From: Jennifer Altier
To: Gibbs, Kelli; Rothschild, Stephen; Owen, Andrea
CC: Lisa Miller
Sent: 6/5/2012 8:50:05 AM
Subject: FW: Ad board - last 45 min
Attachments: Actavis last 45 minutes of meeting file 0999.doc

Kelli, Steve and Andrea,

Please find attached the transcript of the advisory board where the messages and concepts are discussed. There are interesting comments on the messages, our core visual (does the boot say acute pain? Could have it on for 6 weeks. Maybe crutches are better). The last section focuses on the discussion of the current headline.

Steve, as we discussed last night, we need to find a balance between overreacting to the comments and adjusting our current headlines to be cognizant of this viewpoint. If there is anything else I can send you today please let me know.

Thanks,
Jennifer

Jennifer Altier
Marketing Director

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From: Cherie Forchette [mailto:cforchette@genesisassoc.com]
Sent: Tuesday, June 05, 2012 9:14 AM
To: Jennifer Altier
Cc: Eileen Provost
Subject: Ad board - last 45 min

Hi Jennifer,

Just received the attached transcript from the end of the ad board on Sat. This is very rough – and most of the speakers' names are "?" since the transcriber started in the middle of the tapes and hasn't had a chance to learn the voices!

We'll see you at 11am.

Cherie

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PLAINTIFF TRIAL EXHIBIT
P-02348_00001

Exhibit: 006
Allergan - ALTIER
Date: 8/2/18
Reporter: Amanda Miller, CRR

Fax 646-349-2160

Dr. McCarberg: Don't underestimate the NTPA. Somebody said the nurses are the ones that talk about the side effects. So you may, if you're targeting people and education, you may want to go to nursing meetings and talk about that.

If you're looking at the primary care audience and you're looking at new start NUCYNTA as a place to go I think that's a wise thing. Primary care is doing postoperative pain management in a lot of rural communities and you don't want to forget that target area as well. If you go to big cities they are not doing it at all. I haven't done in-patient care in a long, long time because they wouldn't allow me to do it, it's all hospitalist care. So, but you will find primary care that are doing it. You don't want to underestimate the power of what they could do by numbers.

Male Voice: Actually you make a good point there, Bill. I think that if the added value of this drug is dealing with nausea and vomiting and dizziness, that the hospitalists may be a better target than the chronic pain market.

Dr. Fine: Yes, I was thinking hospitalists and orthopedists just because of what we talked about today. And you have to focus on orthopedists, because you've got basically one, even with that targeted population you have 14,500 doctors out of a pool of conservatively 800,000 prescribers you're already cutting down severely. But that's where a lot of the

prescribers are who aren't afraid of drugs so that's good. But you still only have one medical service rep, or whatever, for 100 prescribers. The chance of changing behavior when you interface with somebody for a few minutes every couple of months, which is the most you'll be able to do here, is really remote. I think it better be even more targeted and more focused so you can really follow the results of that interaction and the consequences and manage expectations and really develop a relationship if you want to learn about this. And I think you need to move to the messaging. And I want to sort of segue to that with this comment, which is that we went around the table and we heard that some people thought there was more compelling evidence and some less, but what we're really, I think the sense that I got from the group was that we know that there's something of a problem. But another opioid is not really the solution to the bigger problem. So within the opioid prescribing context the issue is really managing adverse effects. We don't have strong, compelling data that we can market to that ends so it has to be sort of inferential.

So all that said, the marketing strategy really has to be about talking to people who are going to listen to the message in a way that stirs their sense of desire to try and maybe improve upon certain outcomes, but not at the expense of the efficacy they have already been led to expect and think they get

out of mostly hydrocodone or oxycodone. A little bit of NUCYNTA which is probably not of much value to you.

So with that, leading into that I think maybe the question is where does that group of prescribers live? Where and how do you access them so you can get a group of very interested first adapters that might then leave? If that's the one strategy the other is the larger wholesale strategy. But on the retail side, which is what we're talking about now, that's still a big number and a very small number of MSRs. And you have to really shrink that down by about an order of magnitude, I think, to make a difference. Or, I suspect it will go the way of NUCYNTA.

