**Neuromed Growth Plan**

16/12/23

Questions from Bryan Johnson (sorted by topic) / Review of key drivers part II

Working document

Version number 1.0

**Market (Volume and structure)**

1. **We need to verify that Nihon Kohden, Natus and Micromed share an existing $200M a year revenue market of clinical epilepsy services.**
2. The market for clinical epilepsy services in the United States is $200M. It is shared between two major companies (Natus and Nihon Kohden) and a handful of smaller companies. The breakdown is as follows:
   1. Natus - $100M (data comes from personal conversations with Jim Hawkins, CEO)
   2. Nihon Kohden - $50M (<http://www.nihonkohden.com/ir/library/pdf/nihonkohden_annual_report_2016.pdf)>
   3. Cadwell/Compumedics/EGI/Blackrock NeuroMed - $50M
3. The market for clinical epilepsy in the rest of the world is estimated to be $400M broken down as follows:
   1. Europe – $75M
   2. China – $200 M (internal study)
   3. Japan –
   4. India –
   5. South America -

Note: drug markets for epilepsy are: US (2 b USD), EU (1b), Japan (0.5 b), India and China (0.6 b)

1. **Are there similar service providers for DBS?**
2. DBS was initially used to treat the symptoms of Parkinson’s, but it has also been tried in other disease states. There are more and more companies coming online with other forms of stimulation for the brain and central nervous system. Below is a list of different applications:
   1. NeuroPace (RNS) – responsive stim for epilepsy
   2. DBS for Parkinson’s
      1. St Jude (Infinity)
      2. Medtronic (Enterra, Activa PC)
      3. Boston Scientific (Precision Spectra, Precision Plus)
   3. Spinal Cord Stimulators for Pain
      1. Stim Wave (Freedom Spinal Cord Stimulator)
      2. Nevro (Senza) – SCS Pain
   4. Vagal Nerve Stimulation
      1. Cyberonics - LivaNova (Aspiresr VNS therapy for Epilepsy based on heartrate)
      2. EnteroMedics (VBLOC) – VNS for obesity
      3. ElectroCore (GammaCore) – nVNS for headaches (non-invasive)
   5. Other applications for stimulation
      1. NeuroSigma (Monarch ETNS) – Trigeminal Nerve Stimulation for ADHA, Depression, Epilepsy
      2. Synapse (Neurx DPS) - Diaphragm
      3. Neuro Medical (Altius) – peripheral nerve
      4. Inspire (Inspire U2122) – Upper airway
      5. SPR Therapeutics (Smartpatch) – peripheral nerve
      6. NeuroMetrix (Quell or Sensus) – TNS sensitive nerves
      7. EndoStim (Endosim IPG) – esophageal/sphincter stim
      8. Imthera (Aura 600) – Upper airway
   6. Research applications:
      1. Increasing number of researchers
      2. Competitors: AlphaOmega, Neurostar
      3. BRM contacts: ca. 10, eg. Dr. Dees, USC, Dr. Gross, Emory, Cologne, Duesseldorf.
      4. Technical barriers: initial response positive on hardware, but needs proper front-end software. Considered partnership with AlphaOmega and Neurostar.
3. **We need to verify that this market is made up of roughly 3,000 refractory patients, of the estimated 300,000, that engage with hospitals to try and address their medical needs.** (see also: previous document: review of key drivers 161219)
4. 100-500,000 patients per year in the US: [J Engel, Jr.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Engel%20J%5BAuthor%5D&cauthor=true&cauthor_uid=24348103), MD, PhD, Why Is There Still Doubt to Cut It Out? [Epilepsy Curr](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3854719/). 2013 Sep-Oct; 13(5): 198–204. doi:  [10.5698/1535-7597-13.5.198](https://dx.doi.org/10.5698%2F1535-7597-13.5.198" \t "pmc_ext) PMCID: PMC3854719
5. 50 Mio patients suffering from Epilepsy worldwide, surgery now considered more cost effective and efficacious than drugs in Brazil, China, India and Turkey; World Health Organization. Atlas: Epilepsy Care in the World. <http://www.who.int/mental_health/neurology/Epilepsy_atlas_r1.pdf>
