Evoke Pharma, Inc (UPDATE)

April 8, 2021

Corporate Speakers:

- Yale Jen; Laidlaw & Company; Senior Biotech Analyst
- Mathew Moschovas; Laidlaw & Company; Investment Banking Analyst
- Richard McCallum; Texas Tech University Health Science Center; Professor of Medicine Division of Gastroenterology
- Luke Kottke; Laidlaw & Company; Investment Banking

Introduction

Yale Jen: Good afternoon. My name is Yale Jen, Senior Biotech Analyst of Laidlaw & Company. We appreciate you attending our fireside chat this afternoon to discuss the treatment landscape of gastroparesis and the real-world usage experience of a recently launched drug called Gimoti which is a nasal spray of Metoclopramide.

First, we have to apologize that the other invited speaker, Dr. Kostas Sideridis, cannot attend this meeting due to some personal unique circumstances and this afternoon, we are very honored to have Dr. Richard McCallum from Texas Tech University Health Science Center at El Paso to provide his insight. He has a very outstanding career in medicine, both in clinic as a gastroenterologist and in research.

He is the professor of medicine in division of gastroenterology. He also is the founding chair of the Medicine of the Texas Tech Health Science Center at El Paso. He was elected to the American Society for Clinical Investigation and he's also a fellow of American College of Physicians. Dr. McCallum has published more than 390 articles in peer-reviewed scientific journals, 100 textbook chapters and has edited 13 scientific textbooks.

His research has been focused on the physiology, pathophysiology, pharmacology of gastrointestinal smooth muscle relating to disorders of motility and functional bowel disease involving the esophagus, stomach, small bowel and colon. So first, welcome and thank you, Dr. McCallum. So ...

Richard McCallum: Thanks very much.

Yale Jen: You're welcome and first, could you provide us a little bit more information if I'm missing anything and also maybe talk a little bit about your medical practice?

Richard McCallum: Yes. Well, I think the only – we don't want to take up much time. I think two areas are important, that we've had continuous NIH funding for the topic of gastroparesis for the last 15 years and that's always hard to do and hard to sustain. So we're very proud of that and then we just published a major landmark textbook on

gastroparesis. Elsevier was the publishing company. Came out I think last November. So we're very proud of sort of having a major footprint in that world.

My practice, I'm in academics. I've been in this area for the last 45 years or so, running departments of GI and medicine and conducting a research team, teaching and being involved in national societies, but mostly seeing patients. I like to remain in the – in the grassroots, so to speak. I like to see patients and learn from them and try to help them.

So I have clinics each week, I do endoscopies, I do procedures, I study motility tracings of the esophagus and stomach and generally try to juggle a lot of balls at the same time, which we all do I'm sure. So that's a snapshot.

Questions and Answers

Yale Jen: Okay. Great. That's very helpful and I think I'm going to group our questions probably into two groups. One is to talk of general aspects of gastroparesis, the illness and the management. In the second group, we'll be talking about therapies, especially the use of Gimoti in a real world setting. So my first question is in order to level the playing fields for all our participants, could you first just give us a brief description of gastroparesis?

Richard McCallum: Sure. So gastroparesis, in its simplistic form, patients ask me, doctor, what is that term? It's rather a daunting word. It's a lazy stomach. Your stomach is not emptying the caloric contents of your meal on time. It's staying in the stomach longer than usual, resulting in symptoms and the reason it's staying in the stomach is not because of any obstruction or mechanical problem.

This is a problem where your nerves and muscles are not working properly and they can't grind up the food. The term is called vermiculation, mix it up and eventually expel it into the small bowel to be absorbed. That would be it in a nutshell.

Yale Jen: Okay. Great. And how would you generally treat gastroparesis with a patient with a sort of different level of severity?

Richard McCallum: Well, as you've heard already from my statement, it's very key to make sure we have the right target. So we do have to go through the rituals of excluding any other condition, otherwise we never get to the finish line. So we have to make sure that appropriate studies have been done to exclude what's called obstruction or pathology in the stomach.

So these patients have had an upper GI endoscopy, sometimes a radiologic testing, sometimes imaging of the abdomen such as a CT scan because the patients can have some abdominal pain in addition to feeling full after a meal, not being able to finish a meal, nausea, bloating and some sometimes vomiting.

