MELANIE WEST, MODERATOR: Good evening and welcome to our webinar this evening my name is Melanie West and I am the current Chair of the ATA Board of Directors as well as acting Executive Director. I sincerely hope you are enjoying our 2016 webinar series. If you are, “make some noise” and share them with a friend, co-worker or family member. Help others to understand the symptoms of tinnitus and hyperacusis and why treatment options are so important. Tonight we will hear from two experts about tinnitus and Pharmacology – specifically what drugs and medicines have been tried for tinnitus treatment as well as what future medicines may be targeted to treat tinnitus. I want to be clear that ATA does not endorse or recommend any particular treatment or product. What you will learn tonight is for educational and informational purposes only and is intended to provide you with an overview of what types of drugs have been tried for tinnitus management and what has been learned from those trials. So please do not mistake the presentation for an endorsement of any kind for any particular drug therapy. ATA remains committed to curing tinnitus by funding research and, in fact, one of our presenters this evening, has recently been funded by ATA to look at new drug targets for tinnitus relief. So tonight’s topic is particularly relevant to the research that ATA funds and believes is promising.

We are fortunate this evening to have Dr. Michael Hoffer, from the University of Miami Miller School of Medicine who is also current member of ATA’s Scientific Advisory Committee and Dr. James Kaltenbach, from the Cleveland Clinic who is a former member of ATA’s Scientific Advisory Committee to share their expertise on pharmacology as it relates to tinnitus. We also have Sal Gentile, an ATA member who will share his tinnitus experience and Jennifer Born and Jodi Asmus from the ATA staff who will be talking about ATA and helping to facilitate the webinar tonight. But before we begin I’d just like to go over a few housekeeping items as well as direct you to some of the functions you may be asked to use during the course of the webinar on your control panel.

During the webinar you will be asked to answer a poll. To answer the question simply click your answer with your mouse or if you are viewing the webinar on a smartphone or tablet by using your touch screen. If you are on the telephone, you will not be able to answer these questions.
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At the end of the formal program there will be an opportunity for a Question and Answer period. If you would like to submit a question, please use the question feature in the control panel. Due to limited time, we will not have an opportunity to have everyone’s question answered but please do submit. We may be able to use them in future webinars or in the Q and A column in our magazine, Tinnitus Today.

I would also like to address some features in your control panel. You are in control of how you will view the webinar. You have the ability to make the presentation full screen or not and control where you view the webcams on your screen. You may enlarge the screen by pulling down on the notched area on your screen or by pulling the corners of the video. When slides are being shown the video of the speaker view will automatically become smaller – this you cannot control - but you will still be able to see the presenter. Please take a moment to familiarize yourself with these features – they will come in handy as the program progresses.

Before we get to our pharmacology experts, I’d like to introduce you to Jennifer Born, ATA’s Program Director. Jennifer has been with ATA since 2006 and has worked for the organization in various capacities. I’d like to have her tell you a little bit more about ATA’s history and programs – Jennifer.

**JENNIFER BORN:** Thank you Melanie and thank you all for joining us here this evening. As Melanie mentioned, I have been with ATA for nearly 10 years. During that time, I have learned a lot from our members – many of you in the audience tonight - that medications for tinnitus is one of the most frequently asked about and frequently sought after pieces of information that people with tinnitus and hyperacusis ask about. Not only are you interested in what kinds of medications you can use to get tinnitus relief, but you also have concerns about what drugs to stay away from for fear of making tinnitus worse. When ATA was first founded by Jack Vernon and Charles Unice in 1971, those kinds of questions didn’t have answers. This is precisely why after establishing ATA, Jack and Charles made a
decision to make both education and research founding principles of how ATA would serve the tinnitus patient community. Because of that – ATA has directly contributed hundreds of thousands of research dollars toward advancing science in the area of pharmacology.

ATA’s mission has evolved over the years and just recently our current Board of Directors worked diligently on a new mission that encompasses more of what we heard our members telling us they wanted from ATA. This mission guides everything that we do at ATA and while being updated to reflect the current state of tinnitus research and treatment, remains true to the core principles that Jack Vernon and Charles Unice envisioned for ATA in its humble beginnings. If you haven’t seen our new mission, it is as follows: Improving the lives of people with tinnitus and hyperacusis by providing hope of a quieter future through education, advocacy and research toward a cure.

