximately SEK84 million for the same period of 2022. The increase in expenses reflects Hansa’s broadened commercial activities and organizational expansion related to the launch of Idefirix in Europe.

Further inflation and devaluation of the Swedish Krona against the euro and the U.S. dollar have negatively impacted cost in 2023. For the full year 2023, SG&A expenses increased to SEK450.5 million, compared to approximately SEK338 million in 2022, due to the reasons just mentioned, as well as certain one-off costs incurred during 2023.

Investments in R&D amounted to SEK108.3 million for the fourth quarter of 2023, which is a SEK16 million increase compared to the same period in 2022. For the full year of 2023, R&D expenses amounted to SEK411.3 million compared to SEK346.3 million for 2022. The increase was mainly driven by the initiation of the clinical and CMC development program for HNSA-5487.

The ongoing Phase 3 trial in anti-GBM disease and progressing the EMA post approval commitments including the post approval study.

Operating loss amounted to SEK175.5 million for the fourth quarter of 2023 compared to SEK146.2 million for the same period in 2022.

For the full year of 2023, operating loss was SEK788.5 million versus SEK588.6 million for 2022. The increase in operating loss in 2023 over 2022 is driven by increased investments in our operations and onetime revenue recognized under our agreement with Aspire in 2022.

Lastly, net loss for the fourth quarter decreased to SEK124.5 million compared to SEK148.7 million for Q4 2022. The decrease was driven by a SEK51 million positive financial income mainly related to favorable U.S. dollar, euro, and British pounds currency effects.

For the full year 2023, net loss was SEK831.7 million compared to approximately SEK611 million for 2022.

Please turn to Slide 13. Cash flow from operating activities amounted to approximately minus SEK173 million for the fourth quarter of 2023 compared to minus SEK110 million for the fourth quarter in 2022.

For the full year of 2023, operating cash flow was minus SEK755.6 million compared to minus SEK503 million for 2022. The increase over last year is mainly driven by the increase in operating expenses and the SEK50 million upfront payment received under the Aspire agreement in early 2022.

End of December 2023, our cash position stood at SEK732 million, which is expected to provide a cash runway into 2025 as previously guided. For 2024, we do expect both operating expenses as well as cash burn to improve over 2023 driven by increasing sales, the completion of the Phase 2 trials in AMR and GBS and savings from the ongoing restructuring.

I will now hand back the call to Søren for his final remarks.

Søren Tulstrup

Thank you, Donato. Please turn to Slide 14. Hansa enters 2024 in a strong position to successfully execute on our key priorities. In transplantation, our key focus is to continue to successfully launch Idefirix in Europe.

Second, we aim to complete randomization in our U.S. ConfIdeS trial by mid-2024 as previously guided. In our autoimmune franchise, we aim to complete and announce the full data from our Phase 2 trial in Guillain-Barré syndrome and then interact with regulatory authorities to determine the best path forward for this indication.

In our anti-GBM program, it is our aim to complete enrollment by 2025 and as discussed, we currently have strong momentum.

In gene therapy, we expect the first patient to be dosed imminently with imlifidase as pre-treatment to Sarepta's gene therapy Elevidys in patients with Duchenne Muscular Dystrophy. First, high level data is expected later this year.

In addition, Hansa and Genethon expect to initiate later this year a first clinical trial of imlifidase [indiscernible] GNT-0003 Genethon's gene therapy in Crigler-Najjar syndrome following successful completion of preclinical work.

Last, in relation to HNSA-5487, we will assess further immunogenicity data from the Phase 1 trial in healthy volunteers and select the leading indication to be pursued.

Please turn to Slide 15. With this overview, our presentation is now concluded and we would like to open the call for questions. Operator, please begin.

Question-and-Answer Session

Operator

Thank you. We'll now start the question-and-answer session. [Operator Instructions] The first question will be from the line of Johan Unnerus from Redeye. Please go ahead. Your line will be unmuted.

Johan Unnerus

Thank you for taking our questions. Just a few. And congratulations to an improved quarter. And that relates to the first question because we can see both. The quarter was good, obviously, and it seems like you have some contribution from the European program, is that correct? And then also we know that it seems to be an improved dynamics in the post approval study, which has taken it quite significantly forward. Is that also an indication of improved dynamics or acceptance?

Søren Tulstrup

Thank you very much for those questions, Johan. So I think I'll hand over to Matt to address this overall, but clearly we are seeing a good contribution from a range of countries and very encouraging. We're seeing first sales in some of the key countries in Europe, the larger countries, including Germany. But Matt, maybe you can provide some further context.