And then they have to undergo a study called a gastric emptying test. So this is a physiologic test. It can't be diagnosed by endoscopy or CT scans or ultrasounds or other techniques. One has to do a gastric emptying test where you eat a meal that's labeled with an isotope. The gold standard in the country is an egg beater meal, two eggs, piece of toast, some jam and water, 250 calories, 1% fat and that's the gold standard and one of the problems in the country is people don't adhere to the gold standard.

The diagnosis is made by default, by frustration or without objective data and that interferes with the interpretation of how treatment may work or does not work. So having defined the entity, you then have to define its etiology because depending on the etiology, your treatment has to be calibrated to the target. Probably the two – the two big ones are diabetes, probably greater than five to 10 years duration, diabetes mellitus. There's 25 million diabetics in the country and so a percent of those patients go on to get gastroparesis.

And there's another group, the common group, called idiopathic. Patient comes to us and we don't know the exact reason why the nerves and muscles were damaged. They're not diabetic. We assume and sometimes they actually can identify a gastroenteritis illness which we think is a typically virally mediated illness where you have nausea, vomiting, diarrhea, restaurant food poisoning, perhaps traveling, perhaps being involved with camping or drinking water.

Some potential reason, sometimes the patient may have forgotten the exact day and time when they had gastroenteritis. It's a common illness. Most of us bounce back and do well, but a subset go on to have chronic nausea, bloating, fullness, can't finish a meal, vomiting. That's called idiopathic.

And then the other group has had vagal nerve injury. They've had surgery on their esophagus, usually repair of a hernia called a hiatal hernia. So heartburn, common surgery and a small percent of those patients have damage to their vagus nerve from the surgery. So they're the three big ones – diabetes, injuring the nerves and innervation of the stomach, idiopathic, viral injury to the nerves and muscle function and a vagal nerve injury damaging the innervation of the stomach.

So we do want to identify where we're going to put you because we are treating the whole patient. Gastroparesis is in the game obviously, but we have to identify all the factors and particularly in diabetics, glucose control is always on the table. Diabetic control often determines a lot about the prognosis of diabetic gastroparesis.

So that's very important. You have to have the time and interest involved to very thoroughly evaluate the patient and then have the – have the gastric emptying study done and then agree that there's no medications involved. Some people are taking narcotics, some people are smoking marijuana, some people are taking L-DOPA. There are many medications which can alter a gastric emptying study.

So we have to be detectives. We have to make sure that this is not iatrogenic, this is not a man-made cause of gastroparesis. So I'm not going to go through all the details, but it's not as if someone just – you don't just get a menu and order gastroparesis up on the menu. Gastroparesis is a diagnosis you have to work for and you have to be 100% sure that you have the right target or the medications and treatments will not be working.

Yale Jen: Okay. That's very, very [authoritarian] and very helpful. Maybe just a quick [things on] this issue here which is for the gastroparesis symptom itself, is there any difference in term of treatment per se or it's just more of consideration or other comorbidity need to be considered?

Richard McCallum: State that question again.

Yale Jen: Is there any major specific consideration need to be considered for treating, let's say, gastroparesis of diabetic versus idiopathic versus sort of nerve damaged?

Richard McCallum: Okay. Well, symptomatically, the most common symptom we ask the patient is what's called early satiety, the patient's inability is to finish a standard meal that they could finish in the past or that their family is consuming. Premature fullness, premature satiety, that's a very telling symptom that we focus on along with nausea. They're probably the biggest three.

Early satiety, premature fullness and nausea, they are the big three and they're indistinguishable. They're the calling card to get you in the door to sort of justify that your slow stomach is symptomatic and is worthy of further intervention.

As far as the different ideologies, diabetics tend to vomit a lot more than idiopathics. Diabetics, probably because of undulations in blood sugar control, tend to be a little more vulnerable to vomiting in their story, maybe once a week, maybe intermittently. Some could be more frequently as they get very severe. Diabetics tend to have a potential for diffuseness. Diabetes doesn't stop at the stomach. It goes into the small bowel and colon. Some of these patients may have constipation as well.