I think you will find that tonight’s presentations, particularly reflect that mission as well. As you know the talks from our experts this evening will be focused on medications that have been used to treat tinnitus and their degree of success as well as possible future medications. Before we get to that – I want to take a poll of our audience to find out how many of you have personal experience with medications for tinnitus.

**Q: Have you taken or do you currently take medication to help manage your tinnitus?**

**Answers:**

Yes, a prescription exclusively to manage my tinnitus.
Yes, a prescription in combination with sound therapy to manage my tinnitus.
Yes, I have tried an over the counter medication for tinnitus.
Yes, OTHER.
No, I don’t use a medication to manage my tinnitus.

Whatever your experience has been with medications for tinnitus, I know that tonight you will learn much that you didn’t know before about this important, exciting and hopeful area of research.
MELANIE WEST, MODERATOR: Thank you Jennifer for that information about ATA’s mission, evolution which absolutely includes, and will continue to include, advancing research in the area of pharmacology.

Now I’d like you to turn your attention to the main event. Our first speaker is Dr. Michael Hoffer. Dr. Hoffer has been working with tinnitus patients for 20 years. He is an otolaryngologist at the University Of Miami Miller School Of Medicine in Miami, Florida and is affiliated with Naval Medical Center San Diego. He received his medical degree from the University Of California San Diego School Of Medicine and is board certified by the American board of Otolaryngology-Neurotology and the American Board of Otolaryngology. He is a current member of ATA’s Scientific Advisory Committee and has expertise in tinnitus in military populations and co-morbid conditions like traumatic brain injury. He will share with us information about what medications have been tested for tinnitus treatment and the varying degrees of success. It’s my pleasure to introduce Dr. Michael Hoffer.

MICHAEL HOFER: Hello everyone and thank you Melanie for that introduction. I am Michael Hoffer and it is my pleasure to discuss with you tinnitus pharmacology and examine medications currently being utilized to treat patients with tinnitus. We’ll also learn a little bit about the varying degrees of success these medications have had in treating tinnitus.

Slide Two

I just want to say that I have no financial interests to disclose, but off –label use of medicines will be discussed. In fact virtually all of the uses of these medicines for tinnitus are off label. The views expressed here are those of me – the speaker and not those of my employer the University of Miami or the Department of Defense for whom I also perform some work.

Slide Three

Tinnitus is one of the most frequent medical conditions. It is seen in one third of all adults and one of ten individuals has consistent tinnitus. In half of this group or 5% of the total population tinnitus is disabling. So that means 1 out of every 20 individuals is disabled by tinnitus and one out of three know what it feels like. These numbers are far higher than the incidence of most diseases many of which receive far more attention and far more funding.
Slide Four

There are a variety of different treatment options for tinnitus but they largely break down into these four groups. Treat the underlying health condition, utilized noise suppression, tinnitus therapy (in particular tinnitus retraining therapy), and medications. Our talk today will focus on medications.

Slide Five

Medications for tinnitus can be broken up into several basic groups. We will discuss benzodiazepines, anti-depressants, and anti-epileptics as groups of medicines and then turn our attention to Zinc, Gingko, and new generation sleeping medicines.

Slide Six

Benzodiazepines are one of the most common classes of medicines used in the treatment of tinnitus. As a class these medicines produce a sedative, hypnotic, and anxiolytic effect. Some of the most common agents include Xanax, Valium, Ativan, and Klonopin. All of these have been used both in trails for tinnitus relief and to treat individuals that suffer from tinnitus outside of trials. The main uses of these medicines include the treatment of anxiety disorders and insomnia. Side effects include drowsiness, cognitive issues, and the possibility of dependency. It should be noted that these medicines have a long half-life and so once they are taken the effects may not wear off for a significant period of time.

Slide Seven

Benzodiazepines are used in tinnitus to reduce the anxiety associated with the tinnitus. As for the actual ability of this class of medicines to treat tinnitus there is one trial showing the benefits of Xanax and one showing some benefits from Klonopin. It must be noted that these trials were not without flaws and most trials show no benefit from any medicines in this class. More importantly a number of studies reported that there was a rebound worsening of the tinnitus when the medicine was stopped.
Slide Eight

Anti-depressant medicines are another class of medicines used to treat tinnitus. This class of medicines is not truly a single type of medicine but rather a group of medicines with different mechanisms of action that are used to treat depression and a variety of other disorders. The agents are classified by mode of action into groups and common agents include Celexa, Paxil, Prozac, Elavil, Pamelor, Cymbalta, Effexor, and Trazadone. These medicines have many uses including depression, anxiety, and pain control. Side effects from these medicines are common and include mania, restlessness, and mood issues.

