Novartis AG

Novartis AG, PTC Therapeutics, Inc. - M&A Call

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Matthew Klein, Pierre Gravier

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Tiago Fauth, Kristen Kluska, Lee Hung, Brian Abrahams, Eliana Merle, Joel Beatty, Joseph Thome, Huidong Wang, Samantha Corwin, Kyuwon Choi, Danielle Brill, Tazeen Ahmad

Operator Operator

Good day, and thank you for standing by. Welcome to the PTC518 Collaboration Agreement Call. [Operator Instructions] Please be advised that today's conference is being recorded.

I would now like to hand the conference over to your speaker today, Dr. Matthew Klein, Chief Executive Officer. Please go ahead.

Matthew Klein Executive

Thank you all for joining the call this morning to discuss PTC's new collaboration with Novartis. As today's call will include forward-looking statements, I refer you to the slide posted on our Investor Relations website in conjunction with this call, which contains information about our forward-looking statements as well as our Risk Factors section in our most recent Form 10-K filed with the SEC. We are very excited to be working with Novartis on the PTC518 program and believe this global collaboration agreement will accelerate the advancement of PTC518 for Huntington's disease patients worldwide.

As detailed in the press release, Novartis will assume PTC518 global development, manufacturing and commercial responsibilities following completion of the placebo-controlled portion of the ongoing PIVOT-HD study, which we expect to be in the first half of 2025. As part of this agreement, PTC will receive $1 billion in cash once the deal closes and be eligible to receive up to $1.9 billion in development and sales milestones. In addition, PTC and Novartis will share profits in the U.S. with a 40-60 split, 40% for PTC, 60% for Novartis. And on ex-U.S.

sales, PTC will receive double-digit tiered royalties.

The economics of this deal are quite significant. This is one of the largest Phase IIa licensing deals of which we are aware. The economic terms are commensurate with the promise of PTC518 as potentially being the first approved disease-modifying therapy for HD. Importantly, PTC will continue to have an important role in the PTC518 development program even after completion of the PIVOT-HD trial, given our expertise in developing small molecule splicing therapies as well as our expertise in HD. Now a word on how we got to this agreement.

PTC518 has long attracted the interest of the pharma community given its best-in-class profile and success of Evrysdi.

Following the interim PIVOT-HD data readout in June 2024, PTC was approached with an unsolicited bid for the program. We decided that we would run a formal process to determine if there was a potential partner we felt could bring more muscle to the development and commercialization of PTC518 and could provide deal economics that were consistent with the strong potential of PTC518. Specifically, we wanted any deal to include a significant upfront payment as well as provide ability to share meaningfully in the upside if development is successful.

This was a highly competitive process with several parties involved, and it became clear through the process that Novartis fulfilled the 2 key deal criteria and shared our goal of dedicating appropriate resources and experience to advancing PTC518 for the Huntington's disease community. PTC will continue to oversee the conduct of the placebo-controlled portion of PIVOT-HD and will take the lead on the planned regulatory interactions with FDA later this month as the deal will not be finalized until completing HSR review, which we expect will be in Q1 2025.

In terms of use of proceeds from this transaction, we plan to use these funds to continue to expand our leading and unparalleled splicing platform, including leveraging our new PTSeek discovery engine, which can accelerate identification of promising target splicing molecule candidates. In addition, we have several splicing and other therapies at clinical or late preclinical stage that we look forward to advancing. We will detail these programs more in the near future. We will also continue our business development efforts working to identify promising therapies that can complement our existing commercial and development portfolios.

Lastly, I want to share how proud I am of all the PTC team members whose contributions enabled this important agreement from our scientists who have worked for decades, pioneering the discovery and development of oral small molecule splicing therapies to our development teams that have overseen the PTC518 clinical studies and to our finance and legal teams who helped get this agreement across the finish line. We look forward to continuing to work with Novartis to achieve the critically important objective of delivering a safe and effective therapy to the hundreds of thousands of patients worldwide affected by Huntington's disease.

I will now turn the call over to the operator for questions. Operator?

Operator Operator

[Operator Instructions] Our first question comes from the line of Tiago Fauth with Wells Fargo Securities.