Dr. Hartrich: Another thought here is I see a little bit of a mismatch in that I look at this as you guys have a channel of distribution that you got when you picked up Kadian. And if you haven't gotten the channel why not brand extend it and bring out more products through it? The problem is you've got an acute drug here in MOXDUO, but your channel goes really more for chronic pain. So I think you've got a bit of mismatch there that you're not really going to get the synergies that you're looking for.

Dr. Long (?): I would go after plastic surgeons. They don't care about prior authorizations. They don't even understand the concept, and they don't want women retching after they've done all of their extensive work. They don't want any

pressure on the suture line. So I know that was a big success for the tapentadol folks.

Dr. Hertz: That's another issue also because of drug interactions, especially with seizures and people on Wellbutrin and things like that. So, and they have not done a good job in marketing their product, plus the dose is very high. I mean, you're looking at it and people will tell you, "Oh, it's 100mg of a narcotic." I mean, that sounds high to them. It's a different --

Dr. Orth: So one of the things that we have is we're, I don't know about you, but we're part of two hospital systems. But the hospital systems are really making it very difficult for anyone to come and interact with us on a day-to-day basis. So I think a lot more orthopedic (indisc.) are getting a lot more of their information at these sort of regional meetings and that sort of thing. And I think that those are very effective means of getting your word out to the orthopedic surgeons. So if you want surgeons to be doing it you want to have a little focus session at some of these regional meetings that they have. Maybe not that you get to the American Academy and people are too busy, the big, big meetings with 16,000 people, but I've been at five of them already this year. And you know at lunch you sort of, but you need to have some compelling data to push it to them that you're getting people up faster and you get

people who are good representatives in the field. Maybe do a multicenter trial if you're interested in orthopedics. It's easy to run a short duration multicenter trial in knee replacement.

Dr. Cahana: So who I would not talk to are pain specialists and anesthesiologists and PMNR simply because we're too much involved in this and everyone has an opinion. They will just give you a hard time and it will be very difficult. This is just a small example of how disruptive and obstructive we can be. So I believe that, and again based on the literature, that 80% of pain is done in the primary care setting, including acute pain because of the lack of the patient-centered surgical home and because in most rural areas the ERs are attended by primary care physicians and by physician extenders. Another 28% is done in the ER bona fide, and only 2% are done by pain specialists. So at the end however you're going to slice and dice it, it will go back to primary care. That is why other scheduled pain medications have been so successfully distributed because they went straight to primary care. And that we are now reaping the effects of that aggressive marketing. So the question is how to promote this without asking what is the better way to do it? And the answer is simple. Just do what Purdue did. Is go out to primary care and infect them. And if you have a couple of centers of

orthopedic surgeons, plastic surgeons, transsexual surgeons, and all of that then you can work with those selected groups and do that as part of projects.

Dr. Helm (?): Purdue got heavily fined because of what they did.

Dr. Hartrick: I was going to say to save time what I can do is give them a copy of Grassley's letter.

Dr. Cahana: The point is like this. Again, what I'm trying to illustrate is that there are two separate questions that can be as divorced as much as the company strategy. One is what is the right thing to do, and this is what we've discussed all day long. And then the other is what is the most effective way of doing it, which is a different question. And that doesn't necessarily have to be the right way. Now the reality is that medicine is practiced in the United States by primary care. And that's what carries weight. And even though specialty care make more money and think that they have more clout and think that they have more influence in this, at the end of the day in terms of the weight of the impact that they have on the health care system it goes back to primary care. So if you want to make a big boom and a splash in sales and all that go to the source. And just be prudent, because you have previous examples like Stan said of what happened when you were too far from the truth.

Now, personally, what I think you should do, but again that is personally, is go to selected, large medical systems. Go to a couple of universities. Go to group health. Go to KP. Go to the DoD. Go to the VA. Go to United Healthcare and do a couple of phase IV comparative effectiveness research studies and be, for once, a stakeholder that distributes a new intervention the way it's supposed to be distributed.

Ms. Altier (?): Thank you, everyone.

Dr. Fine: Before we go, Nathalie, thank you. You obviously got a lot of interest served up. Thank you for a good --

Ms. Altier (?): Yes, I'm sorry to jump into Nathalie's time here, but before we let you go this afternoon we really wanted to talk about really our short term. This morning we got a lot of good information about other clinicals that we can do and other data we can mine and that sort of thing. My challenge is I need to bring the product to market with the message basically assuming a positive PDUFA at the end of this month we'll be launching in July. So based on what you've heard presented this morning what I was going to do was run through a series of promotional messages. And although we've had a lot of good interaction, in the interest of time I'm just going to go through all of the messages, and then I promise I'll go back and I'll get your feedback on each one. But I want you to sort of

see the full story that we're planning to tell and really get your feedback.