Matt Shaulis

Absolutely, happy to do that Søren. And Johan, thank you for the question. And yes, I think we are very pleased to confirm that within the Eurotransplant highly sensitized program, not only have patients been identified in first waves of reviewing the waiting list, but we have indeed had the first patient now treated. So that is an encouraging sign about dynamics. And then similarly with the post approval study, this is another sign that we believe is positive regarding the dynamics.

Of course, we've mentioned previously that treatment guidelines are in place across Europe with ESOT. And now on a country-by-country basis, we continue to see the major markets with treatment guidelines. This is a positive sign. But also the post approval study, continuing to accelerate, shows that clinicians are identifying these patients. And then as we see organ allocation, it's leading to treatment. So of course we're going to continue to see volatility in commercial activity and sales on a month-to-month and quarter-to-quarter basis. But we certainly believe things are headed in a really good direction.

Johan Unnerus

Great. Appreciate it. And also in terms of the sort of sales, commercial specialist support on your side. Now, earlier, France was in a sort of more dynamic phase and now seems to be like the number of countries are expanding, which is of course positive. Do you sort of mirror that in your supporting efforts or do you need to be more or less equally supportive in the earlier stage as well?

Søren Tulstrup

Yes, well, thanks for that. And Matt, you can talk to this. Clearly, we have the setup we need in all of these countries, right. So we're not scaling up or down in any of these. But it's really nice to see the first sales now coming from the other countries, large countries outside of France. And if we can kind of replicate what happened in France, we're in a very good situation. Matt, maybe you want to expand on this.

Johan Unnerus

Maybe – sorry, maybe I can make it a bit easier because I mean, your object from the commercial side is pretty substantial. But do you sort of go into different stages with your focus in these countries which are more dynamic? Or is it that you need to provide a lot of support in countries which are sort of earlier in this stage as well?

Matt Shaulis

I can certainly talk a little bit to sort of the stages related to our strategy. And certainly, in the very early days, in a particular market, we'll take a focus on just a handful of centers we believe have all the necessary infrastructure for treating the complex immunologic transplant procedures and that have a willingness or a basis for treating [indiscernible]. And then we grow from that point forward. And so obviously, France, has gone beyond that point of just a handful of small number of [indiscernible], and then is now expanding to a larger number. Other markets like U.K., Spain, Italy, Germany, we're getting that initial smaller set of centers up and running. But in all cases, we see that the team that we have in place is really capable of driving larger acceptance and a larger number of centers.

We certainly also put a big emphasis on peer-to-peer engagement, where our commercial and medical teams very regularly ensure that a new center that hasn't yet used imlifidase

able to speak with other thought leaders that have experience using the treatment. That's a big part of the early phases of the work that we do, but there is plenty more for us to do to activate the patient voice and drive further adoption in additional centers as we get into follow-on phases of commercialization. And suffice it to say that we really believe that the team that we have in place is the right size. It is driving activity in the big 5 European markets and then also has the capacity to get to the traditional markets beyond the five.

Johan Unnerus

Great. And finally, from our side, you're clearly engaging in an overview of the OpEx side. And can it be – when can we see traction from these savings or reallocations that – should it be fully in place by the end of the year? And how much can we see by the middle of the year?

Søren Tulstrup

We'll certainly see it very soon. But Donato, will you comment on this?

Donato Spota

Yes, sure. Hello, Johan. Yes, I mean, as we said, we're currently implementing this restructuring. So we expect to see some initial savings from that, maybe in the second quarter of this year already, but then more pronounced than in the second half, and the full effect then in next year.

Johan Unnerus

Great, thank you. That's all from us.

Operator

Thank you, Johan. The next question will be from the line of Gonzalo Artiach from ABG Sundal Collier. Your line now be unmuted.

Gonzalo Artiach

Hi. Good afternoon and thank you for taking my questions. I have a couple of them. The first one, on the U.S. ConfIdeS study, it seems that you're keeping guidance for mid-2024 for full randomization of the study, but you still have 24 patients out of the 64 that are set to be randomized. And based on your update from January 6, compared with what has been communicated today, it seems that no patients or very few patients in the best case have been randomized in January. So how confident are you on achieving guidance? As of today, it seems a bit challenging to get 24 patients randomized in the next five months. Thank you.

Søren Tulstrup

Well, thanks so much for that question Gonzalo. So, overall, what we've seen is that randomization comes in buckets, if you will. So you cannot make predictions based on what has happened over a few weeks or so. But overall, we now have more, as Matt talked to, more than 100 patients enrolled.