Tiago Fauth Analyst

Congrats on the deal. Just 2 for me real quick. Just wondering what sort of data was available for the parties that were part of the process? Was it just a June 2024 update or something else since? And you did mention that Novartis is going to be involved in regulatory interactions upcoming, but I'm assuming the deal is not conditional in any way, shape or form on the outcome of that.

Is that correct?

Matthew Klein Executive

Thanks for the questions, Tiago. Let me take your second one first. No, there is no contingencies in this deal based on the regulatory interactions. This is a collaboration to take this drug forward through the entire development process and commercialization process, whether that's through an accelerated pathway or not accelerated pathway. In terms of the data that were reviewed as part of this deal, the vast majority of the data were what was shared publicly in the 2024 June data announcement.

Operator Operator

Our next question comes from the line of Kristen Kluska with Cantor Fitzgerald.

Kristen Kluska Analyst

Congrats on the great deal. And I think bigger picture, a testament to your team with now 2 $1 billion upfront cash deals with this platform in the last 13 months. So maybe just on that note, you said that you're going to use some of the cash to look at this platform in more detail. With the success you've seen from Evrysdi as well as 518 now, how are you thinking about looking at potential other strategies with this platform?

Matthew Klein Executive

Kristen, thanks so much for the question. There's no question these deals continue to validate how PTC has pioneered small molecule splicing therapies and really have an unparalleled experience and track record in that regard. We continue to do our splicing work and our teams are, of course, learning along the way, and we have made a number of additional insights. I mentioned our PTSeek discovery engine, which is going to allow us to continue to develop -- discover and develop important splicing therapies that would be important not only for things that we at PTC would look to develop, but also could be the source of future strategic partnerships.

Splicing represents an incredibly innovative approach to drug development, and we believe that the splicing approach could lead to a number of important therapies for all different indications, including those core to PTC as well as those that might be core to other companies. So we look forward to continuing to build this platform and leveraging its unique capabilities to deliver meaningful oral therapies for high unmet medical needs.

Kristen Kluska Analyst

And then obviously, you guys are pros at meeting with the FDA, especially this year with all of the approvals and ongoing applications. But just given Novartis' willingness to work with you on this pathway, curious if they gave you any good insights or suggestions as it relates to the upcoming Type C meeting? Will they physically be in attendance with you at this meeting?

Matthew Klein Executive

Yes. So just from a technical point, the deal can't close isn't official until the HSR clearance, which won't occur to the first quarter. But let's just say, big picture, one of the important aspects of this deal was the Novartis experience and successful track record in the development and commercialization of neuroscience therapies. That was a really important part of this deal for us, and they obviously have experience in Huntington's disease development as well. So we look forward to their collaboration and partnership in every aspect of getting PTC518 forward.

Operator Operator

Our next question comes from the line of Jeff Hung with Morgan Stanley.

Lee Hung Analyst

Congratulations. How does the $1.9 billion in milestones split out between development, regulatory and sales? And then for the tiered double-digit royalties on ex U.S. net sales, how many tiers are there? And how are those tiers triggered -- like are they triggered by cumulative sales?

Or do they reset on an annual basis?

Pierre Gravier Executive

Yes. Thank you for the question. So I would say for the milestones, they are equally weighted between development and sales. And then it's double-digit tier royalties and it's based on net sales, they reset every year.

Operator Operator

Our next question comes from the line of Brian Abrahams with RBC Capital Markets.

Brian Abrahams Analyst

Congrats on the deal. Can you talk a little bit more about like your expected next steps beyond PIVOT-HD, I guess, what Novartis will be running when they take over development of the program? And then I guess along those lines, how will the development decisions get made in the future? You mentioned PTC is still going to have an important role. Can you talk a little bit about, I guess, the types of committees that will be involved there and how future data disclosures will be handled as well?

Matthew Klein Executive

Thanks for the question, Brian. So we -- PIVOT-HD, as everyone is aware, is a 12-month

placebo-controlled study that then has an open-label extension portion in which patients will roll over and allow us to continue to understand the long-term safety biomarker and clinical effect. And so that study is going to continue to run.

But of course, now efforts will shift towards the design and preparations for an efficacy trial. And as we've talked about, that would be a Phase III trial that could be a registration trial in the context of a standard approval pathway or a confirmatory trial if we were able to avail ourselves of the accelerated pathway. So those are the key components of the development plan. And of course, there'll be future strategies about how we can think about making PTC518 available for the full spectrum of HD patients, including earlier stage presymptomatic patients. So those all remain a part of the future development of the program.