Idiopathics, these patients tend to have more propensity for pain, more complaint about having a lot of discomfort. We try to make it discomfort. Patient really demands that we call it pain, epigastric pain, and they may be prone to pain elsewhere, fibromyalgia, may have had previous surgeries for gall bladders and hysterectomies. They tend to be more prone to pain, there's a higher incidence of depression and a feeling of anxiety and mood aspects in idiopathic patients.

All these three entities are dominated by females. Seventy-five percent of all these entities are female – are female driven. It's probably 80% to 85% in the idiopathic subgroup.

Yale Jen: Okay.

Richard McCallum: So yes, that's probably a brief – a brief response.

Yale Jen: Okay. Great. Thank you. And at what point do you think the patient, based on their symptoms, that you need to admit them to the hospital instead of just outpatient treatment? What level – what type of symptoms that is worth being admitted?

Richard McCallum: Their story. Yes. Their story. Their story is that I vomit to the point where I actually go to the emergency room. So when a patient says I'm being admitted or I go to the emergency room once a month or I may be admitted or the vomiting – yes, the vomiting has brought me to that point. That may be – they're being admitted anyway. I don't think we – we try to admit them if we can. If we don't have to because at $3,000 or $4,000 a day in the hospital, that's not an economic idea.

So diabetics get admitted because they go into what's called diabetic ketoacidosis. Their diabetes gets out of control. Often, they get a urinary tract infection when the blood sugar goes above 400. It activates vomiting. So they get into the emergency room with diabetic ketoacidosis, vomiting, metabolic problems and they get admitted.

Idiopathic patients are more likely to come in the emergency room for dehydration. They want to get IV fluids, they may need IV anti-nausea medicine, maybe pain. They come of their own volition. We admit patients electively only when it's clear that they're having this once-a-month or so, every six weeks admission to a hospital cycle, losing weight and our medications have not worked and then we do surgery.

We do a procedure called placement of a gastric electrical stimulator and cutting the pylorus, the exit to the – of the stomach into the small bowel called the pyloric sphincter. That's a surgery we do in about 20%, 25% of our patients who fail all medical therapies or can't tolerate any medical therapies. That's the last – that's the last step in the scenario. That's not something we try to – we try to maneuver, but it happens when patients cannot function.

They're not working, they have no quality of life. These are signs that we've moved to the point of very severe and unless we can turn that around, you need to have surgery. Our job is not to torture patients. We have a surgery. We have a surgery that I can resurrect you. Eight percent, 85% of my patients essentially have no symptoms and are functioning well after this surgery.

So there comes a point in medical therapy where you will not respond. It's not – medical therapy is not forever. Particularly in diabetics, the disease goes on. You're a diabetic for life. It's an unforgiving entity, it burns up your nerves and eventually you will not respond to medical therapy. That's not the fault of medical therapy. It's the fact the deck – the deck is stacked against you and you cannot overcome it. So time may run out and you have to have surgery.

Some patients, the diabetic aggression is somewhat more friendly and controllable, and you sort of stay on hold for a while and you remain treatable and remain somewhat – not

reversible, but manageable. A subset, the disease marches on and you have to go to surgery.

Yale Jen: Okay. Great. That's a good description of what's happening there and then maybe the last question about the general aspect of gastroparesis is that what portion of your patient actually fail their original treatment and has to go to the second line therapies? So we have a better understanding in terms of the sort of treatment process or the dynamics there.

Richard McCallum: Well, we really haven't talked about treatment. So the first approach is to – is to control their nausea and that's their main symptom as a rule and in turn, prevent vomiting and then ...

Yale Jen: Okay.

Richard McCallum: So that requires an antiemetic and at the same time, we're going to start a prokinetic. Prokinetics take time. You don't empty your stomach tomorrow morning. It may take a week or two to stimulate and re-motivate and resurrect your stomach. Anti-nausea drugs work tonight. So if I want to look good tonight with my patient, I'm going to give them an antiemetic today. I may also start a prokinetic.