6. 2.4 Mio new patients diagnosed each year: in high income countries 30-50 cases per 100,000 people, in developing countries 7-14 per 1000. <http://www.who.int/mediacentre/factsheets/fs999/en/>
7. US: 3 Mio people with Epilepsy; 10-15% do not respond to drugs; Identification of Potential Epilepsy Surgery Candidates Updated: Dec 15, 2014; Author: Erasmo A Passaro, MD, FAAN;
8. **Following on the previous question, we need epilepsy patient data for major markets starting with US, China, Europe and India.** 
   1. **What are other big markets?**
   2. **How many are there?**
   3. **How # are refractory?**
   4. **Of refractory, what # of patients choose to do (drugs, resection, neuropace) and on what time lines?**
   5. **What is efficacy of procedures.**
   6. **How much do these areas pay for epilepsy procedures (what is the market size)?**
   7. **What are the different incentives in these markets.**
9. Huge growth in China; 9 Mio with epilepsy, 6 Mio with active epilepsy, 30% intractable = 1.8 Mio; 4.4 patients per 1000; 400,000 new every year; 10,000 USD per surgery, [Eur J Neurol.](https://www.ncbi.nlm.nih.gov/pubmed/19968706" \o "European journal of neurology.) 2010 Feb;17(2):189-93. doi: 10.1111/j.1468-1331.2009.02871.x. Epub 2009 Nov 24. Epilepsy surgery in China: past, present, and future. [Xu L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Xu%20L%5BAuthor%5D&cauthor=true&cauthor_uid=19968706)1, [Xu M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Xu%20M%5BAuthor%5D&cauthor=true&cauthor_uid=19968706).
10. [Epilepsy Curr](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4749109/). 2016 Jan-Feb; 16(1): 21–23. doi:  [10.5698/1535-7597-16.1.21](https://dx.doi.org/10.5698%2F1535-7597-16.1.21" \t "pmc_ext) PMCID: PMC4749109 Inspecting Resecting: Examining 20-Year Trends in Epilepsy Surgery [David Spencer](https://www.ncbi.nlm.nih.gov/pubmed/?term=Spencer%20D%5BAuthor%5D&cauthor=true&cauthor_uid=26900371), MD
11. [Neural Regen Res](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4145945/). 2013 Dec 15; 8(35): 3316–3324. doi:  [10.3969/j.issn.1673-5374.2013.35.006](https://dx.doi.org/10.3969%2Fj.issn.1673-5374.2013.35.006" \t "pmc_ext) PMCID: PMC4145945 Treatment of epilepsy in China: Formal or informal [Jianming Liu](https://www.ncbi.nlm.nih.gov/pubmed/?term=Liu%20J%5BAuthor%5D&cauthor=true&cauthor_uid=25206653),1 [Zhiliang Liu](https://www.ncbi.nlm.nih.gov/pubmed/?term=Liu%20Z%5BAuthor%5D&cauthor=true&cauthor_uid=25206653), M.D.,1 [Tao Chen](https://www.ncbi.nlm.nih.gov/pubmed/?term=Chen%20T%5BAuthor%5D&cauthor=true&cauthor_uid=25206653),2 and [Ruxiang Xu](https://www.ncbi.nlm.nih.gov/pubmed/?term=Xu%20R%5BAuthor%5D&cauthor=true&cauthor_uid=25206653)1
12. One Beijing hospital does < 7000 surgeries per year since 2005, Cost 1500 USD for surgery <http://www.bjtth.org/English/NeurosurgeryCenter.htm>
13. 300,000 candidates in India at any given point in time for surgery but only 420 surgeries per year (mostly in southern india) A survey of epilepsy surgery in India Ramshekhar N. Menon a, Kurupath Radhakrishnan, Seizure 26 (2015) 1-4
14. 6M people in Europe have epilepsy, 30% (1.8M) are drug resistant. 10% are good candidates for surgery, but only 3,000 elect to have surgery per year. Main problem is access to optimal care and often times a 1-3 year waiting period. Patients, families, GP, treating neurologists, and policy makers are not well informed about benefits & risks of epilepsy surgery.
15. **Same questions as previous point for DBS.**

**We need a follow up call to confirm specifics of what applications we are looking for (Parkinson’s, DBS products used for other applications,….)**

We have contacts/customers in this space, but do not have detailed data, due to the initial focus on epilepsy.