In terms of how development will be handled, there will be a joint development committee that will include members of both PTC and Novartis. And again, a really important part of the decision to enter into this collaboration with Novartis was their experience in HD, the collaborative nature of their team, their strong, strong commitment from Vas the CEO throughout the organization to work as hard as possible and bring the resources necessary to get a therapy forward for patients with Huntington's disease. So we really look forward to this being a true collaboration where each team can leverage each other's expertise in an effort to accelerate the development of this therapy for HD patients.

Operator Operator

Our next question comes from the line of Ellie Merle with UBS.

Eliana Merle Analyst

Congratulations on the deal. Just curious in terms of the timing. I guess just what's the latest in terms of when you plan to meet with the FDA around accelerated approval or pathway in Huntington's? And I guess, did that meeting happen already? I guess just given the timing of the deal here, what's your latest in terms of like your expectations around the likelihood of an accelerated approval pathway with mutant Huntington's as a surrogate?

And then I have a follow-up question.

Matthew Klein Executive

Thanks for the question, Ellie. So this agreement was not related at all to the timing of the FDA meeting nor to our belief -- our strong belief in the potential for Huntington lowering to serve as a surrogate endpoint in Huntington's disease. The timing here was about making sure that we had the partnership in place as we start thinking about that efficacy trial, which we have to start working on as soon as possible. And just to be clear, the FDA meeting has not occurred yet. It will occur later in the month.

Eliana Merle Analyst

Great. And just a follow-up to Brian's question. Just if you can give us more detail around sort of your conversations with Novartis, I guess, what the latest you're thinking in terms of what a Phase III design could look like? I mean, whether that's for confirmatory or for initial approval, just any more details on those conversations and the Phase III thinking there?

Matthew Klein Executive

Yes. I think the teams are fairly aligned in how we're thinking about the trial, the need for there to be a longer placebo-controlled phase and endpoint strategy that would include the key known established outcome measurements for HD patients. Of course, one of the components of the FDA discussions later this month in addition to discussion of the potential for Huntington lowering to serve as a potential surrogate endpoint in the context of an accelerated pathway is to have alignment with the agency on how we're thinking about endpoint strategy for that efficacy trial.

Operator Operator

Our next question comes from the line of Joel Beatty with Baird.

Joel Beatty Analyst

Congrats on the deal. The first question is, what do you hope to see in the PIVOT-HD readout coming in the first half of next year? And then a second question is, what are your plans for this additional cash that you've got with the $1 billion upfront today and as well as the recent sale of the voucher?

Matthew Klein Executive

Thanks for the questions, Joel. So the key for PIVOT-HD as it has been, as we look at the 12-month data in a larger group of patients is to continue to see what we have observed to date in the first 30 patients, which is evidence of durable peripheral huntingtin lowering, that continued evidence of lowering of CSF huntingtin protein levels. And again, one of the key findings was that consistency in the magnitude of dose-dependent lowering we saw in the blood and in the CSF.

And then, of course, also beginning to understand the signal on the clinical scale. I think we were quite excited to see the evidence of dose-dependent benefit on the TMS as well as the cUHDRS. And now with more patients, it will be important to see if those trends hold. And then, of course, finally, the evidence of continued safety and tolerability, which has been a really important part of the PTC518 story that we've been able to deliver these biomarker effects in early signals of clinical effect in the context of a favorable safety and tolerability profile. In terms of cash proceeds, Peter, do you want to comment on how we're thinking about that?

Pierre Gravier Executive

Yes, absolutely. I mean there will be a number of prongs. One, we'll keep on developing, obviously, our commercial -- we're preparing for our commercial launch next year and developing our internal assets. We talked about our splicing platform and PTSeek, where we believe we have a number of unique molecules that we can bring forward. And finally, we will continue to assess BD opportunities and complement our commercial portfolio as well as our development pipeline.

Operator Operator

Our next question comes from the line of Joseph Thome with TD Cowen.

Joseph Thome Analyst

Maybe first one, even going back to the prior management team, the company had indicated that it did want to kind of keep whole rights to PTC518 given the experience with risdiplam. Maybe can you talk a little bit about just what changed in the management thought process there? And then second, do you have any follow-on compounds for Huntington's that you're working on in the splicing platform? Are you limited in what you can pursue there? And does Novartis have access to these follow-on compounds if they exist as well?