In the case of Metoclopramide and Gimoti, we have a marriage. We have an antiemetic component in the central nervous system by blocking dopamine D2 receptors and we have a prokinetic property in the stomach by blocking dopamine receptors. So we can do two things at once. We can give nausea relief, which works first, and then we can begin to stimulate the stomach as a prokinetic effect which works later.

So we would start that therapy in our – in our patients as our first line therapy. Some people would also give a back-up antiemetic such as Promethazine or the 5-HT3 antagonist Ondansetron to have a plan B to make sure that the patient is happy. Metoclopramide has about a 10% chance that in the first week or two, you will have side effects. You'll have agitation, restlessness, what's called akathisia, twitching of muscles, torticollis, insomnia.

These are issues that may make the patient have to reduce the dose, A, or, B, may have to stop it. So that's a consideration. So you've lost, say, 10% of your patients in the first week or two, so you may call them failed medical therapy as far as your first-line drug, Metoclopramide.

Of the remainder which you've started off on maybe a modest dose, some people use 5 milligrams four times a day and build up to 10 milligrams three or four times a day slowly just because you don't want to have the patient call you with side effects that could be avoided by starting slowly and then the patient has lost faith or confidence in the drug and won't try it again. So we start low and build up a little bit and then so in patients who start at 5 milligrams, which they may by their local doctor, and don't do much better, they may call that failure.

We would not call that failure. We would increase the dose to maybe 10 milligrams four times a day and give them a couple of weeks to see where that goes and then with Gimoti, now we have the option of saying, look, we can guarantee continued absorption, no interference from vomiting intermittently, no interference with a stomach full of food or sometimes old food in the stomach which sits in the stomach for days and interferes with absorption, blood level of [inaudible] in the body.

And so you'd have the opportunity then to say, look, we're not going to give up on 10 milligrams four times a day, you're not having any side effects or minimal. Let's jump to Gimoti and give you another chance to get a more sustained blood level of this drug. So you work very hard at this because the menu is limited. The menu is zero. There's been nothing going on in this area for over 40 years and Gimoti is the only new addition in 40 years.

It's a time capsule. You could dig it up and you'd still be very current. So you can't – you can't be frivolous. You got to make the very most of a – of a limited menu. So you have to work very hard at finagling the dose. In some cases, we would use the backup anti-nausea drug and then if they fail all those tricks, you'd have to consider other medications.

In this country, we only have Erythromycin as an available pseudo prokinetic. It's not approved for that, but we've adopted it. It has some legitimacy, 250 to 500 milligrams three or four times a day as a prokinetic to replace Reglan. It is not an antiemetic.

Some people would then go to a drug called Prucalopride, known as Motegrity, approved from Takeda for constipation in this country, serotonin agonist which might have a role in the stomach. Yet to be proven, no data, but has all the right stuff. You may go to that. Again, not an antiemetic, so you're using two drugs at once.

And then finally, you may go to Domperidone if you have the wherewithal to do it like we do. You have to get a special IND from the FDA. It's not approved in this country. Some people get it from Mexico. We get it from other pharmacies in Canada and New Zealand and you have to have an informed consent and you have to follow the patient and monitor their cardiogram. Probably 1% of gastroenterologists in this country have the ability to do that.

So that's the limited repertoire that we're talking about. Of course this is based also on changing the diet to a liquid soft diet, trying to minimize high-fiber foods, bulky foods, glucose control maximized. I have to have a co-management with a diabetologist. Usually, they're already seeing one and addressing medications. Many people take Tramadol or pain medicine for back pain, miscellaneous pain. That blocks gastric emptying.

Some diabetics take what's called GLP-1 analogues to lose weight and help their Type 2 diabetes. Those GLP-1 analogues slow the stomach and could sabotage your therapy. So that, in a nutshell, is your sort of – that's the playing field.

Yale Jen: Okay. That's very, very helpful and this is a very great segue to Gimoti and this is a just recently launched drug and I understood – I understand that you have already prescribed the drug. So basically two questions here.

Number one, what's your initial experience so far with the drug? And maybe a follow-up here is that I [understand you help patient] to get the refills and what are the typical feedback by those patients to take the – to take the refills and the – and any specific characteristic of those patients that you can sort of extrapolate from with the – at this moment?

