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Galapagos NV Q3 2022 Earnings Call and R&D Update

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PRESENTATION

Sofie Van Gijsel *Galapagos NV - Head of IR*

Welcome all to the Galapagos Capital Markets Day and third quarter results. This presentation is webcast and accessible via the Galapagos website home page. The presentation will be available for download and replay later on today.

I would like to remind everyone that we will be making forward-looking statements during today's webcast. These forward-looking statements include remarks concerning future developments of the pipeline in our company and possible changes in the industry and competitive environments. Because these forward-looking statements involve risks and uncertainties, Galapagos' actual results may differ materially from the results expressed or implied in these statements.

We start today with our strategic and financial updates, followed by a deep dive in our efforts in oncology. Next, we discuss our immunology franchise and commercial capabilities, followed by Q&A. And with that, I'll now turn it over to Paul. Thank you.

Paul Stoffels *Galapagos NV - CEO, Chairman & Member of Management Board*

Well, thank you, Sofie. And all welcome to the Galapagos R&D Day. Happy to be here in New York today and thank you for joining. My name is Paul Stoffels, I'm the Chairman and CEO of Galapagos. I'm a physician, scientist and headed R&D at J&J for the last 12 years before joining -- before I retired from J&J at the end of last year. In April this year, I took over from the CEO, Onno van de Stolpe and have been working with the teams on the renewed strategy since then.

I cofounded Galapagos back in 1999 as a target discovery company, and have been working alongside Onno for a long time, but this was done at a time before the human genome was sequenced. So it was at that moment, a transformational company with a breakthrough new technology. And the company was successful in putting its first medicine on the market, Jyseleca, in Europe which was a big achievement for a company to go end to end, from a start of a new target to getting a product on the market.

Galapagos evolved from a target discovery company to a fully integrated biopharmaceutical company over the last 20 years, focused on small molecule drugs in fibrosis and inflammation. Today, we will talk about our plan to accelerate our path to new medicines, focus on our strategy on immunology and oncology and broadening our platforms, including biologics and CAR-T. We will expand external innovation efforts to bring new medicines in late preclinical or early clinical to Galapagos. And this should result in a strong late-stage portfolio in 2028 and potentially already one new medicine on the market. Last but not least, we continue to build on a strong relationship with Gilead to commercialize outside of Europe.

Next. While we were successful with Jyseleca, we experienced some midterm failures in our pipeline, and we are now embarking on a significant acceleration strategy with the aim to bring multiple late-stage assets into the pipeline as well as one additional product in the market by 2028. We'll focus on our areas with high -- we'll focus on areas with high unmet medical need, from a new target discovery research and development of small molecule medicines in inflammation and fibrosis to a disease area-driven strategy in immunology and oncology, deploying best-in-class targets and expanding into biological modalities such as antibodies and CAR-Ts.

We have a strong balance sheet of EUR 4 billion cash, and we are aiming to use our cash in a disciplined way on the research and development of new drugs to maximize the value creation.

We have -- we can build on a very strong fundamental in the company. On the one hand, we have deep scientific expertise with 20 years of R&D experience and strong teams in our 4 research centers in Europe. We built a European commercial infrastructure, which launched Jyseleca in RA and UC. And that gives us a real strategic advantage now where we have built in a very challenging market, Europe, where every country has different rules, the connection with the payers, the connection with the regulatory authorities and also with the authorities in the countries to distribute drugs.

Going forward, this allows us to bring -- to launch products in Europe fast, and we already will be able to benefit from that with a strong basis in the launch of a CAR-T in Europe.

We are continuing to leverage the R&D capabilities of our partner, Gilead, as well as their commercial infrastructure for the U.S. market for our medicines. I consider this as a strong asset. We can co-develop in Phase III, accelerate the launch and we get high royalties on sales. That allows us to do much more, much faster on a global scale and have significant impact.

Using our financial strength to create a strong pipeline in accelerated time by select BD and disciplined spending will even further accelerate our pipeline. So the combination of internal research, combine that with external access to new assets focused on high medical need, will be able to accelerate the value creation at the company.

So our objectives for 2028. In early stage, by 2028, we should have 10 lead optimized compounds and 5 preclinical assets ready for the clinic. In late stage, it is our goal to have 5 assets in late-stage development, of which 3 are cell therapies and 2 small molecules. We think that is feasible. In the market, very important, we aim to bring at least 2 new indications for Jyseleca as well as 1 cell therapy in multiple indications. Also that, because of the high medical need in oncology, it's a possibility for us, and we aim to do that by 2028.

We will continue to do business development, next slide, please and -- in order to either further accelerate our pipeline. What are we looking for? On the one hand, for fast access to market, as I was explaining, time to market is for us now a critical prerogative in order to make this happen. Late preclinical and early clinical stage to preserve a lot of the value creation from within the company. Buying late-stage assets, very expensive and most of the value you pay out to all the shareholders. We would like to go early stage, late clinical, early preclinical in order to continue to add significant value ourselves.

We have commercial leverage in Europe, which is very attractive for many companies to work with us, with a strong focus on immunology and oncology and within that high unmet medical needs, going for the string-of-pearls approach. How can we bring a number of assets on board from internal or external in the development stage and accelerate them to market? What do we bring for partners? End-to-end development capabilities. We've done it before. We have a strong leadership and entrepreneurial mindset, a proven commercial rollout now adds to the strong capabilities of the company. Where needed and possible, a collaboration partner with Gilead, bringing additional assets and global reach for companies who want to work with that. And last but not least, a solid balance sheet, which gives us the time to make this all happen in the next 5 years. So supplementing internal science with external innovation is the way we want to succeed.

Next. So the portfolio we focus on, immunology and oncology, is a very important one because that focuses us on specific areas in immunology as well as bringing in a new area with high unmet medical need. Filgotinib, which is in the market, and the team will talk about it later for RA and UC, it's approved in Europe and doing very well. We expect big things from Jyseleca going forward as it really solidifies in the market. We will have a Phase III data for Crohn's disease in the first half of next year. And we are starting a new study, a new indication, axSpA, now in Phase II. We have good evidence for a strong TYK2

with '3667, and we started -- we are starting a study in dermatomyositis, followed by one in lupus in the course of next year.

And then from our SIK portfolio, we will continue to further explore the SIK3 '4399 in RA and the SIK -- the rest of the SIK portfolio in preclinical to see how can we bring this very interesting new target into the clinic in a later stage.

Really new for us is CAR-T. And we built CAR-T on the basis of having access and having -- bringing in CellPoint with access to a decentralized production tool. A small company like us could never have the ambition to be a large CAR-T company in the world with differentiated technology. And that's what we do here, combining a CD19 -- two CD19, two existing CD19s on a new platform, testing it out. It's in Phase I/II at the moment. We're entering with the BCMA into the clinic early next year. And then our later-stage objectives are having next-gen CAR-Ts to -- combined with the next-gen CAR-T platform for production, and so being a big player in this space.

In order to do so and to focus the company, we do a pipeline rationalization where we will discontinue fibrosis and kidney and refocus our resources and capabilities on oncology and immunology.

Now I'll leave it to Bart for talking about the financials. Thank you, Bart.

Bart Filius ***Galapagos NV - President, COO & Member of Management Board***

Thank you, Paul, and good morning, everyone here in New York, also from me. And good afternoon for those of you that are in the webcast in Europe. Thanks for joining. Let me say a few words about the financials about capital allocation, but it's also our Q3 release. So there's also a bit of, I would say, corporate housekeeping here in terms of clarifying the numbers for the Q3 report that went out yesterday.

So first, I always start -- let me see if I can get this working, yes, with the cash balance, EUR 4.4 billion at the end of September. A very healthy cash balance, obviously, for our company. We reiterate our guidance for the year, still between EUR 480 million and EUR 520 million, as we announced at the end of Q2. Our cash burn itself over the first 9 months has been EUR 340 million. And you see two additional impacts that sort of wash out. One is that we have had the benefit of the dollar appreciation over the first 9 months of the year that has offset the investments that we've done in -- on acquisitions, most notably the acquisitions for CellPoint and Abound.

On the P&L side, revenues, EUR 440 million. That always includes two noncash items that are recognition of accounting revenue for filgotinib and recognition of accounting revenue for the Gilead transaction that we signed in 2019. But there's also now a significant portion here in cash revenue that's coming to be part of our P&L. And we're very proud with the sales number of Jyseleca. We have EUR 60 million of sales in the first 9 months of the year. And with that, we are also increasing further our guidance for Jyseleca for the full year to EUR 80 million to EUR 90 million. And we started the year off at EUR 65 million to EUR 75 million. This is our second raise in terms of revenues. But with the EUR 25 million Q3

sales number, we feel comfortable that we are in the EUR 80 million to EUR 90 million range when we close the books at the end of December. So good, healthy revenues on filgotinib and Michele, our Chief Commercial Officer, will detail more about the performance in the markets later on this morning.

There's also royalties here that relate to Japan that also includes the UC approval in Japan and a couple of milestones from our partner, Sobi, who is now also launching Jyseleca in Eastern Europe.

Our operating results, EUR 135 million negative. The most notable point here is a depreciation on our OncoArendi transaction in fibrosis that we had done already in Q2. And you also see an increase in sales and marketing expenses compared to last year, which is mainly driven by the fact that this year, in 2022, we're no longer sharing the commercial cost in Europe with Gilead, but we're taking that on fully ourselves. Overall, the net result is almost breakeven. Again, we're helped here by foreign exchange, net other financial income of EUR 130 million.

With that then, maybe a few words about a longer-term perspective on cash burn and capital allocation. First, a view on 2023, and then I'll continue for the longer term as well. So as I've said, the guidance for this year is about EUR 500 million. And you can see here on the left how that's split out between burn that is connected to Jyseleca, and that includes both the investment that we're still making in the development of Jyseleca, for example, in Crohn's disease, where we've got a big trial still ongoing in Phase III, but also the investments in the commercial rollout of Jyseleca in Europe. So that's a big portion of that burden. I'm highlighting that particularly because, obviously, as Jyseleca progresses, as the numbers increase, that burn will come down significantly. And I'll show in the next slides that we actually anticipate that burden to be completely disappearing as of 2024.

In orange, you see the R&D burn. That's actually all the research that we do, but also the activities that Paul was highlighting on our TYK2, on our SIK program and on our cell therapy program and then corporate and G&A cost there as well.

