Meeting the mind: The Neurotechnology revolution

A NEW ERA IN OUR UNDERSTANDING OF THE BRAIN

Throughout human history, the mind has been incomprehensible, other-worldly and beyond reach. The Bible describes all manner of thoughts and emotions but does not once mention the brain. Aristotle thought that the brain was a cooling mechanism for the blood. Centuries later, although the modern fields of biology and medicine have fundamentally transformed our understanding of the body and our ability to heal it, most scientists still think of the brain as the "final frontier" of research.

Yet now, the world had made advances in neuroscience and neurotechnology that, until recently, seemed impossible: brain-controlled prosthetics, neuroimaging technologies that can detect tiny lesions, cochlear implants that restore hearing, and others. Recent advances in science and technology will allow us to address some of mankind's greatest challenges. Imagine a world free of the heartbreak of degenerative brain diseases such as Alzheimer's and Parkinson's. Imagine a world we can reach into with our minds even if our bodies were sick or broken. Imagine a world where the blind can see.

That world is beginning to take shape in Israel today. Israeli companies and academics are playing a leading role in nurturing innovations across the spectrum of neuroscience and neurotechnology. These innovations will transform lives and the world we live in. Here are just some examples:

- BrainsGate, an early stage company, is developing a novel implantable stimulation device that increases blood flow to the brain, significantly reducing brain damage caused by ischemic stroke
- BrainStorm uses stem cell transplants to provide treatment for currently-incurable neurodegenerative diseases, such as Parkinson's, ALS and conditions such as spinal cord injury

This paper elaborates on two exciting opportunities that stem from a technology platform which enables bidirectional communication between the human brain and machines: connecting the brain directly to the outside world (the Brain Machine Interface or BMI) and the development of therapeutic neurostimulation devices.

Together, these two areas hold the promise of crossing a hurdle that has been impregnable thus far in human history. BMI is in its early days, but the already existing advances in research and the trajectory of technological applications will allow us to transcend the body's limitations and overcome physical disabilities. New neural medical devices, many of which are already in different stages of development, would assist in reaching directly into the brain to heal it without damaging surrounding tissue in a consistent and reliable way.

Israel is the right place to make these opportunities more real:

- Israel has a strong tradition of putting science and technology at the forefront of its economic development. The country invests 4%-5% of its GDP on R&D each year, which is the highest rate in the world, and has developed leadership in terms of scientists, engineers and patents per capita. Despite its small size, Israel has become an important centre for innovation, and has a proven track record in fields such as computer science, navigation, nanotechnology and brain research.
- The next horizon for Israel is neurotechnology. We have begun the journey and are looking for partners. It is an enormous challenge but a hugely worthwhile one, with the potential to transform the world in which we live. It is only by bringing together global leaders across many fields that we can collectively rise to this challenge.

In this document we will describe some of the areas on which we are focusing, and several ways in which we can collaborate on this great mission.

OPPORTUNITY 1: BMI WILL ENABLE US TO OVERCOME THE LIMITATIONS OF OUR BODIES

We are on the verge of technology that will reliably and consistently allow our brains to interact directly with external machines. Achieving this will allow us to overcome many of the physical disabilities that limit millions of people. However, the implications are even broader – BMI will allow us to develop new ways for all people to interact with their surroundings.

Some ways that this kind of technology could revolutionise our world include:

- Providing eyesight to 35 million blind people and hearing to 140 million deaf people with artificial sensory systems
- Removing physical disability caused by amputation and spinal cord injury to nearly 20 million people by using advanced prosthetics technology that allows individuals to touch and feel the outside world with all the finesse of a real human limb. This will also alleviate a burden of over \$450 billion on health systems worldwide
- Enhancing the functions of our brains, such as memory and problem solving

■ Establishing direct linkages between the human nervous system and the environment: improving communications and education for billions of people by creating fully-immersive virtual worlds, controlling home appliances, or accessing the internet directly from the brain by developing new ways to interact directly with computers

Israel's capabilities create a unique opportunity to further accelerate and catalyze the applications of BMI to everyday life. Israel:

- Has built a world-leading position in technology and high-tech, especially in electrical engineering and computer science
- Has a proven track record in multi-disciplinary research, which is a major requirement in BMI
- Built a highly-developed defence industry, which contributes to many technologies in the BMI space, such as miniaturisation and imaging, and could, in itself, be a customer for many innovations in the field
- Created a home for world-leading researchers in the field, and holds leading research institutions such as the new Edmond and Lily Safra Center for Brain Sciences in the Hebrew University, the Leslie and Susan Gonda (Goldschmied) Multidisciplinary Brain Research Centre at Bar-Ilan University, and others

Many exciting innovations in the Israeli start-up arena and academia are already underway in the field of BMI. Some examples are

- NanoRetina is building an ultra-small, easy to implant artificial retina designed to restore sight
- Elminda is developing an innovative way to record brain activity at high temporal and spatial resolutions
- Professor Eilon Vaadia from the Hebrew University in Jerusalem is developing a unique brain computer interface to treat severe paralysis
- A group of researchers at Bar Ilan university are conducting advanced experiments where a human remotely controls small animals by thought alone

OPPORTUNITY 2: NEW THERAPEUTIC STIMULATION DEVICES WILL IMPROVE MILLIONS OF LIVES

New technologies in neural stimulation will soon allow us to alter brain biology in a targeted way. These will revolutionise our ability to treat, and potentially to heal, many neurological diseases and brain conditions, such as tumours, trauma, degenerative diseases and psychiatric disorders.