Richard McCallum: Yes. Well, the follow-up is limited. I mean, we've certainly been – we've only been doing this a couple of months. So we do – we do prescribe it. We're still learning some of the tricks. We have to go through a couple of – jump through a couple of hoops with sometimes getting it approved through their insurance, but the company has as – has a helpful connection and that's made it easier.

We don't call patients every day. This is not a private office. It's me and prayer and a couple of medical assistants and we're working 24 hours a day. So we don't call patients every other day and find out how they're doing. We've not had any negative callbacks. I see patients every two to three months. So when I see them, I'll see them, but I have not had any negative callbacks. I assume that the drug may be working and I think we've had – we give a month and then we give a refill.

So again, we don't call up before we refill – before the refill is up and say are you happy? Do you want to push on? So we don't have that kind of microscopic data, but I think in medicine, the general theory is hearing no negative news from patients who tend to be very vocal when it is negative and you'll hear from them, we have assumed that things are running smoothly and I've given it to four or five patients. When I see them back in three months, I'll know more, but that's about all I can say.

Yale Jen: Okay. Great. That's, again, very helpful. And, Dr. McCallum, I understood that you recently published a peer review article highlighting the Gimoti and could you provide us some insight on how should Gimoti to be used going forward? Maybe in what sort of gastroparesis sub-population [may it be] most valuable, at least initially and so we'll get a better sort of overview of it.

Richard McCallum: Yes. I think we've got two sort of approaches here. There's a primary care doctor who generally, very early on, refers to the gastroenterologist. So although it's going to be marketed to the primary care doctor, it's not going to be clear how quickly they can be educated and focused. I think most primary care doctors look upon gastroparesis as being a bit beyond their radar, bit beyond their level and they refer to a gastroenterologist.

Often the gastroenterologist has to do the endoscopy to confirm there's no obstruction, that we do have the right diagnosis and maybe even repeat or do the gastric emptying test in the right manner. So we're mainly talking to gastroenterologists in reality. Although the symptoms may make a primary care doctor refer the patient to a gastroenterologist, most primary care doctors are not in a position to get involved with referring to endoscopy and gastric emptying. They rely on GI.

So most GI doctors then are very tuned into the field and they would probably take two approaches. I think in the early going here, people would probably start with some oral Metoclopramide, but I think as we educate and make it clear about the benefits and advantages of Gimoti, they would be, I think, very interested in getting a good result fairly quickly and having a happy patient clientele and PAs, the nurse practitioners, who manage – in reality who manage these patients in practice.

I mean, GI doctors are too busy doing endoscopy on everyone. So their interest level in treating patients day-to-day is not that high. Nurse practitioners do most of the – of the office work and so we have to educate nurse practitioners as well as physicians that, yes, let's probably start off with oral Metoclopramide in some cases here because Metoclopramide comes in with the black cloud.

When you mention Metoclopramide to anyone in this country, there's a synaptic quivering of the eyelids or the mouth because they've been indoctrinated and brainwashed over the years that Metoclopramide spells trouble and they're not sure what it is, but they've been told be careful and maybe some have actually read the black box warning. So they're going to be doing it with trepidation in the beginning.

So I think they start off with the oral form, maybe low dose, as I said, and go a week or two and the patient has no symptom, no negative side effects and so they're relieved and then they become very, I think, focused and they would then say let's go with a full court press here and ramp up Metoclopramide and/or, in short order, transition to Gimoti.

In academic medicine where we see the patients who have not done that well out there, patients come to me because they've either failed medical therapy, they believe, or they've heard that there's other options and it's up to me to try to establish have you really failed medical therapy or not and do you deserve a second chance?

And so I think at the academic level, and these are patients who are thought to be moderate to severe who come to us to be referred to us, they're not manageable by simple measures, we would probably try Gimoti from the beginning because we want to guarantee absorption and guarantee that we get a result quickly and try to impress the patient that we know what we're doing and we have other tricks up our sleeve. So we would go straight to Gimoti at the more academic level.

Of course, we have GI fellows being trained every day. GI fellows are going to be graduating every year and they will have learnt now that Gimoti's available, they will see

people like me use it and they'll be going into groups and going into practice in this country and they will have to educate the members of their group who have been trained in the last five to 25 years that there's a new kid on the block and we need to go to it.