Now what's happening into 2023, there's actually 4 big elements that I believe are noteworthy here. So it's too early to give a precise guidance. We'll come with that as usual in our February announcement of full year results. But on the Jyseleca side, we should take into account that this year, we're still receiving about EUR 80 million from Gilead in terms of payments for development costs, and also, as I said before, the approval for UC, and that will be nonrecurring. So that's a, what I call, bad guy in terms of the perspective towards next year because we're not going to get that same cash in next year. On the other hand, that's going to be fully and more than offset by the performance that we anticipate for Jyseleca and also the reduction in development costs that we're going to be seeing already in 2023. So overall, we anticipate the Jyseleca burn to go down next year.

On the R&D side, there as well, we anticipate the burn to go down next year. And we've taken the decision to discontinue fibrosis and kidney, not just for the scientific prospects of those 2 therapeutic areas, but also to free up resources to invest in oncology. And we've announced yesterday also to our teams in Galapagos that we will be reducing the workforce with 200 positions. And as a result, we

anticipate a saving compared to this year on those 2 franchises. And that saving will be offset, not fully but will be offset, to a large extent, with investments in oncology as we're building out that franchise in 2023. So overall, again, the message is cash burn in 2023 is going to be lower next year than it is this year, but it's not going to be a significant reduction as a result of those nonrecurring Gilead payments and as a result of the investments in oncology.

Then a look at the longer term. So first of all, 2024. We anticipate in 2024 that Jyseleca can be breakeven. And breakeven here is defined as commercial income and the deductions for R&D on Jyseleca and the deductions for the commercial investments in Jyseleca. So there's no overhead and G&A allocation included there. But overall, from a product point of view, we believe that Jyseleca will be breakeven in the course of 2024. And that's good news because it means that the gray part of this cash burn forecast is going to disappear. And as of 2024, we will be at a significantly lower level of R&D and corporate spend.

Now there's an arrow in there in 2024 going up and down on the R&D side. Obviously, it's very difficult to predict where we're going to land exactly in terms of our R&D spend. This is going to be dependent on the results scientifically that we will have over the next, let's say, 18, 24 months. So it can be a bit more. It can be a bit less. Also, obviously, if we would do significant business developments, this would also change the R&D burden. But everything being equal, if you look at our current spend, we anticipate that 2024 will see a significant reduction in cash burn.

But then if you look forward and you look forward 5 years to 2028, you see that if Jyseleca starts to become closer to its peak and as a reminder, our peak sales expectation is about EUR 500 million, we believe that Jyseleca has the potential to deliver about a 50% product contribution, i.e., deliver actually cash into the company of about EUR 250 million. And again, everything else being equal, which we all know is not going to be the case by 2028, but I wanted to show this to you because it basically tells us that we're going to be significantly reduced by the time we reach 2028 in terms of cash burn, and we have the potential to invest in other R&D from there on.

So I hope this clarifies a little bit the capital allocation from an ongoing cash burn perspective. And with that, I hand it over to Tol to talk about the -- to Paul, sorry, on the oncology franchise.

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***

So let me give a short introduction. Thank you, Bart, for the financial review. Does it work? Can I have next slide? We can operate the CAR-T, but we cannot operate slides. So -- well, thank you. Well, before we dive into oncology, I just want to give a short top line introduction on what we'll talk today. We have 2 opinion -- key opinion leaders here in the field with us, Rimas Orentas and Sébastien Anguille. They will contribute as experts in the areas and physicians treating patients on what we are doing here. And then we have Tol, Tol Trimborn and John Mellors, who will talk about our CAR-T production system in early-stage development as well as our R&D portfolio.

But the aim, what I indicated earlier on our 2028 road map, is that we aim to have 3 next-generation cell

therapies in 3 years. And in the short term, the focus is on how can we validate the decentral CAR-T delivery model with proven therapies. If you develop new technology, you want to have stability on one of the parameters. And that's -- here, we have 2 therapies which are proven in the clinic and where we are going to use the CAR-T, the CAR-T delivery platform in order to be able to show that we can do this on a large scale and bring this to patients.

The medium term, the 2023, 2025, our focus is on how can we get to best-in-class cell therapies for hematological malignancies. And what we learned today is there is a lot of high medical need still even with current therapies, which are coming into the market as well as how can we globally scale the CAR-T platform. At the moment, our CAR-T platform is being tested in Europe. Very quickly, we'll be in the U.S. and later on hopefully, into the rest of the world.

And then in the longer term, we would like to bring the technologies to also solid tumors and other areas, but especially solid tumors, hematological cancers as a potential going forward.

For that, on the next slide, yes. So the ultimate aim is to get to best-in-class CAR-Ts on the next-gen platform. And the challenges are still quite significant. At the moment, limited patient access because it's costly, complex, long manufacturing times, not always fitting the clinical setting and how patients should get access in the short term for saving their lives. Side effects, CRS and neurotox are still quite significant challenge. Also, that can be addressed by different approaches. Relapse is an important matter in oncology continuously, and we have learned from different approaches with CAR-Ts that you can get with bi- and trispecific CARs, you can get to better outcomes as well as CAR-T exhaustion and immune suppression, especially that for solid tumors. So a lot of signs in front of us to be able to approve and to improve products, which are better for patients. And that with an aim for better safety and durability outcomes with especially also broader patient access.

With that, I would like to first invite Sofie and Rimas to give a short introduction on the status of CAR-T and where the medical need and access for patients is. Thank you.

Sofie Van Gijsel *Galapagos NV - Head of IR*

Thanks very much, Paul, and thank you, Professor Orentas, for being here. Maybe you can start with a bit of background. We have your profile there, but maybe where your interest in the cell therapy space lies.

Rimas Orentas -

Okay. Thank you. Okay. I'll use this microphone. Good morning, everyone. My name is Rimas. And I'm here due to a long-term friendship with Dr. John Mellors and Mitko, Dimiter Dimitrov. I came through the Abound portal. I've been creating CAR-T cell products for quite some time at the NCI. This is now more than a decade ago. Mitko and I created a CD22-specific CAR, which is still best in class. And currently, I'm a Professor of Pediatrics at the University of Washington School of Medicine, although that's not the capacity I'm here today, and I'm also a Scientific Director of a nonprofit called Caring Cross. And our job there is to bring cell and gene therapies to low- and middle-income countries. So I have great interest in excellent CAR-T cells, curative CAR-T cells as well as access to them.

QUESTIONS AND ANSWERS

Sofie Van Gijsel *Galapagos NV - Head of IR*

Thank you so much. And how would you describe current patient access to CAR-T therapy?

Rimas Orentas -

Well, I think everyone realizes that access is a problem, and access is driven by lots of things, both by the ability to produce CAR-T cells, to get slots for production, also the cost. So at least 2/3 of the providers or insurers in this country restrict CAR-T access to some degree by how they pay. And just by availability, there's academic studies that are published. I can give you details. It's maybe only 20% of the CAR-T patients who are in Italy actually get a CAR-T due to access issues.

So it's production issues as well as cost issues that's driving a real bottleneck in terms of accessibility for this therapy. And that's why I'm excited to be here because I believe there's a Galapagos solution for accessibility.

Sofie Van Gijsel *Galapagos NV - Head of IR*

Thank you. And do you see point of place, as you have called it in the past, or point of care as a potential solution here?

Rimas Orentas -

And I think that is the solution is point-of-care manufacturing. Point-of-care manufacturing, not just for biologics, but for drug therapies is not the wave of the future. It is the future. And I think it's going to decrease costs just because of logistics and supply chain and including the providers, not just in the decision process of which drug or which biologic to get, but including the providers in the value chain as well because the hospital or clinic that implements local manufacturing then can decide when, where and how to use it and can actually come up with the cost structure that makes sense for them.

Sofie Van Gijsel *Galapagos NV - Head of IR*

Thank you. And then the question that we always get as Galapagos is, how does the regulator look at this? How does the regulator look at point of care, maybe specifically the FDA? Do you have any viewpoints there?

Rimas Orentas -

Yes. I have a lot. And I have specific quotes actually I want to share. I mean Dr. Janet Woodcock, when she was the FDA Acting Commissioner said, "We need to enable regulatory procedures that will accommodate new methods" in reference to point-of-care manufacturing of cell products, specifically CAR-T cell products. Peter Marks, Head of CBER, which is the biologics branch, is also looking to enable point-of-care manufacturing of CAR-T cell products.

Earlier this spring, the FDA issued guidance for production of CAR-T cell therapies. It's a wonderful document. It's only about, I don't know, 6 or 8 pages. Every question you have about CAR-T cell and regulatory aspects and product quality, it's all in there. Whoever wrote it did a great job, so I just want to call out the agency for it. And it'll actually show you that there's lots of room in the regulatory world for point-of-care manufacturing. And that machine over there, I think, is what we're going to talk about later. But I think that's one of the two major ways that are now market-ready, that are already producing CAR-T cells. That's it. There's two.

The U.K. has issued a consultation for point-of-care manufacturing. The point of comment is over, but the U.K. is getting ready to do this. So the U.K. realized is that point of care is the way to create accessibility and affordability for CAR-T cell products. Two other European countries. Switzerland is doing a network of local production of CAR-T cells, and they're predicted to drive the cost down by half. And the best-known example is, of course, Spain, which has multiple centers producing CAR-T cells at multiple sites. And in Spain, that's how you're going to get your CD19 CAR-T cell product. It's through this local network of manufacturing, what's it called? It's -- they have prime designation.. So I think point-of-care manufacturing is here.

So what are the regulators looking for? How is this a provocative new statement? They're looking for not just a one-off, right? The FDA doesn't want to have 100 different hospitals and clinics each making an IND application, right? So what they're looking for is a framework with a centralized reporting showing that at each of these sites, we're having consistent, safe and effective products. And if you can come to that as a single report through those multiple sites, the agency is just waiting for that.

And I think the last comment again to show you how ready the agency is, the CDER, C-D-E-R, which is the drug branch, not the biologics branch, has also issued guidance for local manufacturing, right? So this isn't theoretical. The agency is waiting, whether it's in biologics or in drugs to start approving point-of-care production of CAR-Ts and other products.

Sofie Van Gijsel ***Galapagos NV - Head of IR***

Thank you so much, Professor Orentas. This is very insightful. Thank you for being here.

Rimas Orentas -

All right. Thank you, Sofie.

PRESENTATION

Tolleiv Trimborn ***CellPoint B.V. - CEO***

Good morning to you all. My name is Tol Trimborn, and I'm going to explain to you a little bit about our new manufacturing platform that we have established to be able to make CAR-Ts, in our case, more accessible to patients. And as Professor Orentas already pointed out here, we still -- a lot of the patients are still -- that are eligible for receiving a CAR treatment are not getting it. And that's why we came up

with a new manufacturing at the point of care.

So CAR-T patients, the T cells are at the clinical site where this patient is being treated are converted into CAR-T cells and only 7 days later, that patient will be able to get his treatment. So it's very rapid.