So we've talked a lot about people will want to know where this ratio came from, the 3:2 rationale. So what we'll tell them is it was based on the early morphine/oxycodone combination studies. The 3:2 ratio appeared to provide the best efficacy-tolerability profile. The analgesic potency of oxycodone is approximately 1.5 times higher than that of morphine, and the oral bioavailability of oxycodone is approximately 60% compared to morphine at 30%.

The 3:2 weighted ratio of the two products had limited effects on the kinetics of either opioid. And they have similar half-lives, which supports the co-administration of each at the same dosing interval. Also of note oxycodone and morphine are commonly-prescribed treatments with long, clinical histories and proven efficacy when dosed separately.

Moving on from that, MOXDUO was proven effective. It is an innovative combination of morphine and oxycodone in a 3:2 weighted ratio. It is designed to provide effective analgesia with potentially fewer opioid-related side effects than its individual components. MOXDUO provides equianalgesia with morphine and oxycodone at morphine-equivalent doses, and has demonstrated a linear dose response.

We've demonstrated efficacy in two pain models, first of which being the bunionectomy. In a phase II trial following a bunionectomy the MOXDUO 6/4 dose had comparable analgesic effects to its morphine equivalent doses of morphine 12mg and oxycodone 8mg at 24 hours.

In phase III trial following bunionectomy MOXDUO was associated with statistically significant, dose-related reductions in acute postoperative pain, was well tolerated. There were few SAEs or discontinuations. There were minimal changes in respiration and blood oxygenation, and there were no instances of euphoria. Overall the 6.4mg to 12.8mg dose range of MOXDUO has the optimal combination of efficacy and tolerability. Of note, for all bunionectomy trials MOXDUO was administered on day one post-surgery when pain is most severe.

The second pain model is a total knee. In a phase III trial MOXDUO's flexible dose demonstrated significant analgesia versus a fixed low dose. Flexible dose was approximately 12:8 with a SPID (phon.) score of 137.1. The fixed low dose was 3:2 with a SPID score of 72.6.

Also, we've seen demonstrated tolerability. In combination morphine and oxycodone, the mu and kappa-2 receptor antagonist provide effective analgesia while potentially reducing the side effects versus components. We've seen the 6/4 provide reductions in moderate to key severe or good related AEs at

equally analgesic doses to morphine 12mg and oxycodone 8mg. And we've graphically shown that here with four of the key side effects that we see. This is, so it's less than 12 MUDs every six hours. So that's the 3:2 to the 6:4. In the pooled six trials you see the moderate, a mild moderate to severe, the green is MOXDUO, the red is morphine, and the blue is oxycodone. And you'll see that MOXDUO was lower in all three cases with nausea, with vomiting, with dizziness, and with sedation and somnolence, higher at the mild, and then lower at moderate and to severe.

We have dosing flexibility. It's available in four dosage strengths that we've reviewed. It can be taken 1-2 times every four to six hours. It does not contain acetaminophen. And acetaminophen or ibuprofen may be used concomitantly with MOXDUO. It may be taken with or without food. It is the lowest available solid, oral dose of either morphine or oxycodone on the market. We cite the APS and AAPM Treatment Guidelines recommend for patients who are opioid-naïve or have modest previous opioid exposure, opioids should be started at a low dose and titrated slowly to decrease the risk of opioid-related adverse events. And the 3:2 may be an appropriate initial dose for acclimating elderly patients or those with renal or hepatic impairment.

Although the exact mechanism of action of MOXDUO is unknown it is thought that co-administration of sub-analgesic doses of the two components result in analgesia comparable to each of its components, and a concomitant reduction in opioid-related CNS side effects. This is likely caused by the opioids' interaction on a broader spectrum of sub-receptors. We have the mu and the kappa-2. When co-administered morphine's actions on the mu receptors have been shown to be modified by oxycodone simultaneous actions on the kappa receptor type. And it is thought that this association between the analgesic effects and the side effects for the dual opioid combination are related to different populations of receptors and different signaling pathways that are affected by the two drugs.