So GI wants to get results much more quickly than primary care or practicing GI guys in town, but overall, the practicing GI guys in town learn that there's a new kid on the block, that the academic guys are using it, it's being discussed at meetings, people who do the talks around the country like myself and others are proposing it, are promoting it, are endorsing it and by osmosis, the word gets out.

And so medicine is about osmosis and about believing that something works because the experts use it and it's safe and so they will start seeing that example, start seeing that blueprint and it will evolve. So that's the job we have, is to really promote the qualities and benefits of Gimoti, highlighting the fact that this can overcome what may be perceived as a treatment failure or sub-optimal approach or not totally improved and overcome that.

Knowing that we do have to work under the umbrella of a three-month approval and that even during that three months, we have to monitor for the usual culprits or the usual bad guys here, the tremor, the CNS side effects. Although not reported in the clinical trials by Evoke [Pharmaceutical], still on peoples' minds.

Yale Jen: Okay. Great. That's very, very, very helpful and I think we do have a bunch of questions by investors. So maybe for the next 10 minutes before we wrap up, we probably address some of the issues came from them. So Matt, would you mind maybe ask some of those questions?

Investor Questions and Answers

Mathew Moschovas: Yes. Of course. Thank you, Yale. This is Matt Moschovas here from Laidlaw and, again, thank you all for joining the call this afternoon and thank you for the questions that you submitted. For the sake of time, we got over 75 questions, so we chose a handful that we found to be most relevant for Dr. McCallum to answer.

With that being said, Dr. McCallum, the first question is in relation to the product effectiveness. One investor has asked how significant of a treatment differentiator is the nasal delivery of Gimoti compared to an oral delivery Metoclopramide tablet or quick dissolving tablet?

Richard McCallum: Yes. Well, the quick dissolving still has to get absorbed in the duodenum. It's a nice trick for elderly patients who have dentures or trouble swallowing, but it doesn't bypass what's called the first-pass liver metabolism and getting into the bloodstream. So Gimoti has reached a new level of being able to achieve and guarantee absorption regardless of the status of the stomach, your vomiting status, your nausea level where you don't – you feel you can't really swallow anything.

So it's a major advance and based on blood levels, we know that you get a quicker blood level and it remains sustained. It remains sustained over the time period between doses of Gimoti and achieves the same sustained, if not slightly higher, blood levels than the orals in a normal subject.

Now, we have not studied or there's no available data on blood levels in gastroparetics where we assume oral Metoclopramide would miserably fail and whereas the Gimoti would be sustained and continuous. So I don't think there's any question this is an advance in therapy. No question about that.

Mathew Moschovas: Okay. Second question here is around possible other indications for Gimoti. An investor states that Metoclopramide is used in a number of indications aside from gastroparesis. Are there any additional indications besides gastroparesis where you see Gimoti could be used?

Richard McCallum: Well, Metoclopramide and Gimoti are working 50/50 as an antiemetic. In a given day, if I were to carry out some high-powered microscopic investigation, it's working in the brain and the stomach. There's no dominant player. So Gimoti's an antiemetic. So I could use it from anything from hangovers to chemotherapy to taking narcotics to sea sickness, motion sickness, anything. So it's an antiemetic. Any cause of nausea, I can use Gimoti.

As far as its other prokinetic properties, yes, there's a host of things where the stomach and the small bowel for that matter, but it mainly works in the stomach, may be slow. It can sometimes supplement gastroesophageal reflux where patients have a slower stomach and they don't empty the food at night, so they wake up with heartburn. You can take it before dinner to try to supplement PPIs or the usual treatment for reflux.

We use it in people who have postoperative – in the hospital, may have nausea or postoperative nausea from ileus or narcotics after surgeries. It could be used in that setting. It could be used really, as I said, anywhere where nausea is involved. It's an antiemetic as well.

Mathew Moschovas: Great. Thank you for that. Third question has to do with potential other doses for Gimoti. An investor asks would a lower dose of Gimoti add any value?