As I said, we currently have a short manufacturing protocol, and it's also very scalable. So makes it very easy if there are more patients or if we enter more products into the pipeline to add more fully automated machines. So it's all based on a machine called Cocoon made by Lonza, our partner. There is one example, very kindly provided by Lonza today. We can show you later on how the machine actually works in a bit more detail.

But we feel this is very disruptive and then we are the first and only company that's currently developing this at the point-of-care platform in a very centralized way. We have full control of all the steps and everything that's taken -- taking place at all these different individual manufacturing sites. But I will guide you through it in a bit more detail.

So this is the Cocoon machine that we have decided to work with. It's a fully closed and automated bioreactor that can actually manufacture, in this case, T cells. Of course, it's sterile. So if you put something clean, sterile in there, it remains sterile over the process. We work with disposable cassettes on the left-hand side, that actually do the job. So the machine stays clean. It doesn't need to be wiped or cleaned, whatever, after a run. For every patient, we use a disposable cassette. It's thrown away afterwards.

Currently, it's a benchtop machine as it's shown there, but Lonza is working on the first Cocoon tree, as it's called. So with a very small footprint, you can actually stack quite a number of these machines in the cell and gene therapy facilities that all the big hospitals in Europe and the U.S. already have. So they have these facilities, and that's how we have chosen our first partners on the clinical side in the beginning.

So let me talk a bit more on the relationship with Lonza. It's an exclusive partnership to use the Cocoon at the point of care in the hematological space. And in this model, Lonza is actually responsible for deploying the Cocoons at the clinical sites. And we, as a company, we'll actually deploy all the other materials that are near. All the raw materials are brought in by CellPoint. Lonza trains the people on the machine and CellPoint trains the people on the process and on the QC assays. And in return for giving us these Cocoons, Lonza gets a share -- royalty on the net profit.

The second important pillar of our new manufacturing platform is an IT system that we have developed together with a partner in-house. It's called xCellit, and it basically facilitate the scheduling of patients, the monitor progress on the manufacturing process, on the clinical process. It has dashboarding for all the stakeholders involved in the process. Most importantly, it ensures a high quality of data capture. So all the data that is generated and is needed for regulatory -- have for regulatory documentation is captured in this system, and it allows us for a central QA oversight, real time, during the process at any site. And that's organized centrally through our people locally in the Netherlands.

It also ensures the chain of identity, chain of control. So all steps are barcoded, and people cannot make mistakes. And it has the sort of the cookbook, the electronic batch record in there. So the operators of the manufacturing process or the QC processes have to basically have the cookbook in front of them and have to tick the boxes once they have completed the steps in the process. So this allows for a very scalable process and adding more clinical sites easily, and xCellit will orchestrate all of this.

The third important part of our manufacturing process is a very short manufacturing time. We have less than 6 days actual manufacturing, allowing us a 7-day vein-to-vein time, so just short process. And most importantly, we also have fresh infusion. So fresh cells from the patients going into the machine and fresh cells coming out of the machine on -- after 6 days of manufacturing going into the patient, so no cryopreservation. And every biologist, if there are any in the room, knows that by thawing cells, you'd lose at least 20% to 30% of those cells. So viability, by definition, is quite low and poor. We have very high, but I'll come back to that at a later stage.

Most importantly about this is actually two things. We believe by shortening process and by fresh infusion, we make a better product. And this we, of course, have to show in clinical trials, and that's what's ongoing. I'll come back to that. The other important point is that we might be able to treat patients, different patients that cannot wait 12 or whatever, more weeks. Of course, Kite is doing pretty well with 17 or 20 days turnaround time. And most of the other companies, it takes much longer, but maybe Professor Anguille will say something about that later on.

So, so far, we've done over 100 runs, no failures. Everything sterile. It's a really consistent process. And not only at our central site in Leiden, where we've developed this together with Lonza, but also now in 6 centers that we have up and running in Europe. The first center in the U.S. is currently onboarded in Ohio. So -- and have, by the end of the year, we hope to have opened at least 10 sites.

As I said, we have a very robust and consistent process developed over the past 2 years. It's now in the clinic. The product is really pure. It's over 98% pure, over all those runs. The cells are really very viable, as I said earlier, over 95% viability. We see -- most of these runs, you have to realize were done based on healthy donor material. But now also with the first patients, we see high transduction efficiencies, very important to make enough CAR-T cells to put back into patients. And we consistently are at a very low range of copy numbers. So especially in the U.S., the FDA does not want products to exceed 5 copies. We consistently are between 1 and 3 copies.

And because we have such a robust and short manufacturing process, with no relevant impurities. We have a very nice CD4/CD8 ratio for some of the experts in the room. Again, we believe a very good product that we can give back to the patients.

To update you on some of that, although we have now treated 11 patients in total, I'll update you on 2 of the ongoing clinical trials. Our creative team in the Netherlands came up with butterfly names for these studies because the products are coming from a Cocoon. So the first study is ATALANTA. It's a Phase II

dose-escalating trial, a very typical 3 by -- 3 different doses. We've treated 2 cohorts in this study. And most important, after 28 days, we make a PET scan of these patients to follow them. We cannot disclose too much of the clinical data as yet. The data is being analyzed. We hope to show that at ASH in a month's time. But once the dose escalation has gone one step further, we want to roll over this Phase I trial into an expansion cohort of another 30 patients and hopefully in one of the subpopulations of NHL. We hope to report on the top line data, and then we hope we will report on the top line data in the first half.

To share some of the very exciting data that we got out of the first 3 patients that were treated with our CARs in the NHL study, this is data generated by PCR, where you look at how many CAR-T cells there are in a patient. And the T cell expansion upon treatment of these patients is significantly higher than the currently marketed products. So we're very enthused about these early data and that -- yes.

The second study is called EUPLAGIA. This is running in Barcelona currently only. We're opening other European sites on this study. It's also a dose-escalating Phase I/II trial. Again, 3 doses. Day 28 is the first readout. We follow up with those patients and also in this study, how we intend to roll this over quickly into an expansion cohort. And once we have the data of the first patient in the expansion cohort combined with the dose-escalating part, we'll, of course, initiate a discussion with the authorities in the U.S. and EU on how to design the pivotal study.

Also in the first cohort of this study, we see a very nice expansion of T cells, roughly a similar higher folds of expansion compared to the current products. So the data are really encouraging. We hope to show you data on patients, hopefully of the first 2 cohorts at ASH in a month.

To summarize here, we don't see -- neurotoxicity is very important. We have to realize, we see already very good data at very low doses. So no neurotox. Only grade 1/2 CRS. And on the efficacy side, very encouraging data, hopefully, to show in a month's time. But the data that I showed you are, I think, very convincing with the high peak levels of CAR-T after infusion. All these patients were treated in 7 days.

So as I said, currently, we have 6 sites open in Europe. First site in the U.S. is being initiated. By the end of the year, we hope to end up with 10 sites and building on that towards the pivotal studies. And of course, for the commercial rollout, we hope to have at least 40 to 60 sites open in the U.S. and EU combined.

So the upcoming milestone by the end -- as I said, by the end of the year, we hope to have at least 10 sites up and running in EU and the first sites in the U.S. We'll be submitting an IND for 19 and also BCMA in the U.S. And then early or somewhere in the first half of next year, we want to roll over these dose-escalating studies in expansion cohorts, setting us up for a pivotal trial that we intend to start in 2024.

So I think I hand it over to John Mellors, CEO of Abound.

John Mellors -

Good morning. It's great to be here back in New York. I grew up in New York. I did my training at Yale, so I feel at home. And it's really exciting to witness that this machine is going to revolutionize therapy and save lives. This is the future.

So who am I? I'm the CEO of Abound. I trained and grew up at Yale and Pittsburgh. My co-founder, Mitko Dimitrov, poor guy, everybody butchers his name, but he is well-known internationally as an expert in antibody discovery, engineering and application for medical purposes. His antibodies have landed in really good places.

So what does the antibody have to do with CAR? The binding side on a CAR that directs it to malignant cells is derived from an antibody. I professionally have witnessed the transformation of an untreatable lethal disease, HIV and AIDS, to a currently manageable and life-saving therapy for that disease. And I'm anxious to see that same transformation for hematologic malignancies and for solid tumors.

I only have 3 slides, so we'll get through them relatively quickly. So what are our scientific capabilities at Abound? Abound was acquired in June and is a fully owned subsidiary of Galapagos. Well, rapid antibody discovery and whatever format is potentially useful, single-chain Fab, VH, also known as nanobodies. We have proprietary libraries I'll describe on the next slide and incredible expertise in finding the right binder, and we have expertise in designing state-of-the-art CAR-T cells with the help of many individuals, including Dr. Orentas.

So we have a proven approach to rapid antibody discovery. We have very large libraries of fully human antibodies as opposed to mouse or llama that tend to be immunogenic. These are fully human derived from over 500 donors. By large, I mean, 1 trillion specificities. This is probably some of the largest, if not the largest repertoire of antibodies in the world. We have proprietary panning methods that pull out the diamonds or jewels from these libraries. And they do it fast, within a week, we can get very good binders of high affinity in the nanomolar or subnanomolar binding affinity range with good properties for development. And we also have the ability to find ultra-specific antibodies. What do I mean by that? Antibodies that differentiate a protein that is only different by one amino acid.

So how are we going to apply this? One of the huge issues in cancer and with the current approved CD19 therapies is relapse. And what are the causes of relapse? Well, there are many. The percentage of relapse grows with time. It's approaching 75% at 3 years.

So what's happening? The tumor is not monomorphic. It's highly heterogeneous and there's escape of the tumor from the CAR-T cell by downregulating, one of the mechanisms, downregulating CD19.

So as an HIV and other infectious diseases in cancer, what's the solution? It's combination therapy, and we aim to put the combination on the surface of a CAR by targeting multiple proteins on the surface of a malignant cell and by targeting each protein with more than one binder. So that's called a multispecific strategy, either a dual or a trispecific strategy, multiple targets, multiple positions on the protein. So bi- or multiparatopic or bi- or trispecific.

We then are in the process of engineering CAR cells so that they proliferate more as -- and expand to a greater degree. And one of the limitations of current CAR therapies is the lack of persistence of the CAR long term. And we aim to improve that by engineering the cell as well as the vector used to transduce. And for solid tumors, the key barrier is this inhibitory tumor microenvironment as well as barriers for entry of cells into the tumor. Think of the tumor as having evolved its own space within the human body, its own microcosm, if you will, that -- and it's -- that's enabled it to survive immune attack. So we need to reverse that.