Slide Nine

The theory behind the use of Anti-depressants for the treatment of tinnitus is to treat depression associated with tinnitus. This however comes with significant side effects including dry mouth, sedation, and sexual dysfunction, which make compliance and tolerance difficult. Moreover, when we examine this class of medicines for impact directly on the tinnitus the Cochrane Review organizations looked at the literature and found insufficient evidence that use of this class of medicine improves tinnitus.

Slide Ten

Anti-epileptic Medicines are another common medicine class used in the treatment of tinnitus. These agents, at appropriate doses (often much higher than doses used in tinnitus treatment) have an anti-seizure effect. Common agents include Tegretol, Topamax, and Neurotin. These agents are used to treat seizure disorders and bipolar disorders. Side effects can be significant and include drowsiness, dizziness, mental slowness, and eye and liver disorders.

Slide Eleven

When examining the use of anti-epileptic medicines in the treatment of tinnitus the rationale is developed because these medicines are successful in treating chronic pain which some feel is an analog for tinnitus. However, no trials have shown a beneficial effect of this class of medicines on tinnitus. It should be noted that one of this class of medicines, Topamax, has been shown to be effective in the treatment of vestibular migraines. Tinnitus is one of the symptoms of this
disorder and it is possible that in treating the vestibular migraines with Topamax that the tinnitus might be improved but more study is needed in this area.

**Slide Twelve**

There is a class of new generation sleeping medicines used in individuals who have trouble initiating or maintaining sleep. Well-known members of this class of medicine include Ambien and Lunesta. They are not without side effects that include dream issues in some users and dizziness. The main use of these medicines in tinnitus is to induce sleep when tinnitus is interfering with ability to initiate or stay asleep. There is no direct effect on tinnitus but better sleep may improve tinnitus tolerance. These medicines in contradistinction to the earlier mentioned benzodiazepines have a very short half-life so their effects wear off more quickly.

**Slide Thirteen**

Zinc is a dietary supplement and an essential element for proper body function. It is used for just about everything but really only indicated if total body Zinc is low. There are no proven benefits of this medicine in trials but it may help if Zinc levels are low.

**Slide Fourteen**

Ginkgo biloba is a Chinese herbal supplement with a variety of medicinal uses and a variety of uses as a food source. This medicine may have benefits for individuals with cognitive issue and dementia but there are no proven benefits in the treatment of tinnitus.

**Slide Fifteen**

There are several main issues with current medicines in the treatment of tinnitus. None of these medicines were actually designed to control tinnitus, moreover taking a pill for tinnitus, while it might help the tinnitus, will have systemic side effects and risks.

**Slide Sixteen**

In addition, current medical treatment for tinnitus includes a fascinating array of medicines. Such an array exists because one medicine does not work well,
because if one did we would not have so many choices. It is possible that a particular medicine might work on a particular individual despite what population statistics show, however the trial and error method of discovering this fact can be difficult for the patient and the providers.

In closing, I would say that currently, we do not yet know enough about tinnitus and its related conditions to say that a pill or other form of medication is widely available for its treatment. But as you will hear in Dr. Kaltenbach’s talk, research is helping to advance science toward new possibilities in this area. We may someday soon have a medication that can successfully treat tinnitus patients.

MELANIE WEST, MODERATOR: Thank you Dr. Hoffer for such an understandable presentation about what drugs have currently been tried to treat tinnitus. I know that many of our audience members may have had, or have personal experience with some of the drugs you have mentioned and I know they appreciate your overview of some of the concerns surrounding the varying degrees of success these drugs have in managing tinnitus.

As we have just learned, while drug therapy remains a promising area of research and a viable possible future tinnitus treatment, currently there are concerns about all of the medications that have been tried for tinnitus relief. This is one of the many reasons ATA remains dedicated to funding research to find new tinnitus management strategies and to further optimize existing therapies. Dr. Kaltenbach is going to tell us about the current research he has been involved with. This is an exciting area, but before we get to that – I’d like to bring back Jennifer Born to tell us about ATA’s history of funding research and why it is so important that we continue to fund research in search of a cure.

JENNIFER BORN, ATA RESEARCH/MEMBERSHIP: Thank you again Melanie. Since 1980 when we awarded our very first research grant, ATA has directly contributed over $6 million in “seed” grants to tinnitus investigators around the world. Our grant program consists of funding awarded to both students and to established researchers.

