AURIS MEDICAL AG
NASDAQ: EARS

All EARS For a Transformative Year Ahead

Catalyst Packed Year

2016 presents Auris with a year filled with Catalysts, starting with what may be earlier-than-expected results submission for Auris’ AM-101 which has an SPA and could be approved earlier than 2Q16. But as we will discuss, the music worth listening to for EARS, is AM-111 which is due to have most of the ground work completed in 2016, with results expected as early as 2Q17.

While AM-101 certainly excites us and is a treatment which the acute tinnitus community has been waiting for; we believe that AM-111 is the true game changer. We don’t expect to see AM-111 accelerated, but we would certainly welcome any acceleration in the trials for the drug which is in phase 3 for its primary indications.

Analyst’s Rating:
Accumulate Buy

Price Target:
$5.38+ Per Share
Meaningful Science and Well-Designed Trials

The AM-101 as well as AM-111 trials have been extended and modified to present the most meaningful results possible, while staying true to primary indications. Worth noting is that Auris has led and conducted seminars in prestigious universities on this exact matter. We welcome this and it further gives us conviction and confidence to give a high probably of approval to AM-101.

On the AM-111 side, we believe that most sell-side analysts have unfairly set the probability too low for approval (20-35%, Leerink Swann, Jefferies, JMP). Our take on the preliminary AM-111 readout is that time is a major factor to short term recovery of some cohorts, and that is why placebo data can seem high, although always lagging 20% or more in efficacy, behind AM-111 drug readout.

Equity Cash Shelf

As of September 1st, 2015 Auris Medical Holding AG filed an F-3 Form with the SEC that provisioned an equity shelf of $100,000,000 in common shares with a floor price of $0.40 per share. This equity shelf will allow Auris to safely cushion future cash needs as it rolls out pending approval of AM101 and AM111. AM101 is projected to first post revenue streams in 2017, and AM111 is projected to begin revenue generation in 2019. Our projections show that Auris will most likely use approximately $70.02 million of this cash padding from 2015 to the end of 2019, and then cease usage thereafter.

Balance Sheet Security

In addition to their equity shelf, Auris Medical has a very large cash balance. This cash balance, with consideration of their equity shelf, is shown to be more than enough to cover current liabilities. Furthermore, Auris Medical does not operate with much leverage, with an average compound leverage factor of 1.19 from 2015 to 2020. Finally, our assumptions and dilution schedules do not consider the possibility of any debt raises. Although we welcome debt as a source of leverage and tax shield, we certainly don’t expect it.

Future Cash Flow Strength

Even under our most conservative revenue assumptions, Auris Medical is shown to be intrinsically valued, at a minimum of, approximately $4.50 per share. The average ranges of our DCF analysis turned over values around $5.50 per share. These values were generated using prudent sales assumptions, with consideration of AM-101 and AM-111 individually assessed. We are expecting AM-111 to be far more successful than AM-101 in generating net income, especially at launch. Further, we believe that in the long-term (beyond one year), Auris is worth well over $12 per share. We find this through terminal growth of the cash flow at 4%. Using lower multiples, we find terminal value to be beyond $8, at the very least. Our revenue and income assumptions are based on a weighted average cost of capital of 12-13, assuming Auris does not raise debt to better its capital structure.
Further indications and uses of AM-101?
Our current models do not consider any exotic, or off-label usage of Auris AM-101. In theory we believe the drug could find uses in music (musician use), skilled work involving loud environments (workers’ insurance), and new off-label indications such as Otitis.

Our Guess at AM-102, Long-term Tinnitus Candidate
Through doing some research, we have taken some educated guesses as to the actual candidate of the AM-102 and long-term Tinnitus portfolio. However, since this is a guess, we are not using it as a driver of our investment thesis. Our research is found after this thesis.

Valuation and Modelling Approach
We derive our PT of 5.38 minimum through a discounted cash flow analysis of AM-101 and AM-111 revenue potential. Our terminal growth DCF yields a price target of $11-13 with our same working assumptions.