And then long term, our strategy is beyond CAR-T cells to add different modalities to improve the penetration of CAR-T cells, for example, antibody drug conjugates, which we have a lot of experience with, to provide cell killing and allow penetration of the CAR-T cells into solid tumors. And we will armor the CARs to defend themselves against this hostile tumor microenvironment.

And with that, I'm going to turn it over back to Sofie to introduce Dr. Anguille.

Sofie Van Gijsel *Galapagos NV - Head of IR*
Thanks, John. Hi, Professor Anguille. We're very excited to have you here today.

Sébastien Anguille -
Good morning.

QUESTIONS AND ANSWERS

Sofie Van Gijsel *Galapagos NV - Head of IR*
Good morning. Especially because you are effectively participating in one of the trials that is currently being run on the CellPoint's device. So maybe could you first say what made you decide to participate in the trial?

Sébastien Anguille -
Yes, that's right. So my name is Sébastien Anguille, I'm Head of the Division of Hematology at the Antwerp University Hospital and one of the PIs on this CellPoint CD19 CAR-T cell trial.

Regarding the reasons to participate, let me first describe the context. We have CD19 CAR-T cell therapies on the market. We know these therapies work. They can save lives for patients with a certain type of blood cancer, especially lymphoma. But nevertheless, despite the fact that we have availability of these CAR-T cells, a lot of lymphoma patients do not get the CAR-T cell treatment. And that was, for me, the main reason to participate, that is there are indeed a lot of patients that still do not get the treatment.

We know that only certain types of lymphoma patients, patients with certain types are eligible for

regular CAR-T cell treatments. And actually, this trial allowed us to treat the main types of lymphoma. So more lymphoma types are eligible in this trial. And there is a high need. We know these treatment works also in other types of lymphoma. So that was the main reason actually for us to participate. I will show the story or present a story of Tom, who was the very first patient treated on this trial. And he actually had a type of lymphoma that was not eligible for the current or the regular CAR-T cell treatments.

Second reason, and this is more regarding or about the point-of-care model. The decentralized production is a patient like Tom, whose story will be presented soon, is a patient that would never have made it through the centralized manufacturing process because that takes time. It's quite slow. It's a black box. Here, we have more control. We can go very fast, and this is needed in certain patients with a very highly aggressive disease course.

Sofie Van Gijsel *Galapagos NV - Head of IR*
Thanks so much. So if I hear you, the fact that you give power to the physician to rapidly select patients, that's the biggest advantage of the point of care?

Sébastien Anguille -
Yes. I think that's true. You give power to the physician but also to the patient. We become part of the production process of the entire process. And actually, we now drive the CAR.

It's not...

Sofie Van Gijsel *Galapagos NV - Head of IR*
no pun intended.

Sébastien Anguille -
Yes. It's not putting the patient on a waiting list and hope for the best that we can have the treatment rapidly.

For example, with Tom, we needed to go -- we needed to drive really fast. And what we did is actually, in this case, we did the apheresis, so we took out the cells. The data thereafter, we already started his preparatory chemotherapy. And 1 week after we took out the cells, we already gave them back. So in just 1 week, a little bit more, a little bit longer, we already could treat him with these CAR-T cells.

Sofie Van Gijsel *Galapagos NV - Head of IR*
Which compares to what with the standard of care?

Sébastien Anguille -
Well, it's not only, like Tol said, it's not only the production time. Here, it's 1 week, 7-day vein-to-vein time, but it's the entire process, selecting a patient, having him put on the waiting list, waiting for a manufacturing slot, this can last several months in real world.

Sofie Van Gijsel *Galapagos NV - Head of IR*
Okay. So we're all cognizant. It's early days. It's -- we're still in the trials, but what can you say something about what you see so far in your clinical study?

Sébastien Anguille -
Yes. Not going into detail about clinical results, which look very encouraging, which is what we also expect because these CAR-T cell treatments targeting CD19, it works. But for me, my experience is that in the short time frame, this trial is now 6 months going on, we already treated more patients than we did with regular CAR-T cell treatments. And that proves the point, I think, and also proves the need for a decentralized or point-of-care manufacturing process.

And maybe because my patient, Tom, actually wanted to share his story. Maybe it's good that we -- because ultimately, we do this for patients, we hope to treat patients and save lives. So maybe we can share his story.

Sofie Van Gijsel *Galapagos NV - Head of IR*
Yes.

(presentation)

Sofie Van Gijsel *Galapagos NV - Head of IR*
Thank you. So maybe say a bit about how the patient is doing today. Are you still in touch with him, I assume so, for the follow-ups?

Sébastien Anguille -
Yes. His words were prophetical actually because we're now 6 months later, we just recently, a few weeks ago, we did his 6-month PET scan and he's in a complete remission. So he's actually really doing well. If you looked at him there, he was very sick, and now he is doing really well. He's traveling. He's working back again, and he's living actually a normal life.

Sofie Van Gijsel *Galapagos NV - Head of IR*
Thanks so much, Professor Anguille.

Sébastien Anguille -
Thank you.

Sofie Van Gijsel *Galapagos NV - Head of IR*
Thank you.

PRESENTATION

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***
Well, thank you, Professor Anguille. There are always people like you with a lot of courage to start, for the first time, a new procedure, new technology in your hospital, but having this type of results is really encouraging. And so thank you very, very much for what you do for the trial, also for your patients, and we'll hope to hear more soon.

With this, I would like to introduce Walid Abi-Saab, our Head of R&D, who is going to introduce the immunology topic. Thank you.

Walid Abi-Saab ***Galapagos NV - Chief Medical Officer & Member of Management Board***
All right. Good morning, everybody. Thank you, Paul. Thank you, everybody. It's really been a very exciting half an hour -- the last half an hour, culminating with this wonderful testimonial. So yes, hang in there. Fingers crossed. The future looks very bright and exciting.

So let me tell you a bit about the immunology franchise. As you guys know, Galapagos has been very active in this field for the past 2 decades. We've developed deep expertise. And as you heard in the earlier introduction, we've gone through a series of portfolio assessment and focusing to try and streamline our portfolio and actually focus on medication that will make a big difference to people and add years of life and quality years of life to these patients. And with those foundations, we are moving forward with these key foundations in our immunology portfolio. Of course, filgotinib is on the market and doing very well, and Michele will tell you a little bit more about it in a few minutes. I'll say a few words about it as well. But we also have 2 other key programs that I want to talk about, our TYK2, which is ready to go into Phase II, as you've heard earlier, and our program, the salt-inducible kinase, which is an interesting target that we are now focusing on the next stage of growing it.

So with the pipeline that covers from discovery all the way to Phase IV in immunology and the background that we have, I think this forms a very strong second pillar in the strategy for Galapagos as we move forward.

So the salt-inducible kinases are -- have been an interest to us for a long, long time. We've developed a deep scientific knowledge of that space. It's a novel mode of action, which has a potential for broad potential across a number of immunology targets. So let me talk a little bit why we've been interested in this. As you guys know, for those of you who have been following us for a number of years, we've been very active in this domain for a number of years. And the reason why we've been very interested in this is that the salt-inducible kinase is essentially signaled through 2 lines, as you can see here on the cartoon. And by inhibiting these targets, what you can do is reduce pro-inflammatory mediators such as TNF alpha and the likes, and at the same time, increasing the regulatory mediators such as IL-10 and the likes. And this holds a promise that you're going to have a much better risk benefit profile for these compounds going forward and truly take the efficacy and safety to the next level and address key unmet medical needs that are still out there in this therapeutic area.

So for many years, we've been advancing a number of these compounds preclinically, and we've

advanced a few of them in the clinic, the most advanced being '3970, which is a SIK2/3 inhibitor that made it all the way in patients and a number of proof-of-mechanism trials. And the data indicate that there's clear evidence of efficacy as we saw in psoriasis for '3970 as well as signs of objective improvement in ulcerative colitis. Still, we learned a lot from this and specifically, the degree to which we need to inhibit those enzymes to produce these effects and where to go next. So I think it's fair to say that we took essentially an assessment, a status assessment as to where we are and decided to focus in a very disciplined way about the way forward.

Specifically, what we learned is that SIK3 inhibitors hold promise in rheumatoid arthritis, whereas 2/3 have a broader potential that expands into IBD. What we've also learned is that there are certain number of hurdles that we need to overcome and a certain degree level of inhibition that we need to achieve in the clinic to be able to move these molecules forward.

Lastly, I think we -- and this applies actually to the whole portfolio, we have suffered a series of setbacks with these molecules going forward due to off-target activities or characteristics of the molecules themselves. And as a result, our criteria for advancing molecules from discovery, from research into the clinic had to be set at a much higher rate, and you will see that evidence in the future. So this is our strategy right now, take the focus to develop SIK3, selective SIK3 and selective 2/3s preclinically with the new criteria to advance the right molecule forward while learning more from the molecules that we have and move it ahead. And so one of these molecules, I think this is temperamental, there you go.

One of these molecules is '4399. So what have we learned from the Phase I with this molecule? So this molecule is generally safe and well tolerated. We can give it once a day and with that, have the necessary inhibition to a large degree of the SIK3 isoenzyme. And with that, we should be able to safely conduct a Phase II trial, which will help us to evaluate the potential effect in rheumatoid arthritis for this class of compounds and bring back a lot of knowledge to the whole platform of salt-inducible kinases.

Having said that, it's important that I also say very clearly that we have some challenges with the characteristics of this compound, some potential liabilities. An example would be potentially drug-drug interaction that we think might make it difficult for this compound at the end of the trial to be a potentially commercially successful compound. It remains to be seen. But for the time being, the main goal with this compound is to move forward to be able to allow us to test the hypothesis and in the meantime, work on the new wave of compounds from research with the better characteristics that I mentioned previously. So a very interesting test for us that we will be able to do in the middle of 2023.

The second major project that we have is in the -- in one of our medicine, TYK2 inhibitor, '3667. So why do we care about this? I think we've been very interested about TYK2 because of the way it signals through the type I interferon as well as IL-12 and 23, the blockade of which will unlock a significant number of potential in autoimmune indications. And I think we've known a lot from the -- some of the competitors, particularly deucravacitinib from BMS.

So let me tell you a little bit about our experience with '3667. To date, we have studied approximately

100 subjects with this, mostly healthy subjects, but also some patients with psoriasis. So what you see on the right-hand side panel is from our multiple-ascending dose and an ex vivo assay where you can clearly see in the green line there at the bottom, that we fully inhibit the interferon alpha signaling over a 24-hour period with once a day dosing while in the orange line, which measures GM-CSF/pSTAT5 which is a JAK2-dependent pathway, that is not at all touched in this assay.