The possibilities stemming from this emerging opportunity are enormous, and include:

■ Improving quality of life for over 320 million people suffering from migraine

- Improving care to 30 million people affected by depression that is otherwise treatment resistant, thus alleviating a burden of \$270 billion a year on health systems
- Retarding disease progression and potentially curing the 5 million Parkinson's disease patients globally

Israel is emerging as an important centre for this promising opportunity. Israel:

- Built a world-renowned medical device cluster that includes dozens of startups and centres for some of the major medical devices multinationals, such as J&J, GE Healthcare, and Medtronic
- Established leadership in the fields of nanotechnology, engineering and optics technology in the defence, high-tech and life-science industries
- Is the fourth-largest originator of medical-device-related IP globally, with over 500 patents

There are many exciting innovations in the Israeli start-up arena in the field of neural medical devices. Some examples are

- BioControl is developing implantable devices for the treatment of autonomic disorders using electrical stimulation
- BrainsWay is developing helmets with electromagnetic coils that can alleviate symptoms of psychiatric disorders
- Neuronix is developing a system that employs a unique and accurate combination of Magnetic Stimulation, concurrently with tailor-made cognitive training, to treat Alzheimer's disease

HOW CAN WE JOIN FORCES TO MEET THE MIND?

The new world of neurotechnology is near and it will affect the lives of us all. Now is the time for us to partner in shaping this future.

Israel has already taken steps to promote neuroscience and neurotechnology R&D:

- I-CORE A \$340m program initiated by the Israeli Council of Higher Education to create centres of research excellence in multiple academic fields, including cognitive sciences
- TELEM A cross-ministry forum in charge of large R&D investments including investments in neurotechnology and associated basic research
- New biotech funds New bio-tech funds with Israeli government down side protection
- Chief Scientist The Israeli chief scientist has dedicated funds for R&D in neuroscience and neurotechnology

■ ELSC – A new \$130m multidisciplinary research centre for brain built at the Hebrew University

To accelerate the benefits of this work, we are looking to expand collaborations between Israeli academia, industry and entrepreneurs, and the international community. In recent years Israeli academia, start-ups, investors, and government bodies have begun working together with many international partners to bring this vision of a new world closer. Today we are seeking to enhance our collaboration with others who wish to advance the exciting field of neurotechnology. Israel would happily welcome international medical device players, venture capital firms and other parties interested in joining us on this journey.

We are also looking to launch several new initiatives. These initiatives would bring together more of Israel's talents and resources behind neuroscience and neurotechnology and will serve as a platform for new international collaborations, aimed at bringing the brain revolution nearer.

Presidential "brain challenge prize". As a next step to help commercialise neuroscience research in Israel and beyond, and to bring neuroscience into the start-up mainstream, we plan to launch an international challenge prize to award disruptive innovations in the field that are at or close to commercial readiness. Israel is looking for partners to help design, fund and support this award – and thus benefit alongside us from close and ready access to the most innovative work in this area.

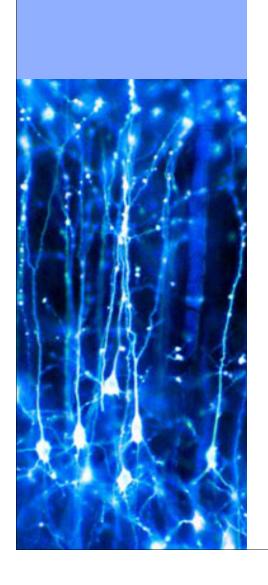
"Meeting the mind" presidential conference. To increase awareness of neuroscience and potentially accelerate the development of nascent ideas into new business ventures or "flagship projects" in brain communications, we plan to initiate a large, international conference for neurotech in Israel, championed by the president. This will bring together engineers, young scientists, entrepreneurs, students, researchers and early-stage investors in an open environment designed to allow knowledge sharing that could develop into new business plans and business ventures.

Attached to this white paper, you will find further information about innovations and advances in Israeli start-ups and research, as well some more information about Israel's perspective on the fields of BMI and therapeutic medical devices.

This is a moment of real opportunity to make what would recently have seemed like dreams into reality. Together, we can lead the world into this new era. Israel is the ideal partner and is looking to team up with others to help shape a better future for mankind.