Once the grants are received, a rigorous peer-review process takes place by our esteemed Scientific Advisory Committee which, as evidenced tonight - is comprised of some of the most talented researchers worldwide who are working on understanding and developing treatments for tinnitus. Each grant is evaluated
through a set of criteria to determine its merits and ability to push science forward. The proposal must also fall into one or more paths of ATA’s Roadmap to A Cure – a document created by our SAC that outlines four paths of research – two basic and two clinical – that will ultimately help lead to new treatments and cures for tinnitus. Once the grants are reviewed and scored, the top-scoring proposals are then forwarded to our Board of Directors for funding consideration.

As Melanie mentioned, all of ATA’s ability to fund research comes from the generosity of our members and donors which consist almost entirely of individuals. That’s something that every ATA member should be proud of. So to those of you here tonight who are ATA members, thank you for your support of the research we have funded and for supporting our programs like these webinars.

For those of you here tonight who are not members, we invite you to join us. By becoming an ATA member you are directly supporting research that is leading to new treatments and cures for tinnitus. You will also get the added benefit of being able to see ATA’s exciting 2016 line-up of webinars which is included in the price of your annual membership donation. You will also receive Tinnitus Today, our magazine that is published three times a year which includes the most up-to-date information on tinnitus, research and treatments, patient stories and Questions and Answers with tinnitus health professionals. We have included the current issue of the magazine as a handout – you can click on your control panel at the bottom where it says “Handouts” and download the magazine at any time during this webinar. By becoming a member you also gain access to the Members section on our website which has 30+ years’ worth of archived Tinnitus Today magazines, the Progressive Tinnitus Management Program and an archive of all ATA’s webinars that you can watch at any time. Membership is just $40 annually and can be done easily online at ATA.org.

We look forward to continuing to work together with all of you toward a future without tinnitus.

Melanie, I’d like to turn the program back over to you to introduce our next speaker.

MELANIE WEST, MODERATOR: Thank you Jennifer for your helpful information regarding ATA’s programs. It is true that our members are and have always been
the backbone of this organization. So I would also like to extend my thanks to all of you.

Now we turn our attention back to medicines for tinnitus - but this presentation will be focused more on the mechanics of what we have learned about drugs and tinnitus through research, and what the future holds in this burgeoning area of tinnitus research and treatment. For this presentation I introduce to you Dr. James Kaltenbach from the Cleveland Clinic. Dr. Kaltenbach has been involved with tinnitus research since 1993. He received his Ph.D. in Biology at the University of Pennsylvania in 1984. After completion of his postdoctoral training in 1987, he joined the faculty at Wayne State University, first in the Department of Audiology, then in the Department of Otolaryngology (1995). He moved to the Cleveland Clinic in 2008 where he serves as Director of Otology Research in the Head and Neck Institute and Department of Neuroscience in the Lerner Research Institute. He has also served on numerous committees at the National Institutes of Deafness and Other Communication Disorders, the American Tinnitus Association, and the Association for Research in Otolaryngology. It is my pleasure to introduce Dr. James Kaltenbach.

JAMES KALTENBACH: Thank you Melanie – and thank you all for your interest in the topic of pharmacology as it relates to tinnitus.

SLIDE 1

In this presentation, I will discuss the search for tinnitus cures in the laboratory, past, present, and future. I will begin with a historic perspective of where this search has been and where it has brought us. I will then speculate on how this search seems likely to unfold in the foreseeable future. My hope is that this presentation will convey a sense that research in this area has shown great progress, particularly over the past decade. It is also my hope that by summarizing this progress, I will help give people suffering from tinnitus a feeling of optimism that the study of tinnitus holds much promise for the development of a cure in the years ahead.

Just a couple of quick footnotes before I proceed. 1) For those of you who may wish to read the script associated with this presentation, I have included the slide number both on the script itself and in the upper left corner of each slide. 2) You
will frequently hear the term ‘tinnitusolytics’ being used throughout this presentation. This word simply refers to treatments that have the effect of either reducing or abolishing tinnitus. I use the term here because it is far simpler than repeating the words ‘anti-tinnitus agent’ or ‘tinnitus-reducing drug’.