On the right-hand side panel, you can also see from a different study, when we look at Tmax, which is the time wherein we have the maximum concentration of '3667, that we have inhibition or rather almost full inhibition of the interferon alpha pathways through pSTAT1 and pSTAT3, whereas we don't touch the IL-2 pSTAT5 which is a JAK1/JAK3-dependent pathway. So the totality of the data show you that at steady state with once a day dosing, we essentially fully block TYK2 over a 24-hour period without touching any of the JAK1, JAK2 or JAK3 signaling in this trial.

What we also have done is look at a number of parameters that we often follow, humoral, so levels, lipids, CPK, those what we call fingerprints for JAK activity. And as you can see, and I hope you agree, we don't see any effect on these parameters from our Phase I study.

And here, I'm showing some gene expression that we did following interferon challenge. So in our multiple-ascending dose, once we reach steady state, we give interferon and try to block its effect with '3667. Again, there's a group that's on placebo. You can see on the far left-hand side. You can see very nicely the time course at the bottom from 0 hour to 48 hours, how you have an increase in expression between 6 to 12 hours coming back to baseline in 24 to 48 hours. And on the right-hand side panel, you see in a dose-dependent manner how '3667 is able to completely block these effects starting from the middle dose on.

So it's not surprising when we took it into a psoriasis trial, a 4-week trial that we've discussed previously, that we saw a very clear effect. As you can see here on the graph, if you draw a line on PASI 75, strictly speaking, we have one patient. If you're generous with me and you allow me to count the PASI 74% patient in, it will be about 20% of the patients. But regardless, at PASI 50, we have about 40% versus 10% of placebo. These results, small study, short duration, tell us that we are in the ballpark of what we have seen with other TYK2 inhibitors that have been studying psoriasis.

So taking it all together, very interesting target, working through pathways that would address some key diseases that we're interested in. You heard a sneak preview before where we're going with this. I hope I have shown you clinical data to show that with once-daily dosing, we provide essentially fully blockade of the interferon alpha pathway over a 24-hour period without touching any of the JAK signaling. We haven't seen any effect in the lab that will suggest that we also affect JAKs. And we believe that with that, we have a very good compound in our hands that will be able to be tested in some key diseases for us that still have a high unmet medical need, specifically dermatomyositis and lupus. And I'll take a couple of slides to go through those, if you allow me.

So dermatomyositis is a chronic and rare autoimmune disease. It has a high patient burden and

treatment failure. Really, this is characterized by inflammation of the muscles with muscle weaknesses, mostly proximal muscles, shoulders and the quads. It has a rare prevalence of about 3 to 10 cases per 100,000. In terms of treatment, there's really not much out there. People get treated with steroids, the usual or immunosuppressants. Recently, there's been approval of an intravenous immunoglobulin IVIg, Octagam, which requires intravenous in an administration over 2 to 5 days every month. So it's a significant burden to the patients. Now this disease is very much driven by type I and type III interferon and IL-23 pathway, making our '3667 a very likely candidate to produce positive effect. So we would like to start a Phase II trial, which is now in late-stage preparation, and we should be starting around year-end.

This is a very brief schematic of the study, a very simple 6-month long trial, double-blind, placebo controlled, one-to-one, one dose of '3667 versus placebo, approximately 30 patients per arm. The primary endpoint is the typical what actually has been used by, most recently, I mentioned Octagam. So essentially, it's a composite score developed by ACR equivalent to the ACR20 that you know in rheumatoid arthritis. So it's called total improvement score. In addition, we will look at a secondary endpoint, of course, the usual safety tolerability at PK, but also we will look at skin endpoint with the modified CDASI, which is also a common in that space.

The other disease that we will be looking to study is lupus. We've been doing a lot of preclinical work and all the knowledge that we have about the pathophysiology of this disease, that it's partly driven by interferon alpha. And we believe that with the potent oral interferon alpha essentially blocker with our TYK2, we should be able to achieve good results. As you know, lupus, there's a high unmet need in this disease. It's -- only 2 treatments have been approved in the past 5 years. It's a very heterogeneous disease, predominantly in women, but the course is -- could be very variable. But inevitably, it leads to very significant morbidity and mortality, the most important, which of course, is lupus nephritis which is of course, very problematic for these patients. So we are aiming to start a Phase II study in 2023 to be able to address this. It will be, again, a well-powered, long enough study that will allow us to evaluate the potential for this compound in this indication.

It's really great to have seen also recent data validating this pathway with deucravacitinib, which showed very good results with their compound in this indication. And as a result, we feel quite confident that with what I've shown you previously, we will have a great potential to show good results in that space.

So last but not least, let me finish on this slide on Jyseleca before I turn it over to Michele. The next big thing for Jyseleca are the top line results for DIVERSITY study in Crohn's disease, which will happen early next year. We feel quite good about it because a number of things. One, we had a positive Phase II data in FITZROY as you see on the slide, which we've published several years ago. In addition, in a sister indication, so to speak, in ulcerative colitis, we had a very smooth path to approval in Europe. And actually, as you will hear from Michele, we're quite happy with the performance of Jyseleca on the market with that.

There's an important issue that's been haunting us with filgotinib for many years, and those of you who

have been following us for a while have been aware of this. This is the issue -- the famous issue of testicular toxicity and having to conduct those studies. And I'm really extremely pleased to see the positive CHMP opinion that we got, essentially validating all of what we've been saying for a while that we do not see any of these concerns translate into the clinic based on the study that was designed specifically to address this concern. And as a result, there will be changes in the label to reflect that, which are actually currently in the making. So we're very, very happy with the way this is turning out.

The next key element is the Article 20. I'm sure you guys are familiar in this development in Europe, where based on results from the oral surveillance study with tofacitinib plus some preliminary data from Olumiant, baricitinib showing some increase in malignancy risk and cardiovascular risk. The European agency asked the pharmacovigilance review committee, PRAC, to review this, and we've been working with them collaboratively. Actually, it's been a very good exercise with very close collaboration, not only with PRAC but also with the other manufacturer to pool our resources together and show the data collectively.

And I'm really quite happy with the initial outcome that came out of PRAC. Of course, we're still awaiting the CHMP opinion, which often follow PRAC. But at least with the PRAC opinion that was made public, I think it's a very good outcome that we don't have any restriction on the indication and also to see that the observations that we're seeing in tofacitinib and Olumiant will be reflected in the label in a way to better educate the prescriber.

And actually, what we like about this is that this is completely in line with what EULAR guidance came up as well as ECCO. And to a great extent actually, and maybe Michele can say a couple of words on this, we see that, to a great extent, reflected by the prescribers. So we believe that already, this has been well known, these adverse events about the JAKs. And these considerations have been actually part of the deliberation and the decision-making that these prescribers are taking when they're discussing with their patient and choosing who is the best patient that they need to prescribe JAK inhibitors for.

Last but not least, actually, it's not small at all. It's a big deal. We have decided to start a Phase III program in axial spondyloarthritis. So I think this is a very important development. We will start this next year. As you know, we feel quite good about our likelihood of success there. We have previously conducted a study in ankylosing spondylitis a few years back, and we had very, very good effects. I think when you look at the performance of filgotinib, when we look at the overhangs from MANTA and now Article 20 being clear and the performance, we feel quite positive about the future of filgotinib, and we are able to invest to bring it to more patients who need it. And that's really very exciting to see that next year.

And with that, I'll actually turn it over to Michele, who will tell us how things are going in the marketplace.

Michele Manto ***Galapagos NV - Chief Commercial Officer & Member of Management Board***

Thank you, Walid, and thanks, everybody. Great to be here with you this morning in New York and then

connected with the folks in Europe for this afternoon. So let's move to some reflections and observation on how Jyseleca is doing actually today with patients and on the market in Europe, especially.

So the profile of Jyseleca is consolidating as the next-generation preferential JAK1 inhibitor and actually being approved in Europe, U.K., Japan, into indications, RA and UC, and actually being the only one approved in both indications with 2 doses, the 100 milligrams and 200 milligrams. And as we expect, also this flexibility in dosing will provide, even more important, with the reflections that Walid also mentioned from the PRAC. That adds, of course, to the convenience of once-daily overall dosing, remembering, so these are patients that are -- have been treated for the past many years with biologics, infusion, subcutaneous injections and of course, oral is a patient-friendly modality.

That adds, of course, to the clinical results from our studies, that confirms the fast onset and lasting activities across the indications and actually adding now with these recent results from the MANTA, MANTA/RAy studies and the CHMP opinion in Europe about the no impact of -- on testicular function. So that was indeed something we had and -- to study. And actually, we are the only drug which has been studied for that, which has demonstrated in the studies that there is no such an impact.

So this has been the profile. But as we launched Jyseleca in these past years, we haven't done just that. Also, at Galapagos, we actually established Galapagos as a commercial operating company in Europe. So we set up in, more or less 2 years, 2 therapeutic areas, starting with the approval of RA in late 2021 and then last year -- 2020, actually, last year, in November with the approval of UC and then now, looking forward to the potential also approval of Crohn's disease. So in the meantime, so we established our operations in most of the relevant largest countries in Europe. Our Galapagos operation also partnered with Sobi to ensure access and sales in Eastern Europe, Greece and Portugal. And actually also, in the process also, we have become marketing authorization holder from -- taking over from Gilead.

So in that process, basically, we allowed the operations -- our operations to supply, book sales, have market access or relationship with payers, and you know it's very complex in Europe, and also have abilities to operate with medical affairs, key opinion leaders, individual physicians and of course, also on marketing and sales. And most of these capabilities actually in infrastructure can be leveraged and flexible for additional therapeutic areas, of course, to support further indications in inflammation, immunology but also looking ahead at oncology, supply, sales, market access, medical affairs especially, are all areas that can be leveraged for oncology as well.

So now looking at this year, this year sales, as anticipated by Bart earlier, are going well. So we have a year-to-date sales of EUR 60 million, last quarter, Q3, of EUR 25 million. So that also gives us the confidence to raise our guidance to the EUR 80 million, EUR 90 million range. Just remember, we started the year with a guidance of EUR 65 million, EUR 75 million. We raised that to EUR 75 million, EUR 85 million after the first half results. And so we are comfortable in raising that again.

Sales are, of course, coming mostly still from rheumatoid arthritis. It was launched a year earlier. Now all the important countries are reimbursed. In Europe, some countries take up to a year to get

reimbursement. We've done that also in very good time, benchmarking with the best of JAK inhibitors, but still now, so we have all the countries with RA on the market and then growing up also with ulcerative colitis with a similar pattern of reimbursement.

Communications, but of course, we look at more. Crohn's disease has been mentioned already a couple of times. If you look at RA, you see in Crohn's, the total market in Europe is about EUR 6 billion. And of course, growth rate in number of patients coming to these advanced therapies. Our ambition is to come in a range of 8% to 12%, depending, of course, of the countries and the indications in total, reaching EUR 0.5 billion of peak sales.