Matthew Klein Executive

Joe, thanks for the question. I think what we've said, at least what this current management team has said is that we believe that we have the team and the resources to be able to take PTC518 forward through development and to commercialize it. This collaboration agreement is really about seeing an opportunity to bring more muscle to those efforts. and not only enhance the probability of successful development and commercialization, but also accelerate those processes.

And we're talking about a placebo-controlled trial that's likely to have hundreds of patients and perhaps hundreds of study sites and a very large potential global HD population that needs to be -- that's going to need access to a therapy if it's approved. So this is really a matter of seeing an opportunity to accelerate both the development and commercial prospects for the therapy. In terms of your second question, this is a deal that really focused on PTC518 and related compounds that are splicing agents that are -- have a mechanism of Huntington lowering.

So this was exclusively about our splicing platform and Huntington lowering as the target. PTC does have other preclinical HD programs, including splicing programs looking at other Huntington's disease targets outside of Huntington lowering that we are continuing to work on and look forward to continuing to advance.

Operator Operator

Our next question comes from the line of Gena Wang with Barclays.

Huidong Wang Analyst

Also add my congrats. That's a great deal. So I have 2 questions. One is, is it fair to say that the base assumption for the Huntington program from the Novartis side to moving forward is based on the Phase III functional approval path. And also did the Novartis see like additional 3 more months data since last June.

I think someone already asked the question, but just wanted to ask again. And then regarding the deal term, the royalty, double-digit royalty, is it fair to assume like low teens to mid-20s range, like what we usually see in other deals? And regarding the profit sharing in the U.S., 40% 60%, will you need to share also the development cost, for example, if moving forward post PIVOT-HD, if there is a Phase III study ongoing, will you need to share also 40% there?

Matthew Klein Executive

Gena, thanks for the questions. I'll take the first 2, and then I'll turn it over to Pierre for the last 2. So your first question was about the assumptions of the development program for PTC518. I think what's clear is that this is a collaboration for the entirety of the program. Obviously, both teams, the PTC and Novartis team will look to see if we can leverage the accelerated approval pathway.

And if not, there's obviously the teams are in place and ready to move forward as we talked about with that efficacy trial that would support a standard approval.

So I think this is a commitment to bring this program forward with whichever pathway can be leveraged to get this therapy to patients faster. As I mentioned earlier, in terms of the data shared, the data were -- the bulk of the data were the clinical data shared in the June 2024 data disclosure. There are obviously additional questions on some of the preclinical data, mechanistic data and other types of things, of course, anyone who is going to be collaborating on this program would want to see.

Pierre Gravier Executive

In terms of the economics, I would say a few things. The royalty, you can assume that they are similar to other deals. And then on the profit sharing and the 40%, 60% in the U.S., development cost after PIVOT-HD will be 100% for Novartis.

Operator Operator

Our next question comes from the line of Sami Corwin with William Blair.

Samantha Corwin Analyst

Congrats on the deal. I guess, what are your thoughts about the best case scenario would be for the pivotal trial design? And do you think it will take multiple interactions with FDA to have clarity on what that design might look like? And do you think it's possible that you would have insight into what the trial design would look like before the data update in 2025?

Matthew Klein Executive

Thanks, Sami, for the questions. Look, I don't know if there's a best case scenario around study design. I think that this is a fairly -- it's fairly clear this is going to have to be a placebo-controlled trial of sufficient length to allow us to detect a meaningful clinical effect and we've said in the past that we believe that would be at least 2 years. And in terms of endpoint alignment look, I think there's a finite set of efficacy endpoints that are well understood and validated for HD patients.

So I think we're not dealing with a situation where we have to invent the wheel here. So I think it's really a matter of alignment with the agency on what they would accept in terms of a light designation of primary and key secondary endpoints that together could provide the evidence of effectiveness on how patients feel or function in everyday life, which is there, what the FDA likes to understand in terms of gaining an approval. I think we'll have the first discussions in December, and I think we'll have a better idea of what additional discussions

could be needed following the completion of those discussions. But again, I think there's a lot already known about how to go about designing that Phase III trial.

Samantha Corwin Analyst

Got you. And does the $1 billion upfront payment change your estimated time line becoming a cash flow breakeven at all?