So that's the MOXDUO story right now that we're planning to have our promotional representatives bring into offices. So I can either open it up to the floor for general reaction, or I can go sort of slide-by-slide and see.

Dr. Fine: I only have one technical comment on the mechanism of action, the second to last slide you talked about sub-anesthetic or sub-analgesic dosing. I think that's going to get people to quibble because you're actually not, each component as currently dosed is really not necessarily sub-analgesic. That is the 3:2 maybe, but maybe not. Two milligrams of oxycodone in a lot of people is still, has an

effect. But certainly when you get to the 6:4, etc., you're not prescribing separately sub-analgesic doses.

Ms. Altier: It's just the terminology there.

Dr. Fine: I just think you have to work on that phrase just to make sure that it's true.

Ms. Altier: Were these --

Male Voice: Or sell it as a replacement for Darvocet (phon.). "That's gone. What do you got now?" "We got smaller doses."

Ms. Altier: I guess, I know I zoomed through the story. Does it seem, does it reflect what you heard Patty present this morning and give a fair picture? Is it any more or less compelling when sort of put together in that way?

Dr. McCarberg (?): You don't know that you can actually say all of that, is that correct?

Ms. Altier: It will be dependent on our final label, correct.

Dr. McCarberg (?): I see. And you haven't had communications with the FDA allowing you to communicate package insert yet, is that correct?

Ms. Altier: Correct.

Dr. McCarberg (?): Because one of the things that you say there is that it's the lowest dose of any available product.

Ms. Altier: Morphine and oxycodone.

Dr. McCarberg (?): But together they're higher than hydrocodone. So if you're trying to get a primary care doctor to say, "Oh, this is the lower dose therefore less risk --

Ms. Altier: Right, so, we just say lowest, solid, available oral dose of morphine or oxycodone.

Dr. McCarberg (?): But they're in combination.

Ms. Altier: Point taken that you're taking issue with it.

Dr. Hartrick (?): Just one tiny thing on the second or third slide where you bring up some numerical information about when you say there were no incidences of euphoria that means zero.

Ms. Altier: In this specific trial.

Dr. Hartrick: But then you don't give the end.

Ms. Altier: Okay.

Dr. Hartrick: So I think if you're going to use numbers someplace you've got to put them in context.

Ms. Altier: Defined.

Dr. Hartrick: Yes.

Ms. Altier: Excellent.

Dr. Hartrick: Say out of all four patients (indisc.).

Ms. Altier: Exactly. Fair enough.

Dr. Fine: The advantage you have in this set, and I don't see anything here that's imminently problematic, and it's very consistent with other products, is that compared with the

NUCYNTA launch that required the majority of its safety data had to pertain to issues around seizure activity, had to pertain around cardiovascular effects, and potentially, even though it was questionable from the data it did have to talk about central serotonin syndrome and get people concerned about things that they are not used to thinking about in prescribing analgesics. So in some ways this brings people back to their comfort zone of what they're sort of used to and familiar with. An opioid is an opioid. That's both good and bad. The good is, "Oh, okay, I'm familiar with this." The bad is, "Well, and so what?" So there's both of that at play here. But I don't see anything that's controversial, or I don't see that there's a lot that's going to be taken exception with. You really haven't pushed the claims in sensitive ways.

Ms. Altier: Right. Is it, are there things we missed? Are there things you heard this morning from Patty that you're like, "Oh, you really didn't bring that out." Or something missing that you'd be interested in hearing from a representative about a new product?

Dr. Cahana: Yes, but they are probably things that you're not interested in disclosing so that's why we're here looking at the material so we know that. But if a representative would come to me and I would start to kind of drill in a little bit into how these studies look like. What is the end? What did we

do? Oh, and actually we're in the hospital and you look at this. So, but I can't ask you guys to go up front and say this was a study that, and I understand that. And the whole mechanism thing is purely conjecture. It's purely by inference all of this mu and kappa and all this is just anyone who is a little bit into morphine biology or opioid biology (indisc.).

Dr. Fine: They'll hand out reprints. They just should be careful which ones they hand out.