This EUR 500 million peak sales in the 3 key indications, so RA, UC and Crohn's by the second half of 2020. In terms of profitability, we expect to have a contribution margin of about 50%, which of course, will lead to the development of cash burn and contribution to the R&D spend in the second half of the decade, that also Bart illustrated at the beginning of this meeting. We expect now to have fully set up our commercial structure this year -- by the end of this year to cover for UC. And with that also for the next indication in Crohn's, when this will come. And with that, again, breakeven in product contribution in 2024. So that, combined with the run of the patent exclusivity until 2035, will allow for more than 10 years of positive contribution from the Jyseleca franchise to the company.

With that, I'll give some more color about the ongoing launch in RA first and then in IBD. So the JAK market in Europe, the JAK class has now passed the 20% mark in advanced treatments, still see a lot of anti-TNFs and other biologics, but you see the class developing nicely. And on the right side, I actually see the share of Jyseleca in the dynamic market. So the switch and naïve markets, the patients that actually get the new therapies are the ones that can be accessed. Now growing nicely, you see a combined effect of more countries coming online and then, of course, also the launch being executed and expanding country by country.

From a qualitative perspective, of course, we keep tracking the perception of the drugs of Jyseleca and competitors. We see nicely how the efficacy rate has been growing. And here, you see that compared with the other JAK inhibitors and also the safety where actually, we are top of the class there in terms of safety perception. And of course, that's important as a starting point, while considering the whole PRAC and Article 20 procedure. So that also gives us confidence for the beginning of the year that we will then be able to keep the Jyseleca trend coming up.

Brand awareness, another important factor, is on the high range, the asymptotic, 80%, 90% level. So also that, we accomplished that in the launch phase.

Moving now on the inflammatory bowel disease, IBD, starting, of course, with ulcerative colitis. The landscape is somehow different if compared to RA. We still hear a very strong predominance still of biologics. The market research here showing doesn't show yet Jyseleca. So the 7% of JAK inhibitors come from Xeljanz. And we see with that also still have high level of unmet need in UC. You may say even, possibly larger than in rheumatoid arthritis because of suboptimal remission rates, safety concerns from

the treatments also linked to the still very high level of corticosteroid dependence associated, actually concomitant to treatment with biologics. And complex treatment paradigms were still in UC, still see with biologics, very high induction rates, 6, 7, maybe subcute injections to be done by patients in their first 2 weeks and of course, the complexity of biologics in terms of cold chain. And so orals have not yet been established, and this is a potential for growth for Jyseleca and the orals in UC.

And indeed, if we look at Germany, Germany is important because it was the first country coming say, with reimbursement in November last year. Also, the largest country in Europe. We said in this first month, Jyseleca has already reached 23%, so almost 1/4 of the share in the switch patient population. And I say here, just to point out, this is all advanced treatments, so the share of all advanced treatments, including biologics, so anti-TNFs, integrins, et cetera. So 23% in the switch market, 6% in the naïve already, and that gives an average of almost 15% in the dynamic therapies.

That's been very quick. Also, we've been positively surprised by that quick adoption. But as in the previous slide, there is waiting by gastroenterologists and patients for new treatments here. And the top drivers for prescription here and it has a demonstrated safety profile from the clinical studies, pivotal studies we had, the sustained clinical remission, also with fast onset of action and indeed, steroid-free remission, which is one of also the results that came out of our clinical studies. So that gives us the confidence that we can establish Jyseleca and then without also the class, but Jyseleca first as a new relevant cornerstone in the treatment of ulcerative colitis.

Moving to Crohn's disease. A few words about that. Of course, this is still potential. We are waiting for top line results next year. But you see here the treatment landscape is all biologics, mostly anti-TNF, integrins, IL-12. And there, there is additional potential similar to UC, and you could say, potentially even more.

We start with filgotinib in IBD. We saw the encouraging starting position and have a positive Phase II study. As Walid indicated also, we have approved and launched in ulcerative colitis on neighboring adjacent indication. Unmet needs here, similar to UC, but also very clear here, sustained remission. Patients here get a remission but then cycle very quickly. There are not so many mode of actions approved in Crohn's so a new one, it's important. And of course, there is no oral -- advanced oral treatment that is available for those patients.

In terms of economics, I alluded to that earlier. For us, it means no incremental resources. We have established our franchise in IBD already with UC. And this is another indication to get that can be managed by our teams across all functions together with UC. Also, the prescribers are the same. And with that also, in terms of economics is important, with the potential approval of Crohn's disease, our royalties to Gilead in Europe also will be reduced. And that, of course, will also improve our profitability. So that's a really positive and expecting another additional growth opportunity with Crohn's.

And with that, I would wrap up the session on Jyseleca as well and pass back to Paul.

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***
Well, thank you, Michele. As we come to the conclusion of the presentations, I hope we have been able to give you a good insight on who we are, what we do and how we are changing the company fast forward into a financially sustainable biopharma.

Starting in '99, as I said earlier, with novel mode of actions, reaching a big step on being able to launch our first drug in Europe and Japan. Now building on that with additional indications as we go forward, bringing in oncology as a new portfolio hopefully by 2028 having 5 pivotal late-stage molecules and one cell therapy drug in multiple indications. As I hope it is really our objective to be able to do that, and I hope we have been able to show you that the company is capable of doing great things, and we'll work towards that.

So with that, I would like to thank all the presenters and our key opinion leaders for the contribution and give it to Sofie for kicking off the question and answers. Thank you.

QUESTIONS AND ANSWERS

Sofie Van Gijsel ***Galapagos NV - Head of IR***
(Operator Instructions) Susan, I think there's a question here. Okay, Brian.

Brian Corey Abrahams ***RBC Capital Markets, Research Division - Senior Biotechnology Analyst***
Brian Abrahams from RBC. Can you talk a little bit more about some of the PK dynamics you're seeing for the CAR-T therapy? And then I guess I'm curious to learn more about the higher peak T cell levels. What you think the implications there might be for efficacy, if you are seeing or expecting to see more robust responses there? And then on the safety side, it seems like you're seeing pretty clean safety with the low dose, but just want to understand the long-term implications for safety as well as durability for the unique PK profile.

Tolleiv Trimborn ***CellPoint B.V. - CEO***
I think this is, of course, a very good question. We are very excited about these higher peak levels. And it's a bit too early to tell what the effect will be. And of course, as we set out to -- on this endeavor, we set up this new platform, the key driver was to try to make a better product with some of the key parameters that we changed compared to some of the other, say, companies that use in the early generation one manufacturing processes. So again, shorter, fresh, mild conditions. I didn't touch on that a lot. But good questions. But to be honest, it's very -- yes, of course, in theory, we hope we have made a better product, and this will result in better persistence. Again, we will show data on ASH on the first patients, on the first cohorts, and that will guide you already a little bit better.

Brian Corey Abrahams ***RBC Capital Markets, Research Division - Senior Biotechnology Analyst***
Great. And then maybe just kind of bigger picture along those lines. Obviously, you have a close partner who is a world leader in the cell therapy space. So just wondering to what degree you can or plan to

leverage your partner's capabilities either in terms of moving the cell therapy program into the U.S. and/or perhaps leveraging some of the constructs and programs they might have to be manufactured using your technology?

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***

We are in constant -- can you hear me? Yes. We are in constant discussion and collaboration with Gilead. They were very instrumental in bringing CellPoint and AboundBio on board. For Gilead, this is an opportunity for next-gen CAR-T going forward. And at the same time, they are very collaborative in being able to -- enabling us to go forward. So further news on that later as we go forward, but it has been a very positive collaboration so far on this space.

Peter Verdult ***Citigroup Inc., Research Division - MD***

Peter Verdult, Citi. Just a few quick ones. Maybe just starting with Tol. Are we going to see anything in addition to what we saw in the abstract yesterday at ASH in terms of more patients or a longer duration of follow-up? I know you can't talk to the data, but will there be anything incremental when we actually see that data next month?

Tolleiv Trimborn ***CellPoint B.V. - CEO***

It's about -- I think we will report on the -- what is it? Roughly 10 patients and...

Peter Verdult ***Citigroup Inc., Research Division - MD***

And 28 days follow-up only.

Tolleiv Trimborn ***CellPoint B.V. - CEO***

And yes, some of them have a 6-month follow-up. Like the first one, Tom. But yes, we will report a bit more detail, there will be a poster at ASH.

Sofie Van Gijsel ***Galapagos NV - Head of IR***

Yes.

Peter Verdult ***Citigroup Inc., Research Division - MD***

Okay. And then, John, just wanted to know when you hope to be in the clinic with your first antibody or, whatever, bispecific from the Abound platform.

John Mellors -

So we started working full time on this in March and by the end of next year.

Peter Verdult ***Citigroup Inc., Research Division - MD***

And then lastly for Paul. Just could you characterize the current environment for doing BD in light of what we've seen happen to the sector, rising interest rates? Just what's the environment looking like at the moment?

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***
Yes. It's -- unfortunately, it's a good time for BD as the markets are closed for a lot of companies, and we are -- we get many inbound calls and approaches for collaboration. So it's -- we are continuously evaluating opportunities at this moment, and more to follow as we conclude on them.

Sofie Van Gijsel ***Galapagos NV - Head of IR***
Question from Phil?

Philip M. Nadeau ***Cowen and Company, LLC, Research Division - MD & Senior Research Analyst***
Phil Nadeau, Cowen and Company. Two questions from us, one commercial and one on the pipeline. First, commercial. I know you said that you're satisfied with the PRAC decision for the JAKs. But can you talk more broadly what you think will happen to the JAK market in Europe now post that PRAC decision? Do you think that it will relieve some pressure and there'll be more growth? Or is it likely to shrink the use of the JAKs?

Michele Manto ***Galapagos NV - Chief Commercial Officer & Member of Management Board***
Yes, take that. Thank you. So what we've been observing this year is that many rheumatologists and gastroenterologists have been very resilient in keeping the use of JAKs during the procedure. And if anything, just they believe in the drug and then they also express the intention to make the discrimination between risk patients and then select which patients actually would take a JAK and for which order of patients, then a biologic will still be the better option. There's still great drugs, and they are being used.

So I think the positive situation now with the PRAC is that -- and the change in label that will come is that this will clarify, takeaway doubt, takeaway speculations that Europe would go the FDA way, which is not. And actually, the -- what we've read from the report is that actually, the PRAC is suggesting something which is very similar to what the EULAR and ECCO community have then published and then communicated during summer, which is, again, putting the physician and the patient at the center and let them decide which is the risk and how to use them.