Revenue Assumptions
Staying true to our conservative approach, we assume that Auris’ drugs take a while to reach the market, but gain adoption fairly quickly. As such, we assume that for its first year AM-101 will do anywhere from 2m-16m, with an adoption rate of 200-300%, tapered by 70% to make growth reasonable.

Balance Sheet Considerations
In our models we assume that Auris aims to burn 7-10m USD per year on the books, while covering the rest of the shortfall with the 100m shelf, diluting at par market price which we believe to be in the range of 3.00-4.00, with aggregate floor of .40USD, minimum. Thus, we use an accumulated deficits account to balance our model. This account grows at a reasonable rate, given our working assumptions.

Other Considerations
We assume that Auris AM-111 will be popular right-off-the-bat due to the partnership with Cochlear from Australia. We further assume that the Auris candidates for long term tinnitus and the rhinology portfolio does not come into the market any time before 2020, although this could very well change.

Risks To Thesis
The most significant risks to Auris are the FDA, execution and transition to an S&M (Sales & Marketing) structure, and enrollment lags in AM-111. While we are fairly confident on the name, we do accept that the AM-111 may be a difficult trial to gather complete data in. This is primarily due to the nature of the trial and indications being tested for primary endpoints: ASNHL - Autoimmune sensorineural hearing loss, Surgery Trauma and Sudden Deafness. However, we do believe Cochlear and Auris will execute these trials well.

The next pages highlight details of our research.
<table>
<thead>
<tr>
<th>Competitors &amp; Players</th>
<th>Mkt Cap</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otonomy</td>
<td>773M</td>
<td>Beyond tinnitus + Hearing loss Not necessarily acute (Trial cancel)</td>
</tr>
<tr>
<td>Autifony</td>
<td>Private</td>
<td>2 candidates Not necessarily acute</td>
</tr>
<tr>
<td>Neuromonics</td>
<td>Private</td>
<td>Device based Not necessarily acute</td>
</tr>
<tr>
<td>MuteButton</td>
<td>Private</td>
<td>Device based, pretty cool they are developing some headphone and waves to help w/ Tinnitus and to create a silence.</td>
</tr>
<tr>
<td>Merz Pharma</td>
<td>Private</td>
<td>Not necessarily acute</td>
</tr>
<tr>
<td>Genvec</td>
<td>33M</td>
<td>Regenerative medical approach to hearing loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Genvec sells delivery technology and has an income</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cash burn is minimal. Has been promoted in pump and dumps</td>
</tr>
</tbody>
</table>
AM-111 D-JNK1

<table>
<thead>
<tr>
<th>Overview</th>
<th>Relevant Links</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM-111 has received an Orphan Drug designation</td>
<td><a href="http://www.aurismedical.com/product-candidates/am-111">http://www.aurismedical.com/product-candidates/am-111</a></td>
</tr>
<tr>
<td>D-JNK-1 is the candidate drug, a synthetic peptide that inhibits JNK-1</td>
<td></td>
</tr>
<tr>
<td>JNK-1 causes cell death, and inflammation, loss of inner-ear hair, and</td>
<td></td>
</tr>
<tr>
<td>inflammation of cochlear neurons</td>
<td></td>
</tr>
<tr>
<td>AM-111 is administered in a single dose intratympanic injection into the</td>
<td></td>
</tr>
<tr>
<td>middle ear,</td>
<td></td>
</tr>
<tr>
<td>completely alleviates hearing loss effects</td>
<td></td>
</tr>
<tr>
<td>simultaneous administration of AM111.</td>
<td></td>
</tr>
<tr>
<td>POST-Noise exposure 1 &amp; 4 hours validated as significantly diff (treated)</td>
<td><a href="http://www.sciencedirect.com/science/article/pii/S0378595506001304">http://www.sciencedirect.com/science/article/pii/S0378595506001304</a></td>
</tr>
<tr>
<td>with AM111 (i.e. with treatment of AM-111 quickly following high noise</td>
<td></td>
</tr>
<tr>
<td>exposure, tinnitus was significantly decreased)</td>
<td></td>
</tr>
<tr>
<td>AM-111 will be entering two Phase III trials and preparing an additional</td>
<td></td>
</tr>
<tr>
<td>Phase II trial</td>
<td></td>
</tr>
</tbody>
</table>