SLIDE 2

The search for tinnitusolytics has a long history that dates back to at least the early Egyptians. Documents from those times indicate the use of various infusions into the ear that included such things as oils, frankincense, tree sap, and honey. Practices of this type were also common in Ancient Greece and Rome and apparently continued for most of the next 2 millennia. A major turning point came fairly recently, (i.e., during the 1980s and 1990s) when the first animal models of tinnitus were introduced. These models allowed formalized study of tinnitus using the scientific method.

SLIDE 3

The availability of these models has had a number of important effects that have propelled the search for tinnitus cures forward. The most obvious effect has been the rapid surge in the number of scientific studies of tinnitus over the past 25 years. These studies have led to a better understanding of the abnormality that underlies tinnitus and the mechanisms by which it is induced. This, in turn, has resulted in identification of potential therapeutic drug targets. And with that has come an increase in the number of drug candidates that have been subjected to experimental test. Many of these candidates have proven effective in reducing or eliminating signs of tinnitus in animals. Drug discoveries, such as these, which have taken place in the laboratory setting have in numerous cases stimulated clinical trials in human subjects and these have begun to show promise in certain subgroups of patients.

SLIDE 4

Before I describe these drug candidates, I would like to show you what tinnitus actually looks like and what it is about the auditory system that needs to be treated. On the left side of this slide, we see normal activity that is recorded when an electrode is placed in an auditory brainstem center of an animal with normal hearing. You see the occurrence of trains of electrical impulses that seem to occur
at random. On the right side we see what activity looks like in the same structure of an animal that was exposed to an intense sound one month earlier. Here you can see that the impulses occur at a higher rate, and their heights are larger. This greater degree of neural firing is what we refer to as neuronal hyperactivity. This hyperactivity is widely believed to be one of the key changes that leads to the perception of tinnitus sounds because it resembles the increase in activity that is seen in normal hearing animals when sound is presented to the ear. In other words, the neurons are behaving as though they are responding to sound, even though there is no longer any sound present.

**SLIDE 5**

Where does such hyperactivity occur in the auditory system? The next slide shows the areas of the brain where hyperactivity has been observed in animals and human subjects with tinnitus. As can be seen, the abnormality is not just in one place but occurs at multiple levels of the auditory system. The earliest stage where this hyperactivity is found is down here in the cochlear nucleus. We also see hyperactivity in the auditory midbrain in nuclei called the inferior colliculi as well as in the auditory cortex, where sounds reach the conscious level.

**SLIDE 6**

As soon as this condition of hyperactivity was defined, scientists began asking whether it might be possible to turn down this activity pharmacologically and thereby abolish or at least reduce the severity of tinnitus. Now, after about a decade of research with drug effects in laboratory experiments, we can answer this question in the affirmative.

**SLIDE 7**

But to understand why we believe this, we need to take a look at the current theory of what causes auditory neurons to become hyperactive. On the left is shown a neuron that is quiet, meaning that its activity is at the low end of its firing range, as shown by the trace in the dark box at the bottom. This state of low firing is due to a healthy balance between two sets of inputs to the neuron from other neurons: One set, shown in blue, is excitatory. By excitatory, I mean that these inputs cause activity to increase (i.e., to be excited). If this were the only source of input, the firing rate of the neuron would be high. However, this excitatory input
is counterbalanced by a similar share of inhibitory inputs, shown in red. These latter inputs cause neuronal activity to go down (that is, to be inhibited). The result of this inhibition is to counter the increase in activity caused by the excitatory input. And the end result is a low rate of resting activity. This low resting activity is what a neuron would normally show in the absence of sound.

On the right hand side of this figure, we see what happens to a neuron after the ear has been exposed to too much noise. Here, the neuron shows a shift in the balance of these two types of inputs: excitatory input (blue) is greatly increased, while inhibitory input (red) is greatly reduced. This produces a shift in the activity pendulum. Because there is weaker inhibitory input and stronger excitatory input, the neuron shifts into a higher state of activation causing it to fire more rapidly, as shown by the trace in the lower right. This is the condition of hyperactivity, and it is widely believed that this is what underlies tinnitus.

**SLIDE 8**

With this theory in mind, scientists have entered the 21st century thinking about new and different ways to quiet neurons. They have developed two therapeutic approaches. The **first** works at the level of synapses. Synapses are the connections between neurons and it is where neurons excite or inhibit each other. Studies at this level are performed with the goal of restoring the normal balance of excitation and inhibition that keeps neural activity low. The theory is that a healthy balance of these two input types could be restored by using drugs that either increase the amount of inhibition or decrease the amount of excitation. The **second approach** is to work at the level of ion channels. This approach bypasses the synapses and work at the level of the cell membrane where ion channels are located. Ion channels are critical to a neurons ability to fire impulses because they are the sites where electrical signals are generated.