Dr. Cahana: So, again, I know, I understand in what environment you're working in. And at the end of the day you need to promote a product that you've probably developed and you want to make that move forward. And I'm just looking at it from an end user. It's yet again we're unable to release ourselves from the culture of where we have to exercise extreme critical thinking in what we do when people comment. I'm not sure that many people in the community have this critical thinking. And this is what we're dealing with now in this morbidity and mortality associated with opioids in our state is because most of the prescribers don't have the critical thinking. Most of them do not have the follow-up questions and take things at face value. So again, a lot of it is in your hands. And it's difficult for us to say what we would or would not put in because obviously our perspective is different. So like Perry said there's nothing in there that is not truthful to the extent

that it's so outrageous. But on the other hand there are some omissions and some word finagling and some stuff that is very nicely put in. Because when you say sub-analgesic doses, but you imply that there is synergy that was never really shown in a robust way. So I understand what you're trying to achieve and that's fine. But I'm just saying to our fellow colleagues here that it doesn't make our life an ounce easier.

Dr. Barrett: If I can interject. I've been in Medical Affairs for a long time and my sole purpose within medical affairs is giving you the right information, the correct information to use this drug appropriately and in the right population. And so any marketing materials that would carry those claims would also carry full descriptions of study designs and things like that. These are top level things. If you see omissions here tell us because it does us no good to hide things that will sell our drug one day but will bite people in another way. That's not our goal. This drug is not for everyone. It's not for every situation. But we're asking you to help us position it in the appropriate way so that there's maximum benefit to the patient and the physician at large.

Dr. Fine: You know one of the, in terms of high level discussion preceding this, and one way of sort of getting at both safety as well as potential value of a new entry into the market in this is to put some top level messages about the

frequency of, if you will, the prevalence of acute pain, the consequences of acute pain, the balance of the importance of managing pain versus managing and prescribing safely. And then fourthly, the frequency and prevalence and consequences of adverse effects associated with not just acute pain but acute pain treatment. Making no inferences, but stating, in a sense giving sort of on one or two slides with four bullets each sort of the reminder that, and that including the multimodal therapy, the paradigm three I think as James presented it is how people should be thinking about acute pain management in any setting now, whether it's a sprained ankle or whether it's a total hip arthroplasty, prescribing, simply writing a prescription, is not the panacea. It's part and parcel of comprehensive care. That I think is the wedge into improved public health, creates a better mindset about the attitude of the company that's getting itself involved.

But also I think to a certain degree mitigates some of the concerns that I think Alex is voicing which is you're part of the solution, you're part of the problem here. Everybody talks, says they're part of the solution but skeptical audience, outside observers might think otherwise unless you present, position yourself otherwise. So that's a thought of a way to do that. It also allows you to really talk about adverse effects and acknowledge them rather than sort of hide around them and

try and soften them. I think that one of the biggest complaints, and this is from the people who are really saber rattling about opioids in any setting is that there has been an apparent, in their word, in their point of view, an apparent effort to soft sell the harms associated with opioids and oversell the benefits. And if you can, I know this was what you were responding to, Jeannette, but if you can be a little more overt about acknowledging the need to be very mindful of these things. Just saying that differentiates you. Is that a fair statement, Alex?

Dr. Barrett: Good advice. Thank you.

Ms. Altier: Anything more on the messages? I think I want to skip ahead. There's just one other thing I wanted to get your reaction to.

Dr. Long (?): You don't mention anything about dependency or addiction potential.

Ms. Altier: We will have nothing to say, nothing different than I have been talking about (indisc.) abuse potential.

Dr. Bennett: (Indisc.) language in the label that we will be required to say in every ad. It's --

Male Voice: That morphine's addictive? Okay.

Dr. Bennett: It's class labeling. It will be in every piece of promotional material.

Ms. Altier: So we can make no claim one way or the other.

Dr. Fine: I know Cherie is going to flog me here, but even that first message, "He can handle his pain. That's the strength of an opioid." Trouble, trouble, trouble from out of the gate.

Ms. Altier: Why do you say that?

Dr. Fine: Why? Because what you've done is you've said that's, you've disclosed the benefit, but there is no risk associated with the statement whatsoever. Now, you don't have to say big paragraphs of risk there, but what you can say is, "I'm -- "

Ms. Altier: Unfortunately, we do have to have big paragraphs of risk all down this whole left side.