Companies who have developed synthetic peptide orphan drugs:

**Aeterna Zentaris Inc.**

**Apitope**

**News Release On Development**

**Recent News**

**June 2015**
**Auris Medical & Cochlear to Collaborate on Clinical Trial with AM-111 for Otoprotection during Cochlear Implant Surgery**

Under the collaboration, Cochlear, the world leader in implantable hearing solutions will support preparations for REACH and provide expertise in cochlear implants and hearing preservation.

ASNHL - Autoimmune sensorineural hearing loss
Facts about Tinnitus

Over 45 million Americans struggle with tinnitus, making it one of the most common health conditions in the United States. 10 million people in the USA and 25–30 million people in Europe work daily in conditions that pose a potential risk to hearing [1].

The Royal National Institute for Deaf People estimates that a novel tinnitus drug could have a product value of US$689 million in its first year of launch [1].

According to the American Tinnitus Association, there are currently no FDA-approved drugs specifically for tinnitus [2].

Tinnitus is the most prevalent service-connected (SC) disability out of all Veterans, according to Veterans Affairs [3].

In a 2012 CDC study on general population (n=9364)

15% of all survey respondents in a CDC study experienced some form of tinnitus
67% of people reporting tinnitus had regular symptoms for over a year
26% of people reporting tinnitus had constant or near constant tinnitus
30% of people reporting tinnitus classified their condition as a “moderate” to “very big” problem in their life
Facts about Tinnitus (Cont.)

In a ATA survey of 1100 members:
What BEST DESCRIBES how tinnitus affects your day-to-day life?

![Graph showing various conditions and their impact on people]


Facts About Tinnitus (Cont.)

What is Tinnitus?
Tinnitus is the perception of sound without an external acoustic source. The name Tinnitus originates from the Latin word ‘tinnire’ which means ‘to ring’ in English and this comes from the fact that a constant high pitched ringing noise is the most common sound perceived by those who suffer from it. Other noises such as whistling, buzzing, and hissing have also been reported. Acute tinnitus lasts for up to 3 months

What causes it?
The most common cause behind tinnitus is inner ear damage particularly the cochlea. To understand tinnitus we must first understand exactly how hearing works in the first place. The process starts when mechanical waves (sound) traveling through the air is funneled through the outer ear canal in order to strike the ear drum. These waves cause the ear drum to vibrate. These vibrations are then amplified by the ossicles in the middle ear and transmitted to the cochlea. The cochlea is filled with a fluid that vibrates in response to input from the ossicles. Lining the inside of the cochlea are numerous tiny hair cells that then encode the waves in the fluid into electro-chemical signals that can then be transmitted to the brain via nerves for processing. Separate sections of these hair cells pick up different frequencies across the acoustic spectrum for human hearing which generally range from 20-20k Hertz. It is the immediate damage to the tiny hair cells lining the inside of the cochlea that are responsible for the majority of tinnitus cases. These hairs are fragile in nature and may be damaged if the cochlear fluid vibrates violently in response to a very loud noise. The hairs may be bent, broken, or completely sheared off. Damage to the hairs may impede or completely destroy their function of encoding sound signals. Corrupted signals are then sent to the brain which results in the classic high pitched ringing or some other annoying sound.