We have a high double-digit number of patients just waiting for organ allocation and then acceptance of new organ. And with 17 centers currently activated and we expect a handful of centers to come online essentially within the next weeks, within a month or so, we are confident that we'll be able to meet the guidance we've given, which is mid this year as we expect additional patients to be randomized over the coming months.

We've also, of course, made sure that we have sufficient resources, both on the external CRO. We are working with in the U.S. as well as using all of the available internal resources so that we have, let's say, face time with the centers and ensure that there is total focus on this important study.

We're very encouraged by the ongoing high degree of interest from the centers. As we've discussed previously, this is not just a way to generate data, but it's actually a fantastic way to generate experience prior to launch in the U.S. in the key centers.

So that's what I can say. I don't know Matt, do you want to add further comments to this?

Matt Shaulis

I think that really covered it. I just would reiterate that there is a bit of sort of lumpiness and how organ allocation volumes take place and how that impacts the numbers of patients that randomize within our study. So we tend not to see sort of a steady flow, but rather a little bit of volatility in the numbers.

And I think, Søren, you've obviously touched on all of the key factors that give us confidence in the study for Gonzalo. The only thing I would add to that is we continue to see our protocol amendment for delisting has definitely been a source of ensuring that patients that are armed on the study that are ready to go, get an expanded number of potential donors that could be an appropriate allocation to them. So delisting is something that has been a very successful part of the study, and we're going to continue to see that be a part of the path forward here through midyear.

Gonzalo Artiach

Great. Thank you very much. And my second question is on imlifidase and the NiceR candidate HNSA-5487. And there is this U.S. company called Cyrus Biotechnology, which in January 16, they presented some animal data on a modified version of imlifidase, and they showed better half-life and less immunogenicity than regular imlifidase or imlifidase. They achieved 80% reduction of IgG levels after 14 days. And they compared it with regular imlifidase, let's say, which after seven days, the IgG levels are back at pretreatment levels.

So in a way, Cyrus Biotechnology, this early data seems to be showing something we have, that aligns, let's say, with what you are aiming with the HNSA-5487 project, as you described before. So my first question here is if you have any comment on how similar or different their approach is versus yours, let's say, with HNSA-5487, and if you have any animal early data that could be indirectly, to put in a way, compared with what they have so far provided.

And second part of the question, could you comment on your imlifidase patent, about the level of protection against this type of product? And if you also could give some words on your HNSA-5487 production? Thank you.

Søren Tulstrup

Thank you, Gonzalo. First of all, I think, it's actually encouraging to see that there is increasing interest in our approach in this space. Clearly, this is what we see broadly, the ability to rapidly and consistently decrease levels of pathogenic IgG, something that can bring a substantial patient benefit, right?

We're not going to comment on what competitors are saying or disclosing at this point in time. We're very, very confident that we have excellent molecules here, not just imlifidase, but they're 5487, and we're certainly moving forward at speed and we're already at advanced stage with these products.

As far as protection of IP rights is concerned, we have 11 patent families around the imlifidase covering many different things, including medical use and dosing and so on. And we have very, very solid patent estate also around 5487. So we – as I said, we overall encouraged by the increasing interest, and I'm sure we'll see a range of approaches, different molecules as well and so on, trying to emulate what we are doing. This is what typically happens when there is a highly innovative product that can potentially bring a lot of value to patients.

Gonzalo Artiach

All right. Thank you very much.

Matt Shaulis

Thank you, Gonzalo.

Operator

The next question will be from the line of Dominic Rose from Intron Health. Please go ahead. Your line now will be unmuted.

Dominic Rose

Hi, thanks for taking my questions. I've got three shorter ones. The first question is, when I look at the cost of goods in 2023 as a percentage of product revenues, it was around 60%. So I was just wondering why that ratio seemed so high and what your expectations are for it over the next few years. Question two was, I think you said there was a one-off in SG&A this year. Can you let us know how big that was? And question three is, are there any upfront cash costs for the restructuring program? And when would you expect those to be booked? Thanks.

Søren Tulstrup

Thanks for those questions. Donato, will you take them?

Donato Spota

Yes, sure. So on the cost of sales at books [ph], obviously, again, I think we just see a situation, or have a situation where the manufacturing and commercial manufacturing capabilities that we have and the batch sizes obviously are reflective of what we expect in terms of sales and quantities needed at a few years down the line, with many more indications being served.

So right now you have a situation where the batch size is higher than what is currently needed. So an excess capacity, and that's why you have these relatively, in percentage, relatively high level of costs. But going on – looking further down the years, I mean this is expected to come down substantially. So the manufacturing cost in absolute terms, if you look at them is not that significant.