Dr. Fine: But I'm talking about what the centers and including in Congress and everybody else, and the FDA who are now really sensitized to this. "He can handle his pain. That's the strength of good, comprehensive pain care," or, I mean, that's bullshit kind of Perry language. But turn that into really good public health language that now becomes marketing language that the public gets and understands. And then you've put balance of risk and benefit into a phrase that's not just saying every opioids are the panacea, which that implies.

Ms. Altier: We're going at, and that's the two phrase I think I alluded to in the beginning. Sort of the balancing act that we're trying to say that we understand between treating the

pain and treating the side effects. So if you read the sentences together we have, "He can handle his pain. That's the strength of an opioid. He can handle his opioid. That's the science of MOXDUO." So bringing into that balancing act that we can help balance the pain --

Dr. Fine: I'm saying I think there's a much better way of messaging around this.

Ms. Altier: I understood.

Dr. Fine: And that should, a lot of thought should go into what that is.

Dr. Hartrick (?): I really strongly agree with you, Perry. I looked at that and said ibuprofen should be just fine. If I were in his situation I'd go to Costco, get Advil, and be done.

Male Voice: Is this a done deal?

Ms. Altier: No.

Male Voice: The message isn't done already?

Ms. Altier: No, that's why we're asking.

Male Voice: It's a very not gender-sensitive. You know that. He?

Ms. Altier: So this will be sort of our launch person. As the campaign evolves there will be lots of other different people and it will be he/she that sort of thing.

Male Voice: But why wouldn't the message be "opioids can be risky?" "Taking a pain drug can be risky, but it can also

help your pain." That's what Perry is saying, is be up front about the fact they are risky and that you've got to be risk averse.

Dr. Cahana: I think, and this is a discussion obviously that you'll have to have amongst yourselves. The context that we're bringing this with you is that we are not 20 years ago. We are 20 years later suffering from the side effects of the overtreatment of pain, be it medication, devices, or surgery. And there's this tension between what are you supposed to do in order to survive, and then what as we are asking you to do as those being on the ground in front of patients who are suffering from the iatrogenesis that has been created by this overtreatment. So you have to come up with a study with the FDA that comes up with a whole bunch of things that we don't understand and are meaningless to us. So you have to come up with certain designs and methodology that is not relevant to our everyday life. And so it pertains also to the marketing material that you have to come out that will sell that will be like any other marketing material that's out there. Open the New York Times and I say, "Okay, come to the Back Institute and everything will go away." All we're saying is that this is not good. This is not helpful. This is why we are in so much trouble. And so you can look at it and say to yourselves, and this is again a strategic discussion amongst yourselves, is this

an opportunity for us to be the first, to be the first and see our research and phase IV research which might extend our immediate goals? Would we be the first ones in messaging showing some situation awareness of the complexity of what's going around, or are we going to do just what our colleagues are doing because that's how ruthless our environment is, and maybe we won't be as the worst but we won't be as the best. And that's an internal decision that we cannot ask you to take. It's just that we want to share this with you, that the role of the corporate world in this is a devastating role. And I'm now involved in some type of legal stuff that have to do with a company that wanted to help but by aggressive marketing has just created a dialogue between a physician and a patient that is just misleading and devastating. I think this is what we're trying to say to you guys. This is really tough and nuanced stuff. So you have an opportunity to be nuanced here and lead the pack.

Ms. Altier: Great. Any other, I do appreciate all of this. I'm taking it in.

Dr. Fine: I know this is not easy stuff to hear because you're on the long wagon train that has preceded you.

Ms. Altier: But that's why we do these. We do the reality check.

Dr. Fine: Yes, but phrases like, "manage the risk," or, "Pain is a problem. Be part of the solution." These are things that may mean entry into an acknowledgement. Things are a little more complicated than we used to think they'd be. We can't ignore pain. The answer is not, "Well, geez, okay great. No problem." Let's just be prohibitionists. Well, there are people out there who are waving that flag. And they've got the ears of some pretty powerful people in this country. That's not the way things are going to go. But as we get down that train you have to have something to fill in that vacuum so that people feel good enough about whatever replaces the past messages which is, "Opioids for everybody, unlimited, no bad can come of it."

Male Voice: How about, "With the help of a good rehab program MOXDUO can get you back on your feet," or something like that?

Ms. Altier: I wish we could say that. Unfortunately, I can't even say that.