Effects
The amplitude of these signals can vary widely. Immediately after a traumatic shock the ringing will be the loudest and the most dominant sound that one will hear. It is the amplitude of the final ringing once the transient response from the initial trauma has settled that leads to the varying adverse physical and psychological effects in the individual. Commonly, ambient noise of the environment is enough mask the ringing but once the ambient noise is removed, for example, by studying in a quiet area or trying to go to sleep in a quiet bedroom, the ringing sound will dominate once again and this can be very stressful to the individual as it inhibits concentration or creates problems when trying to sleep. More severe effects occur when the ringing is loud enough to be heard at all times. Anxiety can easily develop as one may have fears of never having normal hearing again and it is impossible to not think about it when the ringing is always present. High pitched ringing is very annoying so individuals can end up being in an irritable state at all times if they do not get used to it. These changes in one’s mood can also come from the lack of proper sleep. This can make it very difficult to continue to socialize in a normal matter as their personality changes in combination with impaired listening skills. Depression is also experienced by those who simply cannot continue to function in a normal matter as a combination of anxiety, sleep deprivation and lack of socialization severely affects the individual’s mood in negative ways. Some may not even be able to go to work if their job demands high focus, strong social skills, or any other quality that is adversely affected from the persistent ringing or the sleep deprivation that can result from it.
# AM-101 Tinnitus Acute and Post

<table>
<thead>
<tr>
<th>Overview</th>
<th>Relevant Links</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM-101 for the treatment of acute inner ear (peripheral) tinnitus</td>
<td><a href="http://www.aurismedical.com/images/auris/downloads/auris_factsheet_AM101.pdf">Phase 2/Phase 3 Methodology Fact Sheet</a></td>
</tr>
<tr>
<td>following traumatic cochlear injury or otitis media (middle ear infection)</td>
<td></td>
</tr>
<tr>
<td>AM-101 contains Esketamine hydrochloride, an N-Methyl-D-Aspartate</td>
<td></td>
</tr>
<tr>
<td>(NMDA) receptor antagonist, formulated in a biocompatible and fully</td>
<td></td>
</tr>
<tr>
<td>biodegradable gel.</td>
<td></td>
</tr>
<tr>
<td>It is administered in one treatment cycle, comprising three intratympanic</td>
<td></td>
</tr>
<tr>
<td>injections over 3 to 5 days into the middle ear. From there the drug</td>
<td></td>
</tr>
<tr>
<td>diffuses through the so-called round window membrane into the cochlea.</td>
<td></td>
</tr>
<tr>
<td>AM-101 has the potential to be the first drug to gain approval for treating</td>
<td></td>
</tr>
<tr>
<td>acute (&lt;30 days) and post-acute (&lt;60 days) inner ear tinnitus.</td>
<td></td>
</tr>
<tr>
<td>Phase 3 trials scheduled to wrap up Q2 2016 (acute) and Q3 2016 (post-</td>
<td></td>
</tr>
<tr>
<td>acute)</td>
<td></td>
</tr>
</tbody>
</table>

## How AM-101 works

Acoustic trauma and other insults to the inner ear may trigger increased levels of extra-cellular glutamate, which in turn cause excessive activation of cochlear NMDA receptors. This process results in damage or killing of sensory cells and is thought to be responsible for abnormal spontaneous "firing" of auditory nerves, which may be perceived as tinnitus. Under normal circumstances, the NMDA receptors are thought to play no role in fast excitatory neurotransmission, respectively normal hearing. AM-101 is blocking cochlear NMDA receptors to suppress the aberrant excitation of the auditory nerve that is perceived as tinnitus.

## Development stage

AM-101 is currently in Phase 3 clinical development. We have initiated two pivotal clinical trials with highly similar design, one primarily in North America (Efficacy and Safety of AM-101 in the Treatment of Acute Peripheral Tinnitus 2, or TACTT2) and one in Europe, which we refer to as TACTT3.