So now very difficult to drop a number and say what will happen with the class as such, but these are the direction that will give confidence that the class will remain as a good therapy option for physicians and with the Jyseleca profile also that we'll stay ahead of that class.

Sofie Van Gijsel ***Galapagos NV - Head of IR***
Okay. Let's take one more question from the room. Sorry, Phil.

Philip M. Nadeau ***Cowen and Company, LLC, Research Division - MD & Senior Research Analyst***
Just a follow-up on the TYK2 pipeline questions. The 2 indications that you've chosen dermatomyositis and SLE have been historically very hard indications to develop any drugs. Can you talk a little bit more about your decision to move forward in those rather than indications where maybe there's been more success historically?

Walid Abi-Saab ***Galapagos NV - Chief Medical Officer & Member of Management Board***

Yes. No. Thank you very much. Look, in this space, we've been monitoring it very carefully. I think it comes as a surprise to us, probably to also many of you, the decision with the FDA to essentially not to include the TYK2 as part of the broad black box warning that they gave the JAKs, judging from the interactions we've had before and the way this division has behaved. But predicting people's behavior is always very difficult.

And as such, this has actually played a key role in us moving forward. I think we took a decision back about a year ago that it would be, honestly, very risky for us to embark on developing a new drug for psoriasis, starting Phase III at a time when there's that risk and overhang. And at this point, considering also the way the market is and so on and so forth, while one can never say never, I think it has, to a great extent, limited the window of opportunity to go into psoriasis.

So when you start looking at other indications, of course, IBD is one big one. And we continue to be very interested in that space. Of course, we're very active in that space, particularly with Jyseleca, as you heard, but we also cannot completely brush aside the failure of deucravacitinib in the proof-of-concept study in ulcerative colitis. So we're still discussing the reasons for that failure with a number of the experts because, again, we don't want to just march into that space.

There are various speculations. It could be a matter of dose. It could be a matter of maybe hitting IL-10, which is kind of protective. But until we have a much better understanding of this, we're still considering it, and we're not yet ready to move.

Having said that, the other 2 indications, we had much better confidence in our likelihood of success. And actually, we will see what will happen with dermatomyositis once we have results, but the data from Ducra in lupus confirms actually our initial plans. And now we're accelerating the path forward.

So that's kind of the rationale of how we thought about it and why we ended up with these 2 lead indications, but we're not closing the doors on additional ones as we better understand our likelihood of success and prioritize our investment in the portfolio across the board, not just immunology, but also oncology, as you heard.

Sofie Van Gijsel ***Galapagos NV - Head of IR***

Thanks, Walid. Operator, can we open the line for questions, please?

Operator

(Operator Instructions) Our first question comes from the line of Dane Leone from Raymond James.

Dane Vincent Leone ***Raymond James & Associates, Inc., Research Division - MD & Biotechnology Analyst***

Apologies for not being able to be there in person. Maybe, Paul, you could just take us through your

journey since April of evaluating the organization really from top to bottom and making the decisions on strategy that led you to think about allocating significant resources to transition to more of a cell therapy-based organization in oncology versus the long history of immunology and inflammatory research work that you highlighted Galapagos was founded on. The reason I ask that is a lot of us had, I guess, probably hoped that there was a significant compound library available to maybe be harvested for more development work that had already existed at the organization. But at least from the presentation so far today, it seems like that might not be the case. And as you said, going forward, the organization would be more focused on development and possibly external asset acquisition versus homegrown novel identification.

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***

So thank you for the question. Let me clarify that. It's not at all that we discard the whole past. We still have a very strong small molecule research organization focused on immunology, and now also will focus on oncology. And we are in the middle of reshaping that as part of our strategy. And in the next review, we'll definitely come back on that. There is a great compound library. There's great capabilities in the company to harness that, and we don't throw that away. We will build on that.

What we first wanted to show today is that we want to accelerate our pipeline with assets in immunology, which we can -- where we can see the value in the really near future. Second, fibrosis and kidney, as we evaluated that with the team, was a very long path to success and a very high risk path with very limited biomarker and early derisking. And as a company of this size, and now in commercial, we absolutely wanted to make sure we had a certain number of drugs coming in before the end of the decade to grow the compound.

If you then move into oncology, then my experience -- my previous life with CAR-T and Carvykti was like, Wow!, this is transformational immunotherapy. Can we do something transformational in Galapagos? And then looking at, yes, we can because with decentralized manufacturing existing targets and in the future, new targets, we could very quickly build out a portfolio in oncology in a different shaped way than a large pharma company would do.

And so by bringing CellPoint in -- already in June in the early days, combined with Abound, we acquired the people, the capabilities and portfolio to be able to accelerate. It was a huge motivation for the whole company to enter the oncology space with people already entering into a clinical trial where the first patient walked in was Tom, and you have like a result in your oncology.

And so before going to a big change in the company, you have to balance what you break down, what you do not do any more and what you build on. And I think the whole story is working out really well with the results we see in CellPoint and what we now have been able to do with the portfolio, streamlining the portfolio, the good success with the PRAC, the TYK2, all of that now works out as a strong portfolio for the near future. So that's the short and the long of how we went through it. And I found a very strong organization, very dynamic, very entrepreneurial, and I'm happy to be back in Europe, back home with a fantastic team.

Sofie Van Gijsel ***Galapagos NV - Head of IR***
So thanks. Maybe a second question from the phone.

Operator
The next question comes from the line of Jeroen Van den Bossche from KBC Securities.

Jeroen Van den Bossche ***KBC Securities NV, Research Division - Financial Analyst***
Maybe a dual question here. I apologize, but I'll try to keep it very short. First, can you elaborate a little bit more on the choice of going after axial spondyloarthritis for filgotinib how did you come to that decision? It also being already quite, let's say, busy area. How does it look from the small molecules point of view? To be honest, I'm not 100% aware of it.

And then as a follow-up, yes, at the end of the day, you're building now a company in immunology and oncology. You're going after biologicals, small molecules, CAR-T. Those are all very different indications and very different styles of sales. How is that going to work? How do you see the organization develop its sales team? And is that going to be more expensive than, let's say, more close areas for an earlier-stage company as Galapagos kind of is?

Walid Abi-Saab ***Galapagos NV - Chief Medical Officer & Member of Management Board***
I'm going to start with the choice of indication, and I'll pass it on to Michele, because, again, it was a joint effort between R&D and Commercial to decide what is the next step for Jyseleca. We clearly had good data in 2 indications where we had a clear proof of concept, ankylosing spondylitis. And as a result, axial spondyloarthritis and also in psoriatic arthritis. And when we evaluated our potential going forward and the unmet medical need and looked at the competitive environment, we believe that in axial spondyloarthritis, we had a much better chance of success. And maybe I'll turn it to you, Michele, to address this point further.

Michele Manto ***Galapagos NV - Chief Commercial Officer & Member of Management Board***
Yes. So in axial spondyloarthritis, there are similar elements of unmet need as actually we'd see more in the IBD scene, right? So a more limited number of mode of actions. And actually, so the opportunity for also orals to bring additional options for patients. Also -- well, we -- it was a recurring theme from our interaction actually with rheumatologists that during the launch of RA, when are you coming with axial SpA? Why are you not coming with axial SpA? And that's actually, so it was a decision that we've taken now after we have the proprietary rights for that for Europe. And I think actually, it's very -- it's a very important fact, we found a way to run a study for approval in Europe at the moment that way.

Also, our operational capabilities allow us to launch in axial SpA, when the time will come very effectively, leveraging our resources and teams that we have for RA in a similar way that, of course, we can leverage the resources for UC.

I mean for your second question, I wasn't sure if I got it correctly. So it was about the actual use of

resources for -- across immunology and oncology. Yes, I alluded to that in my presentation. So there is a core -- sorry.

Jeroen Van den Bossche ***KBC Securities NV, Research Division - Financial Analyst***
I'm mostly interested in how you're going to build synergies between those people because they do seem quite far apart.

Michele Manto ***Galapagos NV - Chief Commercial Officer & Member of Management Board***
Yes, indeed. So I would say I would distinguish 3 kind of categories of resources. So the headquarter international strategic part, that's normally a more compact team. That -- well, we have already people who have worked both in oncology and immunology inflammation that can also pivot from one to the other, and definitely we'll hire some experts the way we've done in inflammation.

Looking at the countries, there are core capabilities, which are, say, the office base, I would say, the central in the countries like especially market access and also core or Medical Affairs there, the whole infrastructure that we'll be able to leverage. And then there are some specific roles, which are the roles of, you could say, the customer-facing, the NSLs, the sales team and then for the Cocoon, we'll see how that also will connect with the Lonza teams. But that part will not be, say, shared with the inflammation, but that part also is very small. That tends to be very small.

We've seen that we have, like, few centers per country. So that we can cover with the little teams at a totally different scale, different order of magnitude, smaller from what you need in specialty care for, say, rheumatology and gastroenterology.

So in summary, we'll have synergies where it comes more in the central roles. And when it's a more diffused area, we'll have very small teams to cover the oncology part.

Sofie Van Gijsel ***Galapagos NV - Head of IR***
Let's move back to the room for a couple of questions. Sebastiaan, I think you have a question.

Sebastiaan van der Schoot -
Sebastiaan from Kempen. It appears to me that the success of the CAR-T strategy highly depends on the reproducibility of the Cocoon system across different clinical sites. Can you maybe expand on how many clinical sites you will have during the pivotal trials? Can you also maybe give an indication on what you expect that the different regulators will demand in terms of efficacy, endpoints and the time of follow-up? And then can you also speak to the differences that the EMA and the FDA want?

And then also maybe a question for John. I'm just wondering -- you also mentioned CAR-Ts in the solid space that you want to go into in that space. Can you maybe speak to the -- what the current hurdles are in that space and how you plan to circumvent those?

Tolleiv Trimborn ***CellPoint B.V. - CEO***

Maybe I'll start here. So good question. So as I said, we are ramping up now for the expansion phase to have at least 20, 25 sites up and running and then building on that. So in the beginning, on purpose together with Lonza, I decided to not -- to make sure that the quality of all the sites is really high, carefully selected them. And now where everything is set up, our training has gone up. We've boosted that level up. So we'll be opening up at least 10, 15 sites next year and build on that to -- in a commercial stage, at least have 20 to 30 sites in Europe and 20 to 30 sites in the U.S. And then again, it's very scalable, starts to do really well. For example, Ohio treats 400 patients every year. Relatively easy if Lonza has the tree -- to put a tree there instead of 5 individual Cocoons.

For us, quality is most important. With the 20 to 30 sites during expansion at the beginning of pivotal. We can treat a lot of patients. You simply multiply it by 30 to 40. So typically, in a pivotal stage, you need to treat 100, maybe 150 additional patients.