Dr. Hertz (?): What you are supposed to be marketing for is acute therapy to help you get back --

Male Voice: Sorry.

Dr. Hertz (?): This picture is not marketing acute pain. This picture is marketing chronic pain.

Ms. Altier: Why do you say that? He just had a surgery.

Dr. Hertz (?): Yes, but nobody is going to see that.

Ms. Altier: Why don't you see that?

Male Voice: (Indisc.).

Ms. Altier: I was going to say this is unfortunately a projection.

Dr. Hertz (?): You can have someone with a boot on that's had that on for six or eight weeks because they have a stress fracture. This picture to me looks like a chronic pain --

Ms. Altier: What visual would say acute pain to you?

Male Voice: Crutches.

Male Voice: The man is on crutches. That says more acute pain than --

Dr. Hartrick (?): Where is that glass of wine?

Ms. Altier: Crutches and what? Crutches and a boot, or just like crutches because he just had a --

Dr. McCarberg (?): And tears. So, Ronny, we only have 10 minutes left. And I want to go around the room one more time. And let's assume that the top challenge is money, cost of the drug formulary. So let's take that out of the picture and say that's not the top challenge. What do you think the top, the best opportunity for this drug is? Just single sentence and what's the worst challenge that is not formulary?

Dr. Hertz: I think to try it out in the acute pain setting and major institutions and really see if there's any problem

with it and see whether or not it really does what it's supposed to do.

Dr. McCarberg: Challenge, Ronny?

Dr. Hertz: The challenge is to get it in those institutions and do the studies.

Dr. McCarberg: Jim?

Dr. Crews (?): I'd say again the greatest opportunities are going to be for patients who have not tolerated other opioids, single entity opioids. And the greatest challenge is going to be, other than costs, I don't know that I see a whole lot of other challenges. Just at having a side effects profile that's brought out in longer-term use comparable to what you're showing here on the initial studies.

Dr. Gebhard: The biggest advantage I think is if you can really demonstrate that there are cost savings. If you can do that I would really, along the lines like with what Alex went and it's worthwhile investing that money in my opinion. So if you can show that then you have a slam dunk. And the big challenge is really these days not even the cost. The P&T Committees are so critical of adding anything. And the opioids especially in Florida have such a negative reputation these days. So that's where I see a really big challenge. I'm not sure I mentioned this already because I'm a bit sick. There are

pharmacies in our area who don't carry OxyContin anymore. Patients can't get it.

Dr. McCarberg: You can't write it if they can't get it. Yes.

Dr. Gebhard: Pharmacies have decided to actually not carry those drugs, which is kind of amazing.

Dr. McCarberg: Too much risk. Craig?

Dr. Hartrick: Yes. I would just add that, learn from Ortho-McNeil, whatever they did you should do something different. And maybe it's what Alex is saying and maybe it's what Ralf's saying. Maybe it's go directly to the primary care guys, but try something different.

Dr. Long (?): I think this medication can be used for acute pain management in the hospital as well as in a pain center. And sometimes the way to introduce them to the hospital is to go to the out-patient pain center first. And I think the difficulty getting it in is really showing a difference between what's out on the market now and really convincing people that this is different. And I think that's the biggest challenge, because it's two narcotics that we already prescribe and convincing people that it has lower incidence of side effects and increased efficacy is going to be difficult.

Dr. McCarberg: You want to take that hat off and get another hat on?

Dr. Cahana: Can I say before you? And if you use it then please cite me on this. The opportunity is to say what you do. That's the opportunity. You have an opportunity now to go out and say which are the challenges to do what you say. That's a big difference. And we are in a reality where people say a lot of things, promise a lot of things, and they don't follow up on it. And it's to the detriment of our patients and we feel that every day. And I think this was, from my perspective, a wonderful day because any meeting that has Truvia as the artificial sweetener is on my best list. So well done.