## Efficacy

Notes on effects from Tinnitus Talk.... Tinnitus talk posts seem to make it easy to tell open label and placebo cohorts. One of the biggest concerns is that the Santa Monica center is shit. However, the latest posts in late October and early November are very promising. We note that OddV rated his tinnitus loudness at 8/10 and is now at 2/10 after 3 rounds. Shantelle stopped receiving it at 2nd rounds as she saw her problems completely gone. Shantelle makes a great point on tinnitus and resting: “Today I took a long nap with my 2 year old and when I woke up it was completely gone! This is the second time this has happened. This lasted for 3 hrs and it came back but its a 1...last night [though] I was extremely tired and I swear it was almost a 4! So weird.” Some cohorts report that although previous annoyances do come back, they are "less annoyed by them", by as much as 90%. Last week Thomas Myer, CEO of Auris addressed potential investors about their upcoming products. He mentioned that they made a preliminary examination of the incoming AM-101 trial data last Spring and it appears that the drug loses its efficacy for injections made approaching the 12 month mark, and therefore they are focusing their efforts on studying the 3-6 month period. It sounds like after 6 months the viability of the drug falls off. Therefore it
appears the best outcomes are for patients who have the injections in the first six months since onset. It may work past six months in some patients, but my takeaway is they are hoping to get approval for its use in the first six months.

In the TACTT0 clinical trial, patients with tinnitus following acute acoustic trauma or otitis media treated with 3 x AM-101 0.81 mg/mL showed a gradual and statistically significant improvement to Day 90 in patient reported outcomes (PROs) such as tinnitus loudness, sleep difficulties and overall tinnitus impact over placebo. At Day 90, mean tinnitus loudness improvement was 48%; 62% of patients reported much or very much improved tinnitus severity (unilaterally affected and treated). In contrast, results in the subgroup of idiopathic sudden deafness related tinnitus were inconclusive.

The dose regimen applied in TACTT0 (3 doses given over 3 consecutive days) showed larger therapeutic effect sizes than the administration of single doses or three doses over two weeks, which were evaluated in the TACTT1 clinical trial. This suggests that repeated and concentrated treatment with AM-101 provides the best treatment benefit.

**Safety**

Non-clinical toxicology and tolerability studies as well as the clinical program conducted to date show that AM-101 has no impact on hearing or balance, even at much higher doses than those needed for suppressing tinnitus.

Ketamine has been used clinically for decades as an anesthetic and analgesic. Esketamine is the S-enantiomer of Ketamine and was introduced in a small number of markets outside the United States as a more potent NMDA receptor antagonist with more favorable side effects than racemic Ketamine. We are using Esketamine in doses that result in systemic exposure several orders of magnitude lower than those seen when Esketamine is used as an anesthetic at clinically safe doses.

**AM101 has received a special protocol assessment:** Which means that that an uncompleted Phase III trial's design, clinical endpoints, and statistical analyses are acceptable for FDA approval. But Auris has stated it plans to pursue it until the end and be very thorough with the results and study.
AM-102 eCB Receptor Activation & Tinnitus

<table>
<thead>
<tr>
<th>Overview</th>
<th>Relevant Links</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target is separate from that of AM-101, and likely a CB-receptor.</td>
<td></td>
</tr>
<tr>
<td>The collaboration project draws on earlier work performed for Auris Medical by the Wolfson Centre for Age-Related Diseases at King's under the leadership of Professor Patrick Doherty and Dr Gareth Williams. (Wolfson trial listed Right)</td>
<td><a href="https://clinicaltrials.gov/ct2/show/NCT01969474?term=Cannabis+for+Tinnitus&amp;rank=1">https://clinicaltrials.gov/ct2/show/NCT01969474?term=Cannabis+for+Tinnitus&amp;rank=1</a></td>
</tr>
<tr>
<td>Wolfson Trial looked to use Cannabis capsules to treat non-acute-tinnitus, &gt;3 mo.</td>
<td></td>
</tr>
<tr>
<td>This is still in discovery stage, the molecules have not been named publicly</td>
<td></td>
</tr>
</tbody>
</table>

Prof. Patrick Doherty Background

The main interest of my lab is endocannabinoid (eCB) signaling in the nervous system, and this stems from our interest in regeneration, and in particular the role that adhesion molecules play in promoting axonal growth.