**SLIDE 9**

The next three slides summarize the results of these therapeutic approaches: The studies have identified no less than 11 drugs that work at the synaptic level which show promise in experimental studies of tinnitus. Some of these drugs were specifically selected because of their well-known ability to activate inhibitory synapses, either directly or indirectly. Five drugs, including vigabatrin, gabapentin, taurine, carbachol, and pilocarpine fall into this category and all five have been
found to have tinnitusolytic effects in animals. The other drugs were selected because of their well-known abilities to block excitatory synapses. Six drugs were found in this category to be effective in reducing tinnitus in animal studies, including memantine, ifenprodil, MK-801, Gacyclidine, 7-Chlorokynurenate, and AM-101.

**SLIDE 10**

In addition, some success was also experienced in studies targeting ion channels. Three drugs that fall into this category include lidocaine, retigabine and AUT3. Lidocaine blocks sodium channels and by doing so, blocks impulse generation and nerve conduction. Two others, retigabine and AUT3, promote the opening of potassium channels.

**SLIDE 11**

Now putting these together, you can see that we have a list of some 17 agents that have been shown to be effective tinnitusolytics in animal studies. These are divided here into three categories based on what they have been shown to do. The first group of drugs have been found to reverse behavioral evidence of tinnitus in animals. This means that evidence that animals have developed tinnitus-like percepts following things like noise exposure or ototoxic drug treatment is weakened after the animals are treated with each of these drugs. The second category includes drugs that reverse tinnitus related activity. This means that the condition of neuronal hyperactivity, which I mentioned earlier, and which consists of increases in resting activity in silence, can be reduced by treating the animals with these drugs. And lastly, we have drugs that prevent induction of tinnitus following noise exposure. These drugs have been found to protect animals from developing tinnitus after exposure to loud sound.

**SLIDE 12**

Now it is fair to ask, do any of these 17 agents that work in animals also reduce or eliminate tinnitus in human subjects? **Six agents** mentioned are still awaiting clinical trials in human subjects, so their clinical potential has not yet been determined. These include Ifenprodil, 7-Chlorokynurenate, Taurine, Retigabine, AUT3, and Sildenafil.
**SLIDE 13**

*Four agents* mentioned (Vigabatrin, carbachol, MK-801 and Lidocaine) cause dangerous side effects when administered systemically. Vigabatrin causes vision loss, while carbachol and lidocaine both have side effects on respiration and heart rate. These side effects limit their clinical usefulness to intratympanic tests, meaning that the drug cannot be given intravenously or orally, but can be injected into the ear cavity. When these agents are tested in this way, they have been found to have some efficacy in reducing tinnitus symptoms. Unfortunately, the effects are usually short lived. Despite these shortcomings, the use of these agents has been extremely important in providing a proof-of-concept that it is possible to eliminate or reduce tinnitus by using drugs that target mechanisms suspected of causing tinnitus.

**SLIDE 14**

*Two agents* (ginkgo extract [EGb-761] and gabapentin) have been tested in clinical trials but have yielded mixed results. Some studies suggest that these agents do not have any more efficacy in humans with tinnitus than a placebo. Gabapentin works well in a subset of patients with tinnitus from vascular compression but not in the larger population as a whole. *Another agent*, memantine, failed to show evidence of a tinnitolytic effect when taken orally. *Three others* have been tested intratympanically and shown to have tinnitolytic effects, but the effects for pilocarpine and gacylcidine were generally short lived (<72 hours). However, the tinnitolytic effect of AM-101 lasted up to 90 days.

**SLIDE 15**

In view of these accomplishments, what can we expect to see on the tinnitus horizon in coming years? We should expect to see clinical trials with agents that showed efficacy in animal studies. In particular, look for studies of NMDA receptor antagonists, such as ifenprodil or AM-101. We hope also to see follow-up trials with Taurine and Sildenafil, both of which completely or nearly completely reversed tinnitus in animals. And we should be hearing more about potassium channel promotors (Retigabine, and EGb-761) as preventative agents that protect against the damaging effects of noise exposure.
SLIDE 16

Lastly, we can expect to see an increasing effort to define drug targets that do not cause major side effects when activated. You should stay tuned for more about cholinergic receptors that go beyond the unsafe and dangerous drug carbachol which targets all cholinergic receptors. Studies presently underway are examining effects of drugs that are selective for individual subtypes of cholinergic receptors. These have the potential to be far superior to carbachol, because some of these subtypes are found in more restricted areas of the brain and body and therefore do not have the powerful effects on the heart or respiratory system. These drugs are likely to have far fewer side effects than the more generally acting drug carbachol. We should also look forward to hearing about the effects of potassium channel modulators, such as AUT3 which has been shown to reverse tinnitus in animals.