Richard McCallum: No. I don't – I don't think that. The side effect issue was never an issue in the trials. It was extremely well tolerated. There's no red flags. So I don't think you'd want to sort of waste time fiddling around with those doses. I think the company did some very good Phase 1 work on pharmacokinetics and, no, I think we're on target.

You may – you may argue that three times a day, maybe you could start off a bit more gingerly at twice a day and get your feet wet and not push all the buttons. That would be – that would be acceptable. It may be after a month or so when the patient's doing well, you could say, gee, let's skip one dose, see how you're doing. Again, we've not seen a

pressure to do that because there's no side effect profile we've seen and, quite frankly, these folks, it's not like a touch of heartburn.

Gastroparesis can limit your quality of life, limit your ability to work. Nausea is a terrible symptom. Nausea is the most underestimated and under-respected symptom in GI. We call it the – for those of you old enough to know about a comedian called Rodney Dangerfield, we call it the Rodney Dangerfield syndrome. I get no respect. Nausea gets no respect. So we tend to be very aggressive.

Mathew Moschovas: Thank you for that. This next question is in relation to feedback that you've received. An investor asked what has the feedback from patients of Gimoti been? Has it made their diabetic gastroparesis condition more manageable than taking pills or ODT and has it avoided and prevented expensive ER visits, thereby saving a significant amount of money getting hospitalized?

Richard McCallum: Yes. So that's going to be kind of the next step. I've talked to about one or two patients informally and they seem to be better and they're taking it, but as far as are we going to stop ER and hospital overhead over the next 12 months, it makes good sense that if you're feeling nauseated and maybe contemplating a hospital visit because the oral medicine will likely not be absorbed or will be vomited, you can take Gimoti knowing that I won't be vomiting this medicine back.

It's going to work in 15 to 30 minutes. The nausea will start getting better. I can avoid an ER visit. So we would hope that that data will come out, but I don't have access yet to sort of my patient scenarios at this point, but we are – we are obviously hoping that that will be a selling point, that you can stay home maybe for the day.

You may not feel like working, but you could stay home and take your Gimoti, drink liquids and just hydrate and sort of tough it out that day and avoid an ER visit where all they're going to give you is IV Reglan and, quite frankly, the blood level for IV Reglan is not much higher than the dose – the blood level achieved by nasal spray Gimoti. So it's not day and night.

Mathew Moschovas: In addition to that, do you see Gimoti becoming the standard of care and replacing the much cheaper pill or OFT form for all cases of diabetic gastroparesis?

Richard McCallum: Yes, I see that evolving. I mean, we want to start – we want to start strong and make it different. We've had the same old story for – I told you. It's been approved – Reglan was approved in the early 1980s. So yes, we've been 40 years with Reglan and I think everyone's interested in trying to look better and have a more aggressive strategy and I think just having that sort of upbeat approach that we've got a good drug for you and make the patient feel that we have a higher confidence level that you're going to do well.

It's no question that it will be the drug of choice for GI doctors. As I said, the average primary care doctor will probably eventually get the patient back. Some GI doctors start the treatment and say, well, we've made the diagnosis, we've got the treatment plan and I'm going to refer her back to the diabetologist who sent her to me or the primary care doc who sent her to me.

And, yes, by osmosis they get the message that the GI docs are the experts in town and they're using this new drug, new route of treatment and we're going to – we're going to tag on, we're going to be giving this prescription, we're going to be refilling it because the patients have been – will be sent back to us eventually. GI docs don't tend to maximize long-term care. They tend to make the diagnosis, get a treatment plan and refer the patient back to the referring doctor. So it will go down – trickle down stream and the word will get out.

Mathew Moschovas: Great. Thank you for that. That is all the questions that we'll be asking for now. At this point, I will turn it back over to Yale. Yale?

Yale Jen: Okay. Great. Thanks a lot, Matt, and I think we are reaching to the – to the ...

Luke Kottke: Yale, it's Luke. I just wanted to know if you guys had any perspective on the tardive dyskinesia TD black box warning or if Dr. McCallum might have any information on that at all.

Richard McCallum: On dyskinesia?

Unidentified Company Representative: Yes.

Yale Jen: [On] dyskinesia.

Richard McCallum: In dyskinesia ...