Matthew Klein Executive

I think, look, I think what it does is it reinforces our confidence that we have the funds we need to get to the cash flow breakeven. That remains a key priority for the company. We have a number of important regulatory milestones to come over the next few months that I think will help define that time line for reaching the cash flow breakeven, but we've said it's in the not-too-distant future and certainly will be accelerated by favorable regulatory decisions in the coming months.

Operator Operator

Our next question comes from the line of Paul Choi with Goldman Sachs.

Kyuwon Choi Analyst

Let me add my congratulations on the deal, nicely done. My first question is with regard to ex-U.S. development and I think the European clinical trials registry is currently only listing the 5-milligram and the 20-milligram doses. Can you maybe just comment on the status of the 10-milligram cohort and what's going on with regard to international development? And my second question is for your plan to update on the PIVOT-HD trial next year.

Can you just confirm that the 20 mg dose cohort is fully enrolled and that you'll have both Huntington biomarker data and TMS clinical data endpoints when you report that update.

Matthew Klein Executive

For the question, Paul. Just to clarify, as we said all along, the only 2 doses that are in development are 5 milligrams and 10 milligrams. Those are the only 2 that are being studied in addition to the placebo subjects in PIVOT-HD. There has not been nor as they're currently a plan to initiate the 20-milligram dosing cohort. So the data that we read out following the completion of the 12-month portion of PIVOT-HD will be from the 5, 10-milligram and placebo cohorts.

As we mentioned, we expect last patient last visit to be in the first quarter, and that means that we will likely have the data readout in the second quarter.

Operator Operator

Our next question comes from the line of Danielle Brill with Raymond James.

Danielle Brill Analyst

Let me extend my congrats as well on a great deal here. And just a quick one, Matt. You said the deal is highly competitive in your prepared remarks. I'm curious if you could elaborate on

how many parties were interested.

Matthew Klein Executive

Yes. Thanks for the question, Danielle. Look, obviously, it was a confidential process. Let's just say there was interest from a number of parties, which is not surprising given the promise of the therapy. This included pharma companies that have worked in HD and others that had not worked in HD that we're interested in getting into the field.

Operator Operator

Our next question comes from the line of Tazeen Ahmad with Bank of America.

Tazeen Ahmad Analyst

Congrats from me on the deal terms. I was just curious, Matt, as to how you're thinking about time lines. You talked about the specific reasons why you're excited about Novartis coming on board. And it seems like a lot of that is with regards to the potential for commercial opportunity. How are you thinking about the potential for narrow time lines, let's say that you don't get an accelerated path to approval and you have do a traditional Phase III.

Relative to the time lines, you were thinking about if you were running the study by yourself versus now with Novartis involved. Can you give us a sense on whether or not that time line has now accelerated as well even for a traditional approval. And then secondly, I just want to clarify, based on your PRB sale and based on the cash received from Novartis, do you expect to need to do any financings going forward?

Matthew Klein Executive

Thanks for questions, Tazeen. So this was a deal that we believe accelerates and as I said, brings more muscle to both the development efforts and to the commercialization efforts, and that's the development efforts, whether this goes down an accelerated path or the more traditional path. When we think about the size, the extent of that efficacy trial for a Phase III trial, I think having the muscle and the experience of the Novartis team will be incredibly important for not only the accelerating that Phase III trial, but we also believe heightening the probability of success of that trial just given the neuroscience expertise that Novartis brings to the table.

So we view this very much as a deal that is significant not only for commercialization efforts but also for development efforts. And that speaks to the timing of this because now is the point in the program based on the data we had from PIVOT-HD in June that we need to start moving full speed ahead now with the planning of that efficacy trial. And on your second point, I think it's -- I think we are very comfortable saying, we don't anticipate any need to raise additional cash to get to our cash flow breakeven and beyond.

Operator Operator

I would now like to turn the call back over to Dr. Matthew Klein for closing remarks.

Matthew Klein Executive

Thank you all again for joining the call this morning. As I mentioned earlier, we are very excited about this agreement and look forward to continuing to work with Novartis to achieve that critically important objective of getting a safe and effective therapy to hundreds of thousands of patients worldwide affected by Huntington's disease. Thank you all again, and have a great day.

Operator Operator

This concludes today's conference call. Thank you for your participation. You may now disconnect.