SLIDE 17

I can summarize this brief review by stating the following: We have more knowledge than ever before about the mechanisms and substrates of tinnitus. Numerous drug candidates have been introduced for use in animals that are awaiting clinical trials. New drugs with more specificity are likely to be introduced in the near future that offer hope of relief from tinnitus with reduced severity of side effects. At some point in the more distant future, we can expect improvements in pharmacotherapy that will reduce tinnitus symptoms with minimal side effects. But because tinnitus has multiple mechanisms and multiple causes and profiles, it is reasonable to expect new drug therapies to be effective for specific subgroups of tinnitus sufferers who share common causes and symptoms, rather than for the more diverse patient population as a whole.

Thank you for your attention.

MELANIE WEST, MODERATOR: Thank you Dr. Kaltenbach for that encouraging presentation outlining what areas of the brain are being targeted for tinnitus drug therapy. Clearly research has made some excellent progress in this area and all of us in attendance tonight have hope for a possible future medication to treat tinnitus. One of the ways we are going to effect change is to “make some noise to silence tinnitus.” Share your story of tinnitus or hyperacusis with your doctors and
your Congressional representatives. Encourage them to vote for more funding towards tinnitus and hyperacusis research.

And now we have an ATA member who is willing to share his story in the same way we’d like you to share yours. Someone who has been through the trials of tinnitus and who has turned adversity into positivity. While it’s true that some people with tinnitus still haven’t found a treatment or therapy that works to help them there are some who have and we want to provide those stories to our audience to provide information that can help you as well as provide hope. I’d like to introduce Sal Gentile, a retired IBM executive who is also an ATA member, support group leader, fundraiser and avid bicyclist to share his journey with tinnitus with all of you.

SAL GENTILE, ATA MEMBER HIGHLIGHT: Thank you Melanie, and thank you all for listening. I have been challenged with tinnitus and hearing loss for the last 4 1/2 years. It started while celebrating my birthday - I was out with friends at a noisy restaurant. That night I could not sleep because I was hearing noises in my ears.

The next morning I when I awoke the sounds were worse. I seriously considered calling 911 thinking I had a brain injury. I couldn’t get out of bed and stayed there for a few days before realizing I had to get help. Previously I had been on anti-depressants for a General Anxiety and Panic disorder. I had successfully weaned myself from them and I thought I was having a relapse.

I went to my regular doctor and he diagnosed me with an anxiety attack. After seeing a dozen health professionals - the message that came loud and clear and cold was: “You have tinnitus, learn to live with it.”

That was not good enough for me, I wanted my life back. My psychiatrist insisted on putting me back on antidepressants but I refused because I wanted to keep moving forward – not go back.

I then found the American Tinnitus Association. I became a member and used their website to identify a seasoned audiologist and assistant tinnitus professor in my area. I spent 4 hours with him, and was diagnosed with high frequency hearing loss and tinnitus. He taught me how to disconnect from the noises by using sound therapy and white noise. I ordered a pair of hearing aids with amplification and sound.
To further deal with the anxiety I was experiencing, I also started keeping myself busy by taking long walks, spending long hours at the health club, and doing long distance bicycle rides. I continued Yoga, Cognitive Behavioral Therapy, and mindfulness meditation instead of antidepressants which I feared might interfere with the progress I was making with my tinnitus. Sound machines were placed in each room of my home, and I used a sound pillow to sleep. My wife was there to support me along with my two rescue dogs.

I slowly began to socialize again - I knew I was on the path to habituation. As part of this, I wanted to give back and help others so I became a volunteer for the American Tinnitus Association. I started a support group in Tampa, Florida where I lived then, and started one in The Villages, Florida where I live now. I also became involved with the Tour de Tinnitus bicycle ride – an annual fundraiser for ATA. I raised well over $20,000 on two tours and organized an event that raised approximately $6,000 in one evening. Being a volunteer for ATA and helping others with their tinnitus has been instrumental in managing my own tinnitus.