**Unmet needs (part II)**

1. **What are the unmet needs for clinical epilepsy? What do they want the most? What do doctors, technicians, hospital administrators, insurers and patients want?**
2. **Doctors**:
   1. More accurate identification of seizure location.
   2. Faster analysis of EEG data
   3. Better outcomes from surgery
   4. More biocompatible electrodes (less tissue response)
   5. Wirelessly monitor people and stimulate with higher channel count than NeuroPace or Medtronic (this would revolutionize things)
   6. The current model is very limited and many clinicians just accept things the way they are.
   7. Sometimes can be a long waitlist
   8. Drug pipeline is not working – many are being developed, but no game changers in a long time.
   9. Lack of social support with related partners (psychologists, psychiatrists, nurses)
   10. Surgery is very underused and appears to be stagnant
   11. If you can get to patients early likelihood for success is dramatically increased
   12. Starting to get very expensive with increased deductibles and out of pocket maximums
   13. Better ways to move ideas from academia to the clinic with meaningful expectations.
   14. Standardized acquisition and interpretation of data, better ways of sharing data.
   15. Better ways to measure patient outcomes. We currently look at very little concrete data.
   16. Shift towards epilepsy prevention, not just seizure (symptom) treatment
3. **Technicians**:
   1. Ease of set-up, electrode application, glues, adhesives
   2. Artifact rejection
   3. Easier software, cleaner data
   4. Better cable management when connecting patients, getting wires crisscrossed
   5. Customer support/technical support available 24/7
   6. Alerts for when there are problems with the recordings
   7. If they do ambulatory they want video
4. **Admin**:
   1. The are looking to expand, but no specific unmet needs (they do not understand the technical problems the rest of the hospital struggles with)
   2. Very price sensitive
   3. Scalable without being too expensive
   4. Better technology for the same price
   5. Ease of ordering
   6. Very comfortable with the status quo
5. **Insurers**:
   1. We do not have that information at this stage.
6. **Patients**:
   1. Better outcomes
   2. Less surgery
   3. Less drugs (hate side effects)
   4. Nothing really works
   5. More comfortable monitoring – hate the cosmetic appearance (same concerns on take home device)
   6. Less weight in the head wrap
   7. Less time in the hospital
   8. Better interaction and feedback with the doctor
   9. Expense
7. **What could improve efficacy? What are their incentives?** 
   1. We need more data and more information about the seizures.
   2. It would be helpful to collect data in the natural environment.
   3. Incentives are difficult because hospitals are currently reimbursed a fixed amount for the total care. They are very reluctant to provide additional treatment (more expensive) if there isn’t some kind of guarantee it will work.
8. **Do hospitals want more epilepsy procedures?**
   1. Yes. They recognize there is a very large population that is still not being treated and could see benefit from these procedures. The procedures are also very profitable for the hospital based on reimbursement from insurance. EMU expansion is very common right now in the US as hospitals are trying to better prepare for increased patient procedures.
   2. Vast majority of patients don’t do anything. They don’t know about treatments and when they do they can’t afford it.
9. **How does epilepsy rank in terms of hospital revenue relative to other procedures?**
   1. Not very high right now, but growing. LTM, ICU, networking are all growth areas. Hospital is only getting reimbursed once so any additional expense (for additional monitoring) can be difficult to implement.