Our current focus is on the role of endocannabinoid (eCB) signaling in adult neurogenesis. eCB signaling, driven by activation of the CB1 and/or CB2 cannabinoid receptors, has widespread functions during development and in the adult.

Side Note (Not Prof. Doherty's research): Endocannabinoids released by a depolarized neuron bind to CB1 receptors on either pre-synaptic glutamatergic or GABAergic neurons, resulting in a respective decrease in either glutamate or GABA release. Limiting glutamate release causes reduced excitation,

Dr. Gareth Williams

Novel drug delivery systems based on inorganic and polymeric materials / The use of electrospinning in tissue engineering / Synthesizing new vaccine adjuvants to inculcate enhanced immunity / The application of in situ synchrotron diffraction to study pharmaceutical transformations
Research Appendix:

Notes on AM-102

1. Small molecules, so no protein based candidates
2. The Wolfson trial specifically mentions cannabis capsules, which means
the candidate is a phytocannabinoid (cannabinoids naturally occurring in the
cannabis plant) or a phytocannabinoid analogue. Can someone sanity check
me on this?
3. The press release specifically mentions its a RANGE of small molecules, so not just
one?
4. Small molecule makes sense, because what else could cross the blood-brain barrier?
P Doherty talks so much about the potential role of the hippocampus in attenuating
non-acute tinnitus.
5. P Doherty talks a lot about 2-AG and to a lesser extent AEA in his adult neurogenesis
research.
   a. So maybe the candidates are phytocannabinoids similar to these
      endocannabinoids.
   b. Or they can try to go the synthetic route?
   c. Or the other possibility is a compound that upregulates DAGL activity
5. Some companies to look at to quantify costs? Look for companies using
natural extracts or synthetic derivatives of cannabinoids. The $$$ info?!?

Viva Spain (using phytocannabinoids for multiple sclerosis):

Phytoplant Research (natural cannabinoid supply chain/extraction):
http://www.phytoplant.es/research-and-development/research-lines/

Loss of Retrograde Endocannabinoid Signaling and Reduced Adult Neurogenesis in Diacylglycerol Lipase Knock-out Mice
http://www.jneurosci.org/content/30/6/2017.long

Summary of Findings:
- Cannabinoids are observed to promote neurogenesis (regrowth of neurons).
- Loud sounds can disturb neural growth in brain
- Loss of function/disruption to areas of the brain (mainly hippocampus) can be
  responsible for tinnitus
- Perhaps cannabinoids can be used to alleviate tinnitus caused by neuronal disruption?
- Anandamide [N-arachidonoylethanolamine (AEA)] or
  2-arachidonoylglycerol (2-AG) are endogenous (naturally occurring) ligands (binders)
  to CB1 and CB2 cannabinoid receptors
- We don't exactly know what enzymes and how they make Cannabinoids in the brain.
- We do know DAG lipases (DAGL-alpha and DAGL-beta) are observed to make 2-AG
  in responses to circumstances where eCB signaling has been observed.
- Our results imply DAGL-alpha helps make 2-AG and is involved
in adult neurogenesis via CB1 receptors

**Backing evidence**

Wolfson Trial:
https://clinicaltrials.gov/ct2/show/NCT01969474?term=Cannabis+for+Tinnitus&rank=1