In closing I want to leave you with a saying that has helped me in my tinnitus journey: “Life is 10% of what happens to you and 90% how you react to it,” this is true with tinnitus as well. If you are struggling with your tinnitus – find something to help take your mind off of it – join a club, start an exercise regimen, or volunteer – but don’t be passive about your tinnitus – make some noise about it in your communities. In my experience it has changed my entire perspective on living with this condition.

MELANIE WEST, MODERATOR: Sal, thank you for sharing your experience and thank you for all you have done for ATA. I know those are just some of the many contributions you have made to ATA and the tinnitus community. Thank you for making noise about your tinnitus in a very positive way.

And now it is time for the Question and Answer portion of the evening. We are going to bring back up all of our speakers so that any question you have – whether regarding the research segment, or something specific about ATA can be answered accordingly. While we are doing that I just wanted to remind you that to submit a question, you need to use the question feature in your control panel. Please be sure to include who your question is for when you send it in. I will read each question aloud and then direct it to the appropriate individual on our panel.
QUESTIONS:

1) Many states have legalized medical marijuana and several states have legalized it for recreational use. Has anyone ever reported if using marijuana will reduce my tinnitus?

2) Dr. Kaltenbach, where did the term tinnitus come from?

3) Why haven’t the big pharmaceutical companies come out with a drug that treats tinnitus? Does ATA ever communicate with them to find out if they are working on it?

4) Anxiety is my biggest problem. I was not an anxious person before the tinnitus. Will anti-anxiety pills make the tinnitus worse?

5) When I go to sleep at night I wake up and can’t go back to sleep because of my tinnitus. Are there medications that will keep me asleep and won’t make my tinnitus worse?

6) I have seen several over the counter medicines available in my local drugstore for tinnitus. They make claims that they will make my tinnitus go away. Are these medicines I should try? And are they FDA approved?

7) I know that many medications list tinnitus as a side-effect. There are literally hundreds of drugs listed in the Physician’s Desk Reference interaction guide that list tinnitus as a possible symptom. If my doctor prescribes me one of those medications – should I avoid it at all costs because I have tinnitus? Will it definitely make my tinnitus worse?

8) I have read that Briviact, an epilepsy drug, may be helpful for tinnitus. What is your opinion of Briviact treatment for tinnitus?

9) I know that there are drugs being tested for intratympanic delivery as well as those in pill form. What are the benefits and disadvantages of each of these different kinds of drug delivery?

We have time for one more question – if your question wasn’t answered please be sure to attend the next webinar as it may be one that is answered by another presentation or speaker, or we may use them in future issues of Tinnitus Today. Ok – the last question is......

10) How close are we to having a drug for tinnitus treatment? If you had to give it a timeframe – 5 years? 10 years? More?

MELANIE WEST, CLOSING REMARKS: I want to thank you all for attending our webinar tonight on pharmacology. I hope you learned as much as we have and
that you have taken away from this webinar all of the concerns with existing tinnitus drug therapies as well as the hope for the future of a tinnitus medication. As stated, there are some concerns and cautions with existing tinnitus drug therapies, but there are great hopes for targeted pharmacological treatments and medication for tinnitus in the future.

Our next webinar will be on May 17, 2016 and it will be on hyperacusis. For those of you who don’t know, hyperacusis is an extreme sensitivity to every day “normal” sounds that can cause physical pain in severe cases. That webinar will feature Dr. Richard Salvi, from the University of Buffalo and Bryan Pollard, an ATA Board member who suffers from hyperacusis and who is the president of Hyperacusis Research, an organization he founded after he and his wife both developed hyperacusis to help further research on the condition. Hyperacusis is common in tinnitus patients and recently ATA has incorporated hyperacusis into its mission statement since there is a high correlation between the two conditions.

Registration will be available for that webinar soon at ATA.org. But, attendance is limited, so register early. In the meantime, go to ATA.org and check out the list of speakers for 2016 or refer to the back page of Tinnitus Today. If you are not a member, please consider joining and enjoying these valuable benefits.

Also, I want to thank our presenters again, Dr. Michael Hoffer and Dr. Jim Kaltenbach for volunteering their time and expertise tonight. We are truly fortunate to have had them with us here and to have them helping to further research in this important area of study.

Thank you again for joining us and we hope we will see you in May at our next webinar!