Luke Kottke: Is that a kind of – is that a discouraging adoption, the black box warning of the tardive dyskinesia?

Richard McCallum: Yes. Yes. Yes. So as I say, I use the most Metoclopramide in the country. I use it like water and a lot of this unfortunately was a – is a misperception. Doctors, primary care doctors were filling Reglan monthly, their PAs were calling the pharmacy, giving whatever six-month refills and patients were not coming in and being seen. I've never had a – had a case of tardive dyskinesia in my life and I've treated thousands of patients.

The reason why tardive dyskinesia got started was essentially malpractice. The patient was deserted, was not monitored, were not seen frequently. The family was not informed and if the patient develops twitching, tremoring, tongue movements, quivering, then this is a sign of early dyskinesia, you should call me and stop the drug. That word never got out.

So this figure that's quoted, typically by psychiatrists who think it's even more dangerous, this figure is highly inflated and erroneous. If physicians do their job and nurse practitioners do their job and patients are seen at some interval and monitored and the family is informed from day one, very carefully informed on day one, this is a 15-minute office discussion about the side effects of Gimoti. It's not you'll love this drug, good-bye, I'm busy. That's not going to work.

The responsibility of the doctor and the PA is to inform the patient about early side effects or warnings. If those things are done, which is what's supposed to be done by a good doctor, really tardive dyskinesia is vanishingly rare, but it's already too late. The horses have left the barn. It's sort of teaching for medical students on. For those of us who use the drug, know the drug, we respect it, but it's not a dangerous drug, but because of the negativeness caused by basically malpractice, we have this issue.

We have to address it, we have to teach it and make it very clear that this drug is safe and there's a rare percent of patients, if mismanaged, deserted, not followed and the drug has continued for months without being monitored, something might happen, but that's not going to happen if you inform the patient from the beginning and we have this three-month window.

Even after three months, it won't be that Gimoti, in the future, is going to be stopped like one morning, I'm going to call you and say it's over, Mrs. Jones. You're one minute over three months. That's not going to happen. If Mrs. Jones is doing well on Gimoti and has no side effects, just like with Reglan, we will continue the drug based on a risk-benefit ratio. We have no options and gastroparesis is a bad disease.

So we're not just going to play games and say, well, good luck, Mrs. Jones, we're going to stop everything. Maybe we'll start the clock running again next month and we'll get another three month window. No, we don't do that. We talk to the patient, examine the patient, there's no side effects, the disease is worthy of treatment, diabetic gastroparesis doesn't go away over time, then we're going to continue it.

That's not going to be something we're going to talk about day one, but this is reality. We are treating a – it's like treating hypertension. This is long-term maintenance. Things don't get better alone without some treatment. So that needs to be discussed. Primary care doctors are a victim of reading the box warning and they believe it. For those of us who know what went into the box warning, we know it was basically malpractice. Doctors did not take their responsibilities appropriately.

Yale Jen: Okay. Great. And I really appreciate that. I think we have run almost all the questions and we know that pretty much we are reaching an hour mark. So, Dr. McCallum, we really appreciate you come to this presentation – to this discussion and provide your deep insight on various aspect and the real-world experience of using the drug and we thank you for attending and look forward have chance talking to you in the future in different venues as well. So thanks a lot well.

Richard McCallum: Thank you and thank our colleagues on the call, particularly our Yankees fan. He may need to get some Prozac. We're going to have to see what lies ahead.

Luke Kottke: Well, Gary Sánchez just hit a two-run home run, Dr. McCallum. So we're in good shape so far. Really appreciate your time and thank you to everybody else who took some time out of their day to listen today. Feel free to call the folks over at Laidlaw with any questions you have and thanks again, Dr. McCallum. Have a great day.

Richard McCallum: Yes. It's a pleasure, guys. This is a great new era in the gastroparesis world, so it's good news.

Luke Kottke: Absolutely.

Yale Jen: Thank you very much. I appreciate it.

Richard McCallum: All right. Thank you.

Yale Jen: Thank you.

Luke Kottke: Thank you, operator.

Richard McCallum: Bye-bye.

Operator: Ladies and gentlemen, this concludes today's conference call. Thank you for your participation. You may now disconnect.