

CONCERT PHARMACEUTICALS, INC.
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SCHEDULE 14A
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Concert Pharmaceuticals, Inc. March 16, 2017 P9:30 AM EDT

Roger Tung: Good morning. Well, thank you. It's a

pleasure to be here today, speaking on behalf of Concert Pharmaceuticals. I am very pleased to share with you the advancements that we're making with our clinical pipeline, including the recently-announced deal that we have with Vertex Pharmaceuticals on CTP-656, our next-generation CFTR potentiator.

Now, during the course of the presentation today I will be making forward-looking statements, and for the content and the meaning of those statements I refer you to our 10-K statement filed with the SEC. I will also be talking about the transaction that we have pending with Vertex Pharmaceuticals, and those details -- the details on that transaction will be available in the proxy statement which will be filed shortly with the SEC and can be found on their website or by contacting the Investor Relations group at Concert Pharmaceuticals.

So, the news of this month is really around CTP-656, again, our next-generation potentiator for the treatment of cystic fibrosis. We recently entered into an asset purchase agreement with Concert -- with Vertex Pharmaceuticals for cystic fibrosis assets that we have in our pipeline, including CTP-656, and we feel that this is a tremendous deal for patients in that it will allow the compound to progress, we believe, significantly more rapidly and treat a much broader population than were we to develop it solely ourselves.

We also think that this is a great deal for shareholders. We're very excited about the fact that associated with the deal is a \$160-million upfront payment to Concert, which will give us the ability, based on our current projections, to get into 2021, and to see a number of important potential inflection points without having to do a further dilutive equity raise.

I'm happy to say that there's a lot going on in the company right now. CTP-543, which will become our lead compound for the treatment of moderate to severe alopecia areata, will be moving very shortly into Phase 2 efficacy studies, and our intent is to get a readout on that during this calendar year. CTP-656 is also moving along currently in Phase 2, and I'll talk about both of those programs more in coming slides. And AVP-786, which is being progressed by our partners, Avanir Pharmaceuticals -- that contains deuterated dextromethorphan, which Avanir has licensed from Concert.

So, before I move more into the specific entities along the pipeline, I'd like to note that there is a lot going on that we have started to -- and brought into development over the course of the past years; and to note that in terms of the way that we use the technology, there's really two prongs of attack that we have. The first of those is exemplified by CTP-656, and that's to take a compound with well-understood pharmacology and a well-understood use clinically, and to enhance the properties of the molecule in such a way that it has the potential for superior clinical properties. And in -- with respect to CTP-656, those

include the potential for once-daily instead of twice-daily dosing, the lack of need for a high-fat meal to be taken with the compound for optimal absorption,

and the potential for, we believe, greater efficacy or potency based on the unique metabolic

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profile that we've demonstrated for the compound. The other way in which we are applying the technology is to start with a compound that has well-understood safety and pharmacological properties in humans, but to use deuterium in this case both to change the metabolism of the compound and create a new chemical entity, and to take it into a new clinical utility for which it, in the case of CTP-543 and the case of CTP-78 -- or, excuse me, AVP-786, are both situations where the entity could be first in class in a new indication. And again, I'll speak more to those in subsequent slides.

Now, moving on to CTP-656, there's a tremendous amount of progress that's being made in the cystic fibrosis area, and the most exciting work arguably is that involving small molecules that affect the CFTR, which is the protein which is defective in the case of cystic fibrosis. Now, there are many mutations -- in fact, several thousand -- which lead to lesions in the CFTR protein. A portion of about 5% to 6% of the patients have what are referred to as gating mutations, and those individuals are treated effectively with a potentiator such as Kalydeco, which is the only approved treatment for the gating mutations, and we believe CTP-656 would fall in that category, potentially with better properties than ivacaftor, or Kalydeco. The largest percentage of patients with cystic fibrosis are the so-called homozygous delta F508 patients, and those are -- that comprises about 50% of the CF population. And those patients are not indicated for monotherapy treatment with a potentiator, but instead require a combination, at least as at present, of two different entities, a CFTR corrector and a potentiator.

So, the asset deal that we are entering into with Vertex is a good one in the sense that it not only can address the gating mutation population but also has the possibility of accessing Vertex's very broad pipeline of corrector agents to create combination therapies that can access the largest delta 508 homozygous population. And that agreement was signed earlier this month. A little bit more in terms of detail is shown on this slide. The total potential consideration to Concert in this asset purchase is \$250 million. Importantly, a very large amount of that, \$160 million, will be transferred on signing, and that leaves two potential milestone payments to Concert to make up the potential \$250 million. Those include a \$50 million milestone that is due on US approval of a combination therapy including CTP-656, and \$40 million which is due to Concert based on a pricing and reimbursement agreement by Vertex, and one of three European countries -- the UK, Germany, or France -- and based on the first of those reaching a pricing and reimbursement agreement, \$40 million will be owed to Concert. Now, this deal is pending based on shareholder approval and other clearances, including HSR clearance. We anticipate that this will be ongoing through the next quarter or two. The deal is by contract to close by October 31st and can be terminated by either party after that. We anticipate that it will be closed by that time, and we have the opportunity to extend it on mutual agreement if that's not the case. The pro forma cash that we will receive based on that will leave us at over \$250 million, which we anticipate will take us into 2021, based on our current projections, which will