Wolfson Trial:
https://clinicaltrials.gov/ct2/show/NCT01969474?term=Cannabis+for+Tinnitus&rank=1

http://ir.aurismedical.com/phoenix.zhtml?c=253572&p=irol-

https://en.wikipedia.org/wiki/Blood%E2%80%93brain_barrier

Both Doherty and Gareth on research


Retrograde eCB signaling in the hippocampus is lost in mice lacking DAGLα

**Figure 4 (above)**

DSI in the hippocampus of wt, DAGLα−/−, and DAGLβ−/− mice. a, DSI is absent in DAGLα−/− mice. Average time course for eIPSC amplitudes after depolarization in wt (+/+), DAGLα−/− (α−/−), and DAGLβ−/− (β−/−) mice. DSI for each genotype is averaged across all cells sampled, four to five DSI protocol repeats per sample (+/+, n = 35; α−/−, n = 21; β−/−, n = 21). b, Peak DSI value is expressed as a percentage of depression in eIPSC amplitude after depolarization. Insets are representative recordings from a single CA1 neuron in wt (+/+), DAGLα−/− (α−/−), and DAGLβ−/− (β−/−) mice: the average of eIPSC traces (n = 4–5) just before
DSI versus the average of eIPSC traces at the peak of DSI (second trace after 5 s depolarization; \(n = 4\text{–}5\)). Scale bar, 50 ms, 400 pA. *** \(p < .001\), one-way ANOVA. Error bars indicate SEM. c, (RS)-Baclofen (10 μM) displays a robust inhibition of eIPSC in DAGLα−/− mice, as indicating here the eIPSC recordings of a single CA1 neuron in a representative experiment; each point represents the average of six eIPSCs.

Diacylglycerol lipase-α (DAGLα): key enzyme in the biosynthesis of the endocannabinoid 2-arachidonoylglycerol.[1] It catalyzes the hydrolysis of diacylglycerol, releasing a free fatty acid and monoacylglycerol.

**Tinnitus and the Hippocampus**

As tinnitus is often associated with sensorineural hearing loss, it’s easy to presume the cochlea is responsible for tinnitus. However, studies with Positron Emission Tomography (PET) have identified regions within the auditory cortex, the medial geniculate body, and the hippocampus, which demonstrated increased activation when tinnitus was volitionally increased via oral-facial movements in four selected patients. Of note, Salvi et al report that approximately two-thirds of all tinnitus patients may be able to modulate their tinnitus through volitional activity.

The authors note that the hippocampus is a major site of neurogenesis in the brain and imaging studies show decreased grey matter in the hippocampus (the hippocampus is associated with mood, memory, and spatial navigation) in patients with tinnitus. In lab animals, unilateral noise exposure (resulting in deafness) suppressed neurogenesis in the hippocampus and led to memory impairment. Salvi et al report peripheral damage can/does lead to neuroplastic changes in the central nervous system that may produce phantom auditory sensations (i.e., tinnitus).

**Programming of neural cells by (endo)cannabinoids:**

http://www.ncbi.nlm.nih.gov/pubmed/25409697 (behind paywall ask @euclid1767 for copy)

**Summary of Findings:**

- Endocannabinoids play a part in adult neurogenesis
- The Endocannabinoid family of small signalling *N*-acyl-amines and 2-acyl-glycerols, which typically contain an arachidonoyl moiety* play a role in nerve development but also maintenance and growth into adulthood
- eCB signalling not only promotes adult neurogenesis but also plays a part in regulating synaptic efficiency

**Related Papers to Analyze**

P. Doherty - Regional effects of endocannabinoid, BDNF and FGF receptor signaling on neuroblast motility and guidance along the rostral migratory stream.

Disclaimer:
The information and opinions in our reports are prepared by and are a product of Polo North Securities (“PNS”), a research division of Surge Traders and participates in discussions, research, and due diligence of various equities. PNS is a research team formed out of personal interest of seasoned investors. PNS is not a registered broker/dealer. The reader should assume that the members of PNS may have a conflict of interest and should not rely solely on our reports in evaluating whether or not to buy or sell securities discussed therein. Neither PNS or any of its members will be receiving compensation, directly or indirectly, for this report (other than from Surge Traders), and are not receiving compensation for the formation of opinions stated herein. PNS does not have a business relationship with any company whose stock is mentioned in this report.