So -- and coming back to that question, there is a little bit of difference between EU and the FDA requirements. We're filing the IND now. We have already had discussions with the FDA. We can be -- currently, we cannot answer the question in -- we first have to await the data of the Phase I and the early expansion cohorts to actually enter into a little bit -- into the next level of discussions with the authorities, how a design of a pivotal would look like.

But clearly, if you do the analysis, you can see how others have done it. So it's quite straightforward. Typically, up to 30, 40 patients in the early stages, then a pivotal of roughly 100, 120 patients.

John Mellors -

Thanks for the question. We could spend a couple of hours talking about this. Before I get to solid tumors, we aim to improve durability of response in hematologic malignancy. That's our first goal.

In terms of solid tumors, there's SSPP, okay? Specificity of the target for tumor versus host. That's essential because off-target toxicity is very difficult to manage and could be lethal. Sensitivity. We want to be able and we're able to design CARs that detect very few molecules of the target on a cell. So balancing specificity and sensitivity is key. Penetration of the cells into the solid tumor is a major challenge. There are physical barriers to that, and we aim to overcome that. And probably the most important barrier today is preservation of function once they penetrate, and there are various things we can talk about how to do that. The major initial one is prevent shutdown or exhaustion of the T cell. So we rev it up, ready to go, gets into the body, goes where it's supposed to. The door is not open. We need to open the door, get it in and not have anybody else slam on the brakes. And there are various players that try to slam on the brakes.

The reason the solid tumor is successful, creating its own niche, is it -- is an immune sanctuary, right? And we need to break that down and there are various approaches to do that. We favor some over others.

Sofie Van Gijsel *Galapagos NV - Head of IR*

I think you had another question from Jason.

Jason Matthew Gerberry ***BofA Securities, Research Division - MD in US Equity Research***
Jason Gerberry from Bank of America. Paul, a question for you. You had a front row seat really to the challenges that Carvyckti faced scaling up. And so I'm just curious if you can speak to the point of sight model and how that perhaps is free and clear of some of the challenges that the traditional CAR-T approaches have had or are facing in terms of scaling up. And then as we think about the value proposition of this -- sort of point of sight model, is it greater in certain geographies than others?

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***
Well, first, on all the first-generation CAR-Ts, people had a discovery process, which they put into an upscaling process, which people put into a manufacturing process, which was multistep, multi-quality control, and therefore, a lot of handling in the labs as well as sending the cells in and sending them back with cryo preservation. So long process, cumbersome.

Now some companies have been able already to upscale well and have got a lot of efficiency, but the capacity is limited by the size of the buildings and the number of the people you have in those buildings in the large companies who do it today. So what the point of care and so the Cocoon can do is instead of the -- of doing this step-by-step, reengineer the whole process into one continuous process in a fully sterile environment, which takes out the -- a lot of manual handling as well as a separate instrument, which does it all, which you can put -- as was evidenced by TOL and the team, you can put in different hospitals. That takes away building buildings, having a large number of people recruited and the whole logistics. And that's why we think and we are convinced that the scalability of the Cocoon is really significant as you can bring it to the hospitals in all parts of the world.

Of course, in certain countries, you have good -- like in the U.S., you have good distribution and for CAR-T sending around. So it will stay next to each other, the central manufacturing and the decentralized manufacturing. Where it will be a difference is also in the rest of the world. If you go to the whole of South America, the whole of Asia or the Middle East and other countries, there's very limited access today, while there is as many -- as much need as in the West. And therefore, we'll see how it goes, but the process, the Cocoon is absolutely adapted to the fact that it could go in different countries, and we can build on that. So it's a, yes, next-generation process, which was not inhibited by the old thinking on step-by-step, reengineered the process and had the right tool to do it in an integrated way. That is a short and the long of it.

Sofie Van Gijsel ***Galapagos NV - Head of IR***
Thank you. So a question from Matthew, and I will go back to the phone line.

Matthew Kelsey Harrison ***Morgan Stanley, Research Division - Executive Director***
Okay. Great. Matthew Harrison, Morgan Stanley. I guess 2 for me. So one, Walid, just on SIK. I guess it wasn't entirely clear to me. It sounds like you're hoping to achieve proof of concept in RA, but then you'll go back and look for another compound with better qualities to potentially move it ahead. And I guess

the same thing on SIK2/3 targeting. Any sense for where those compounds are preclinically at least?

And then the second one is just for Bart. As we think about sort of the bridge to 2028 as you're thinking about spend, I guess one of the questions I get a lot is just if you -- I mean -- I guess the real question is, I mean, are those the parameters that you would expect to be in, in terms of not really -- having a little bit of flex on R&D, but not a tremendous amount of flex on R&D? Or is there a reason where you would flex R&D pretty dramatically and ramp up the spend somewhat significantly versus where you are?

Walid Abi-Saab ***Galapagos NV - Chief Medical Officer & Member of Management Board***
All right. Thanks, Matthew. So look, I think -- as you know, the company over the past 12 to 18 months has gone into a sort of self-reflecting period, and the salt-inducible kinase has been a major program with us that we had to reevaluate our investment there and the speed with which we're bringing molecules and why they're failing in the clinic.

I'll spare you all the details. We can discuss it offline if you want. But the bottom line is that what's very clear to us is there are some inherent criteria that we need to improve about the compounds themselves, I'm talking like simple things such as a better therapeutic index, no drug-drug liability, no QT liability, no cardiovascular risk, those elements, which are inherent to the molecule itself and not the target, but there are also certain learnings that we got about the targets and where are challenges in development.

So we decided, and I think you've seen the evolution of our portfolio, that a number of the molecules that we had already in there as potential to move in the clinic when we apply these new set of criteria and really set ourselves the higher standards to move forward so that they don't crash after Phase I, a lot of them actually fell out. And then we need to come up with better molecules. So we're faced with the decision.

So you wait until the next molecule comes, which could take another year or 2, or actually, you test the hypothesis with a molecule, which actually can test the hypothesis. And you can never say never because depending on the result, it's all a risk-benefit assessment that we need to make. But it's important for us to say that '4399, there are some liabilities that it has. I will mention potential drug-drug interaction that will make it less likely to be able to be successful to move forward. But all of this will have to be evaluated at the end of the proof of concept.

Having said that, we believe that the proof of concept will generate extremely important data to test some of the fundamental hypothesis that we've been working on and moving medications -- compounds from discovery into development. And if we are on the wrong path, then this will have a major implication for the whole platform. And therefore, it will teach us tremendously. And potentially, if we're heading the wrong path, it might be time to say, okay, stop it, guys. We're not going to continue here. Because up until now, we've kept on investing a lot without having the benefit of the return and learning. And now we did. Time out. Let's do a check.

So it's very important that our investments right now are targeted. We're not just marching as we've done before and throwing everything at it, including the kitchen sink. Actually, we're taking a measured approach to do that. So I hope this addresses your question.

Bart Filius ***Galapagos NV - President, COO & Member of Management Board***

Let me take the second part of the question in terms of R&D spend. Maybe distinguish, Matthew, between, let's say, what I showed on 2024 as opposed to 2028. Obviously, if you're looking at the shorter term, 2024, let's say, any variances compared to what I was showing should be rather moderated. The one caveat that I would put on the table is that if there's business development, things can be different, right? If you do an acquisition, and that acquisition comes with a good investment case that will come on top, we will not be necessarily able to then completely replace that from the existing envelope. But indeed, in the shorter term, the R&D spend should be in the range of what I was showing.

When you go to 2028, it becomes very difficult to predict. I think that was more symbolical of, I think, where the company is going. If we have a chance to get the cash from Jyseleca in, I think it will significantly help us to fund our R&D operations. But let's see where we are by that time in terms numbers of the pivotals and in terms of the numbers of molecules in the pipeline to define the precise burn in 2028.

Sofie Van Gijsel ***Galapagos NV - Head of IR***

Thanks. Operator, can we have a question from the line, please?

Operator

Our next question comes from the line of Emily Field from Barclays.

Emily Field ***Barclays Bank PLC, Research Division - Research Analyst***

Sorry, I couldn't be there today. Just 2 questions from me. The first thing, I know you mentioned the string of pearls earlier, that's a strategy that's worked for a number of companies in the past. I was just wondering if you could give any more details perhaps on the length of the string or the size of the pearls, i.e., sort of what size deals would be a right fit? And how many do you think of them you could take on given this new movement into cell therapies, the company has got a lot going on?

And then secondly, just on the BCMA CAR-T, assuming success in the CD19 efforts, could that have a faster speed to market? Would you have to bring on a lot of incremental sites and capacity to move that forward? Just kind of thinking about that in context of being behind the CD19.

Bart Filius ***Galapagos NV - President, COO & Member of Management Board***

Yes. Thanks, Emily. Let me take -- Emily, thanks for the question. Let me take the first one on business development. I think what I heard you ask was to give a little bit more feeling to what the size of any type of BD could be. Look, what we tried to signal, I think, is that we are not intending to come out with a suddenly multibillion dollar acquisition. That's not in the books. It's not the way we want to build the company. We think and Paul called it the string of pearls approach, we think it's much more sensible to

add selected assets to our pipeline. This can be through M&A as well as through licensing, but we will do it on a measured skill, i.e., this is on really the sub EUR 1 billion level in terms of cash layout. And we'll be very, very careful in doing so.

Cash is an extremely important asset for the company. Let me emphasize that one more time. Even if the market for BD currently is good, if you're on the acquisition side, we still want to make sure we get good value for money here, both scientifically and in terms of financial investments. So maybe for the CD19 speed to market, can you take that one, Paul?

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***

Well, I think the BCMA -- was the question on will that be able to go faster. Once the center is accredited and validated for making the CAR-T for the CD19, it's easy to add new CAR-Ts -- to new Cocoons to facilitate additional clinical trials. So it will definitely benefit the speed of being able to do new studies, we'll benefit from the fact that we have the front run of CD19 now paving the way in different countries with the regulators as well as in all the hospitals. So we hope that, that will be a smooth and fast pathway for BCMA.

Sofie Van Gijsel ***Galapagos NV - Head of IR***

Thanks. I'm just checking if there are more questions in the room. Then I think we're good to go. So our next financial call is on February 24, 2023. I would kindly invite you - Tirza, maybe you can stand up and wave. So Tirza of the CellPoint team joined to showcase the CellPoint machine, the Cocoon. So please, by all means, go have a look, it should be fun. We did a lot of effort to get it here. So please go and check it out. Thanks very much, everyone.

Paul Stoffels ***Galapagos NV - CEO, Chairman & Member of Management Board***

Thank you.