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enable us to bring CTP-543, again for moderate to severe alopecia areata, through Phase R and we believe into pivotal or registration studies. We also intend with that money to strengthen the pipeline and bring more entities into it. And finally, as I mentioned about AVP-786, that compound is currently in Phase 3 studies and we anticipate, based on success of those studies and approval of the compound, that we may be beginning to realize a royalty stream based on sales of that compound for agitation in Alzheimer's disease. Now, with this deal in the works with Vertex, we are continuing our US Phase 2 study with CTP-656 that we initiated in December of last year. That study is ongoing; is actively enrolling patients. We continue to anticipate, based on current projections, that we would be able to complete it this calendar year. Consistent with the ultra-orphan aspect of this disease, of this very small population of the gating mutation individuals with cystic fibrosis, the study is compact, with about 30 to 40 patients anticipated for enrollment. The primary endpoint is a 4-week endpoint looking at sweat chloride relative to baseline, and it will be a non-inferiority of the different doses of CTP-656. We'll be looking at three active doses -- 20, 100, and 150 milligrams versus placebo -- and we will have concurrently running with that an open-label, active arm of Kalydeco. So, this, as I mentioned, is ongoing. The completion of it will be pending the transfer of it to Vertex. On completion of the asset purchase agreement, all responsibility and expenses associated with it has the study will be transferred to Vertex. With that, I'd like to move to CTP-543, which is our proprietary Janus 1 and Janus 2, or JAK1/2, kinase inhibitor. This is a compound that we're very excited about. We believe that it has the potential to be the first oral treatment for moderate to severe alopecia areata, an indication for which there are currently no approved treatments and substantial population with an unmet clinical need. So, alopecia areata is an autoimmune disorder similar to psoriasis or atopic dermatitis in that it is autoimmune in origin, but the manifestation of this disease is cytotoxic T cells attacking the hair follicles, resulting in loss of hair. And this can be either patchy in nature or very substantial, as you can see in some of the pictures behind me. It's a fairly common disorder, and the population, we believe, is significant, as I'll talk about in the next slide. The compound that we're taking forward in it is a deuterium-modified version of ruxolitinib, which is currently marketed in the US as Jakafi for the treatment of blood disorders including myelofibrosis and polycythemia vera. The fact that Jakafi has demonstrated what we believe to be compelling proof of concept in the treatment of alopecia areata makes us very enthusiastic about the likelihood of our deuterium-modified compound to have similar results, and to go forward with, again, the potential to be the first-in-class agent for that indication. We have completed our Phase 1 single and multiple ascending dose studies and anticipate initiating a Phase 2a study in the disease in approximately 100 patients, starting later this month. Now, our estimates are that at present there are probably between about half a million and 500,000 patients that have active alopecia areata. We don't have a good estimate on the number of patients that are in the moderate to severe range. Our best guess is that it's about a quarter to a third of that patient population, but the epidemiology of the disease is

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not well-determined as of now. This is a disease that can either be relapsing, and particularly in the milder forms of the disease; in the more severe forms of the disease, it's fairly uncommon for it to relapse, and it tends to be chronic in that more severe patient population. While it can affect individuals of all age, from young childhood through late adulthood, the most severe forms of the disease tend to be seen in the first three decades of life, and therefore there's a relatively young population that is likely to have chronic therapy based on the experience with Janus kinases to date. One of the things that we are very excited about in terms of this indication is the clear interest that FDA has in the indication. This is one of eight areas that they've selected for a Patient-Focused Drug Development Initiative meeting, to take place in the 2016/2017 timeframe, which is a fair amount of effort on, of course, both the part of the agency as well as the patient community. This is a way of educating FDA as to the patient needs in a different area, and is a clear indication of their focus on this as an area of unmet medical need. Now, as I mentioned, there is what we believe to be clear clinical proof of concept for the effectiveness of ruxolitinib and the -- therefore the Janus kinase 1 and 2 subtype effectiveness in this indication. This comes from a publication that came out last year from Columbia University with the senior author Julian Mackay-Wiggan, where her group tested a cohort of nine patients in an open-label study looking at 20 milligrams twice daily of ruxolitinib, which is the approved dose for myelofibrosis. And what they found is that in the course of approximately three to six months, they had some pretty remarkable results, which you can see in this set of pictures, each one of these being a before-and-after shot of individuals who were treated with ruxolitinib. As you can see, many of the individuals had quite substantial hair loss, and after three to six months had remarkable regrowth of hair -- again, which would not be expected in this patient population in these numbers for a placebo. So, we feel that this is quite impressive results. The individuals appeared to retain hair quite well during the treatment period. We do know that in a period of several weeks to several months following cessation of treatment, that there is a significant amount of loss of hair. So, we believe at this point that the treatment with JAK inhibitors will be a chronic one. Now, one thing that was very good to see in this study is that the treatment was well-tolerated. There were no serious adverse events noted in the study, and no dropouts associated with it. There was one incidence of reduced red blood cell count, which was ameliorated by dose reduction. On rechallenge at full dose, that did not recur. Now, as I mentioned, we have conducted and recently reported out the single and multiple ascending-dose studies with CTP-543, the deuterium-modified version of ruxolitinib, and we saw the results that we were hoping to see with the compound. It is well-behaved as an oral agent. We believe that the profile that it shows is fully consistent with its use, similar to what you saw with ruxolitinib with a lower dose to get the similar kind of AUC exposure. We conducted multiple doses for up to seven days at doses significantly higher than we intend to use in the Phase 2 that we'll be embarking on recently, and we saw in that study that the drug was well-tolerated, with no dropouts, no dose reductions, and no serious adverse events. We saw, as we expected to, some evidence of reduced blood neutrophil