Then the one-off cost that I've been mentioning, yes, I mean we're not disclosing the individual elements, but they are more substantial. There's different factors that play the role here, so – and that's why I mean it's as substantial as it's worth mentioning it on the call. So there were a few projects, a few activities that reflected into that, but that's not expected to be coming again this year.

And then with regard to the cost on the restructuring – we are not expecting any significant upfront costs. Basically there will be some, but nothing that is really significant. And that had to be booked already for 2023, for example. Does that start up the right, what we're looking for?

Søren Tulstrup

I think that was. Yes, let's move on.

Donato Spota

Yes.

Operator

Yes. He just disconnected. So the next question will be from the line of George Young [ph] from William Blair. Your line now will be unmuted.

Unidentified Analyst

Hi, this is Eric on for Matt. Thanks for taking the question. Just two questions on 5487. So one, was wondering how frequently and for what duration samples are being collected in the healthy volunteer study, in order to monitor immunogenicity over time in IgG recovery. And secondly, will you guys be analyzing whether auto antibodies generated in response to 5487 are neutralizing? Thanks.

Søren Tulstrup

Hitto, will you comment on this?

Hitto Kaufmann

I can't comment on the second part of the question. That's a yes. I cannot give you the detail of when samples are being collected, but it will be done in a very similar manner as we have done it in previous studies of this kind.

Unidentified Analyst

Yes. Great. Thank you.

Operator

Thank you, George. [Operator Instructions] The next question will be from the line of Douglas Tsao from H.C. [Ph] Please go ahead. Your line will be unmuted.

Unidentified Analyst

Hi, good morning. Thanks for taking the questions. Just first on HNSA-5487, do you think you will be able to go into a patient sort of Phase 2 study with having just done a single dose study or do you envision doing a multiple dose study ahead of that. And then [indiscernible] just I'm curious, do you think euro transplant will sort of represent a bolus of volumes that will be realized over a period of time and we'll sort of see a dip after those patients are worked through treated or do you anticipate sort of seeing that sort of smooth into just regular commercial adoption? Thank you.

Søren Tulstrup

Well, thanks for those questions. To the first one regarding whether we would need to do another dosing study before going into patients. The answer is no. We could potentially go straight into patients, so that's certainly an option. And then on the second one, as understanding, you said the post approval efficacy study centers, whether we expect immediate commercial uptake from those, was that the question?

Unidentified Analyst

No, I was talking more about the euro transplant pilot program and the 20 patients that are enrolled or they expect to include in that. Does that sort of represent sort of like a big bolus? But do you expect that overtime, that study is completed or that pilot program is completed that we'll just sort of see a continued pickup through normal commercial activity in Europe and in those markets? Thank you. Does that make sense, Søren?

Søren Tulstrup

It does make sense. So this – the euro transplant program is really a great way to really initiate the uptake of the associated countries Germany, Benelux, and some eastern European countries. And this is typically commercial patients. There might be some patients that are then actually added to the post approval efficacy study instead, but in general, it's commercial patients. So we see this as a great way to start, let's say, the therapy practices in these centers and really help the uptake overall. I don't know. Matt, do you want to add some to this?

Matt Shaulis

Yes. I could just make two other comments related to the question, one around the 20 patient pilot and then the other around a bolus concept. And the 20 patient pilot is not to sort of evaluate whether they're pleased with imlifidase or not. That pilot is really intended for them to optimize their process. How their IT systems are working, how the interface between the organ allocation system and the centers is working. They're going to work to an additional group of 20 and then look for opportunities to really optimize the process for those patients to get treated.

And then with regard to bolus, it's an interesting thought. I think our view is that it's more likely to just be sort of a gradual uptake into commercial utilization. It's simply less likely that there's a situation where there's this big number of patients and then the clinicians would very rapidly treat them.

We think that the uptake of physicians understanding the product, understanding the right patients, and then implementing into clinical practice in their institutions is essentially just going to take a little bit of time. And I think that is a gradual process that we've seen play out in other markets like France. And so it suggests that there wouldn't be sort of this big bolus that would take place, but definitely will anticipate the clinicians will continue to identify additional patients, and that'll lead to sort of a steady flow over time. So hope that that addressed some of the specific elements of your question.

Unidentified Analyst

Yes, it did. Thank you so much.

Operator

Thank you, Douglas. As no one else has lined up for questions, I'll hand it back to the speakers for any closing remarks.

Søren Tulstrup

Thank you very much, operator, and thanks, everyone, for calling in. Exciting times indeed, and we look forward to keeping you updated on progress as we move further into 2024. Thank you.