Dr. Fine: The only thing I wanted to add to everything else that I've thought of and I think I've talked endlessly about, I appreciate the fact that you guys, and you know me well enough when I get on my soapbox is to back off and let me vent. So I appreciate that. That one of the big issues is that simply the number of pills that are out there, and the availability of those pills for either sitting on people's shelves and being diverted or redistributed or used for other purposes. Something novel that might be useful and something to discuss with the FDA as a part of a safety plan, even though REMS, and we've never even talked about REMS, and REMS are not being required of immediate release formulations. But you could be a first, you could actually suggest that we're now not 20 years ago. We're now in 2012. That MOXDUO in two strengths, the 2:3 and the 4:6

may be available in the equivalent of a Z pack. The vast majority of acute pain conditions, even postsurgical ones and the ones that we talked about today, most people are only taking their oral analgesics for three, four, five, maybe six days post-op. Then most of it either gets, they never use more than the first few doses, or they are better enough where they really don't need them or want them, but just continue to use them because they are supposed to. There is a fraction of people that really do need them for two weeks, maybe three weeks in the long (indisc.) period, or for bigger procedures. But perhaps if this came in a 12-pack or 16-pack or a 24-pack, something that it was day 1, day 2, day 3, day 4, day 5 and 6 is half, you know, and that's it. And then instructions on if not use how to destroy the rest of the contents, that might be it, it sounds it's totally different than anything we talked about. But again as a negotiation about why and what's it advantageous about, something new in the market that's maybe not as new as we would like it to be, but has a different aspect of newness that focuses on safety. That's my last (indisc.).

Dr. Orth (?): Well, I don't know if this is the biggest challenge but (indisc.) as far as the challenges the current environment you're trying to come out in is just really different now. There's a big opiate phobia out there. And then not only are you trying to present a drug that is a Schedule II

drug but it's got two scary sounding names in it. It's got oxycodone in it and morphine in it. And if you're going to try to market this to primary care doctors that are already being stressed to not write these type of medicines any longer, I mean there are just whole segments of my state where primary care doctors are just flat out refusing to write opiates. I think it's just going to be a challenge. I don't know what you can do about it. I think it's just bad timing more than anything else. But that's going to be a real challenge.

And I think the biggest potential for it really is you have to be realistic. This is going to be a niche drug. This is not going to replace hydrocodone so you should focus on those niches. Those individuals that have known opiate side effects, and believe me those are not difficult to define, so if you try to market this to physicians in a way of like, "Here are some screening questions you can ask your patients before you take them to the OR." Maybe you can help surgeons identify patients that this might be advantageous to it, and just be realistic about what your sales goals [are]. I can tell you that the tapentadol NUCYNTA folks are not grumpy about being only 1.8%. In two years they're 1.8% they made a lot of money on that drug. I would just be realistic.

Dr. Fine: They are grumpy.

Male Voice: Maybe not your rep. But the company (indisc.).

Dr. Cahana: And I don't think we live in an opioid phobic age. Last week 167,000 prescriptions were written only in (indisc.) medicine. So if anything I do not think that we're opioid phobic.

Dr. Orth (?): Well, Alex, in my state --

Dr. Cahana: I think some of us are concerned about the emergent public health problem (indisc.).

Dr. Orth (?): I'm not saying it's a bad thing to be opiate phobic. I'm glad a lot of my primary care doctors are no longer writing 250 tablets of Percocet a month.

Dr. Cahana: I think that in the continuum we are still, and like Perry said, there's a lot of pills out there. And I think that there will be a true sense that you are trying to help us out with this public health emergency it can be, and enrich the REMS strategies which have been very myopic in how they are going towards in terms of their solutions, you can distinguish yourselves as a different entity not on the fact that you came up with a co-administration of two (indisc.).

Dr. McCarberg: The lights are dimming. We better get one more comment in.

Dr. Hartrick (?): This is an acute pain drug. I think it should be marketed for acute pain, which would be hospitalists.

It would be orthopedic, other surgical specialties. It would be the acute pain services. I see nothing in this evidence that shows any reason for it to be used in a chronic pain settings.

I really like your idea, Perry, of putting in, particularly for the primary care. Put it in a blister pack. "Okay, here's your dose of medicine. You get your 5 pills, 10 pills, whatever it is. And then we expect you to be done." Because that deals with the weaning problem and it also creates the company in a situation of being talk about a public health epidemic. You're now Dr. Snow to the Broad Street pump (phon.) by coming up with this innovative approach.

Dr. McCarberg: I want to thank everybody for coming. I know that everybody has planes they have to catch and everything. Final comments, Perry?

Dr. Fine: Thank you. Travel safely. Godspeed.

Dr. Barrett (?): Thank you, Perry, for doing such a great job.