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count, particularly at the highest doses of the drug, which is mechanism-related and would be expected at high doses of a JAK2 inhibitor. We saw some evidence of pharmacodynamic effects with the compound as well. JAK -- excuse me, STAT phosphorylation is known to be inhibited by interfering with the JAK kinases, and JAK -- both STAT1, excuse me, and STAT3 phosphorylation were seen to be inhibited. STAT3 phosphorylation is more indicative of what would be expected to occur in hematopoiesis, whereas STAT1 is more along the interferon gamma pathway and therefore more likely to be involved in the efficacy of the drug. I'm pleased to say that the effects on interferon gamma-mediated STAT1 phosphorylation were particularly profound, and we saw full inhibition of that pathway at all doses tested. So, we will be shortly initiating our Phase 2a study, and this is a double-blind, placebo-controlled, multi-dose, multi-center study, looking at four different active doses of CTP-543, namely 4, 8, 12, and 16 milligrams twice daily, with the highest of those doses, 16 milligrams, providing essentially the same AUC as 20 milligrams twice daily of ruxolitinib. So, what we're doing is starting with the dose that we have good evidence is effective, and then going down to see what the minimal effective dose will be, so we can get the widest possible therapeutic window. We intend to carry this out in approximately 100 patients with moderate to severe alopecia areata, which we're defining as loss of at least 50% of scalp hair, and we'll include patients that have both a complete loss of scalp hair, which is referred to as alopecia totalis, as well as complete loss of scalp and body hair, which is referred to as alopecia universalis, both of which are considered to be particularly severe forms of disease. The primary endpoint for this will be a 24-week endpoint looking at a responder analysis of individuals who have at least 50% remission in their loss of hair, or in other words 50% regrowth of hair or more. Given that in the study that was done with ruxolitinib the responders had on average 90% or greater regrowth of hair, we expect that to be a very reasonable bar to be able to see differences between the placebo group and the active groups. We will continue the study out for a full 12 months in order to get continued efficacy as well as safety data at that timeframe, which we think will be important as we're choosing doses for our later studies. We think that this will be a very fast-to-enroll study and are hoping to have completion of the study with top-line data this calendar year. I'll move very briefly now to AVP-786, which is a potential first-in-class treatment for the symptoms of agitation and aggression in patients with dementia secondary to Alzheimer's disease. There are, again, no approved agents for this indication. We believe that there is a tremendous unmet medical need for it. We do know that a number of different types of agents, including atypical antipsychotic agents as well as benzodiazepines, are used off-label. We think that -- well, we know that in the case of the atypicals, they're black-box-labeled. We also believe that the benzodiazepines are inappropriate, and I think that's a generally-agreed medical sentiment. So, having an agent which is labeled for the use in this patient population, we think will be a very important addition to the treatment of this patient population. The deal that we struck with Avanir, now a subsidiary of Otsuka, involves our taking the compound through the preclinical work and then transferring it to them, which we have

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done. They now have the compound in Phase 3 and are responsible for all of the development and commercial support for the compound.

We stand to receive both milestones which are largely sales-based in nature, although there are some regulatory milestones, as well as mid-single to low-double-digit royalties, which for a company like ours could be extremely meaningful, given the potential market size for this compound, which we believe is quite substantial. In terms of our cash position, we exited last year with slightly over \$96 million in cash, and based on the closure of the Vertex deal we would have a pro forma -- excuse me, \$250 million -- yes, \$256.2 million available to us, which would be, again, able to take us into 2021 based on our current projections. So, in terms of what we have going on this year, we are entirely focused right now on closing the Vertex deal. We think that we're in good shape to do that, but of course we will be working hard to make sure that that happens. And with respect to 543, we've checked off a couple of these boxes and we'll be moving shortly into Phase 2. There will be a breakout session immediately after this talk, and I'll be happy to take any questions there. Thank you for your attention.