**Barriers and strategies for market entrance**

1. **What are the barriers to build, sell and manage a product?**
2. Enhance existing technology and include single unit recording:
   1. The barriers for the standard EEG products are relatively low, but need to have the appropriate funding and resources. It is important to understand the user needs and dramatically improve the user interface.
   2. The sales cycle is very long and slow for these products and requires direct contact with many levels in the hospital. In order to monopolize this market, you need complete coverage with direct employees in all regions. The US market could support upwards of 30 regions.
   3. It is important to stay ahead of the curve with regards to software and analysis in order to dominate the market. This would require new updates and new versions every 6 – 12 months.
3. Cervello I (both in hospital and in home)
   1. Very difficult to build the technology with full capabilities in such a small package.
   2. Significant concerns in providing adequate hermetic seal.
   3. The early adopters and leading researchers are already screaming for this product, but main stream clinicians PROOF[list of cereplex I users?] will need to see supportive data on how it improves patient care prior to moving forward.
4. ECoG electrodes – consumable product
   1. Relatively easy to build products as good as existing products on the market. Requires some investment in capital equipment to manufacture devices. There is some innovation involved in development higher channel count electrodes and interfaces.
   2. This is currently almost a commodity business. With improved technology and reliable delivery we can clearly differentiate ourselves and drive towards a business that will have automatic reorders for hospitals.
5. **What are the component parts of this solution?**
6. Enhance existing technology and include single unit recording:
   1. Amplifiers, software and accessories to meet the following product types:
      1. Ambulatory EEG
      2. Routine (mobile) EEG
      3. Long Term Monitoring/Epilepsy Monitoring Unit
      4. ICU
7. Cervello I (both in hospital and in home)
   1. Implant package which includes implantable electronics connected to electrodes (ECoG, SEEG, Utah Array, other…)
   2. Pigtail to go through the skin and interface for data to get to the computers.
   3. Pigtail that gets tunneled to the chest to an implantable transmitter (wireless).
   4. Belt pack to receive the signals from the transmitter.
   5. Software to collect and process the data from the Cervello I
8. ECoG electrodes – consumable product
   1. Grid electrodes (all configurations)
   2. Strips (all configurations)
   3. Cables to interface between the pigtails and the amplifiers (with quick disconnects to make it easy for technicians)
   4. Depth electrodes for SEEG
9. **If we gave hospitals the solution for free, without a contract, and only charged them for data processing services, could hospitals say yes to a deal like this?**
10. Receptive to the idea, but concerned the price might be too high to justify
11. A very unique idea and great way to make sure the customers always have the latest and greatest software.
12. Could be some apprehension about hospitals signing up for fee for service. If hospitals have the money they should pay for it. If they don’t have the money they probably can’t afford it.
13. **Would they have a reimbursement code to submit for processing data instead of having the equipment as capex on the balance sheet?**
    * Cardiology may have something like this now??
    * NeuroPace also may have started something like this??
14. **Would we be able to use the data for our commercial purposes?**
    1. unknown
15. **We want to get similar data relating to their idea of an at home epilepsy monitoring product.**
16. **do doctors, technicians, insurers, hospital administrators and patients want it?**
17. **what are pros and cons?**
    1. Move the whole paradigm to outpatient environment, more natural, patients less tied down
    2. More information is better
    3. More accurate complete view of the patient over longer periods of time
    4. Patients don’t want to be off their meds during monitoring (scared)
    5. Hospitals would be fearful of losing revenue.
    6. Might take a while before clinicians felt comfortable sending patients home
    7. Other safety issues:
       1. Interference with cell phones
       2. Other environments (trains, …)
18. **would insurance pay for it?**
    1. We believe we could use the same reimbursement codes for now and it would remain very profitable for the hospital. There could be changes to the codes which would limit the reimbursement, but still make it a reasonable procedure.
    2. Hospital will get reimbursed a set amount for treatment no matter what is being done for patient.
    3. Important: Doctors are paid separately by the insurance and that needs to stay that way or else there is no incentive
    4. WARNING – Laser ablation – set the price too high and required too much additional technology to be used effectively that the hospital would no longer pay for it.
    5. If you can make a compelling argument with the full scope of treatment the hospital and insurance companies would be receptive.
19. **would this increase demand from patients who want surgical intervention.**
    1. This will significantly increase the demand from patients. They will be driven by the increased success rate of the procedure as well as the ability to undergo the monitoring in their own home.
20. **how much could be charged? How big is this market?**
    1. We are targeting a price point of $10k for this product. That doesn’t include the cost of the surgery or other support services. The potential addressable market is the number of patients with refractory epilepsy, but this market will grow significantly when the successful results begin to get published and patients will begin to elect to receive this treatment in lieu of additional drug choices.

**Additional sources (selection, only) for the above were personal conversations with:**

Dr. Paul House (MD, Neurosurgeon, University of Utah)

Dr. Syd Cash, (MH, Neurologist, Harvard/Massachusetts General Hospital)

Dr. Nathan Crone (Neurologist, Johns Hopkins University Hospital)

David Grauer (former CEO of Intermountain Medical Center (Hospital), now Consultant at Health Catalyst (spin off from Intermountain)– all about data analytics/databases)

Dr. Kurt Hecox, (Neurologist) Children’s Hospital of Wisconsin

Dr. Geoffrey Chung, (Neurologist) Cedars Sinai

Dr. Nitin Tandon, (Neurosurgeon)Texas Medical Center

Dr. Moisha, Goyal, (Neurologist) Children’s Hospital of Alabama

Dr. Christi Heck, (Neurologist) USC

Dr. Peter Wong, (Neurologist) British Columbia Children’s Hospital

Dr. John Wittig, (Researcher) NIH

Dr. Zareem Zoghloul, (Neurosurgeon) NIH

Dr. Cathy Schevon, (Neurologist) Columbia

Dr. Gehuda Sepkuty, (Neurologist) Swedish Medical Center

Dr. Andreas Schulze-Bonhage (Neurologist) (Freiburg University Hospital/Director Epilepsy Center)

Dr. Philippe Kahane (Neurologist) (Grenoble)

Dr. Philippe Ryviln (Neurologist) (Lyon)

Dr. Margarita Saek, (Neurologist) (Geneva)