For more information please contact Ido Sharir from the Office of the President of Israel, at ido@president.gov.il

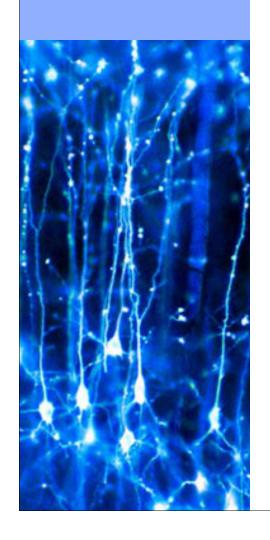
We would like to thank the academics, industry leaders, government officials, entrepreneurs and angels – in Israel and abroad – who have generously dedicated their time and thought to this initiative. We would also like to extend our gratitude to McKinsey & Company, which has worked closely with the office of the President of Israel to develop this report.



Meeting the mind: The Neurotechnology revolution



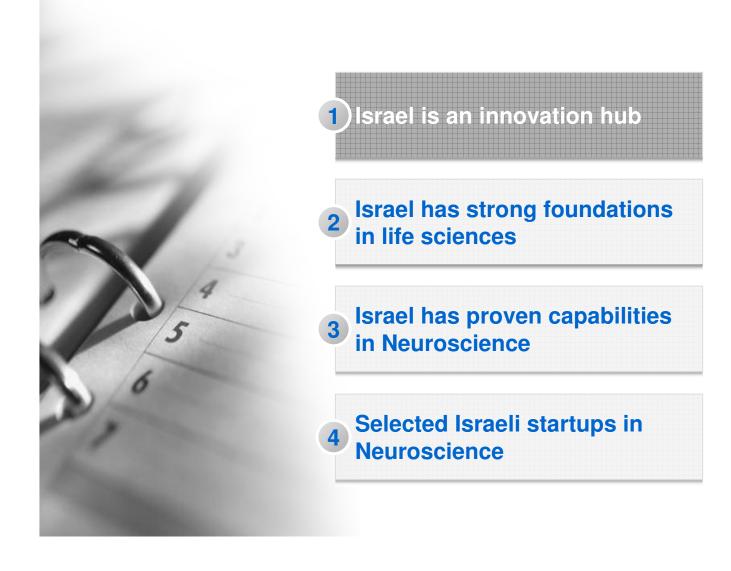
Supporting materials for discussion document



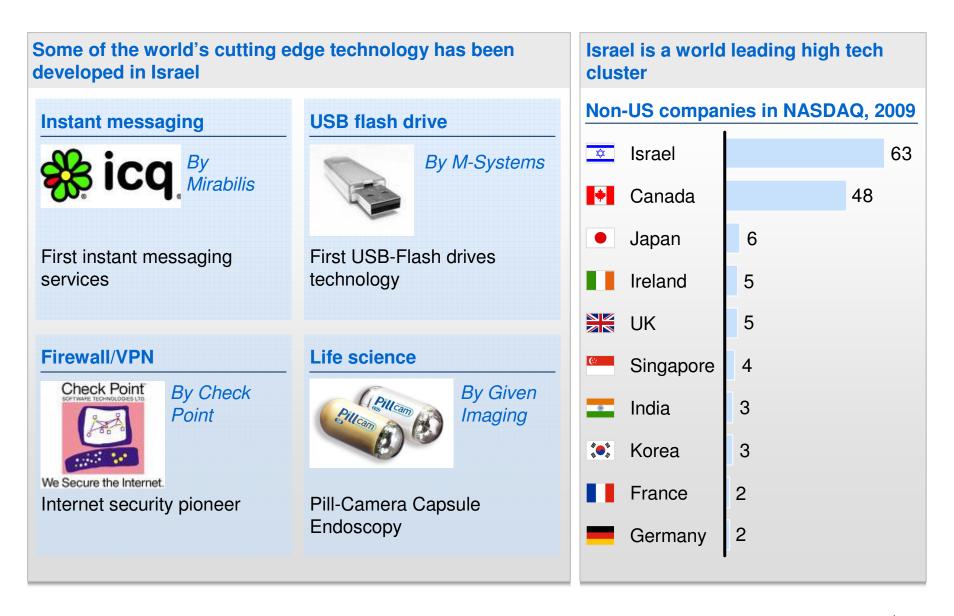
Chapter 1 – Israel's competitive advantage



Israel is the right place to lead in neurotech because of its legacy in innovation, existing excellence in life-sciences, and emerging NS excellence



1 Israel has a rich legacy leading world innovations



1 High-profile executives acknowledge Israel's capacity to innovate



"Israel is important to our goal, because it has historically been a hotbed of new raw technology and scientific developments."

> Matthew I. Growney, Managing director, Motorola, September 2003

"Israel is an Incredible opportunity for us. It provides a growth engine for innovation"

> Richard Nottenburg, Motorola's executive VP chief strategy officer, June 2006

"Some Americans have come to the Middle East looking for oil. We came to the Middle East looking for brains, and we stopped at Israel"

Warren Buffett, Berkshire Hathaway, September 2006

"Outside the USA, we only invest in Israel"

Julien Ngyen, Managing Partner, Applied Materials ventures, September 2003 "It's no exaggeration to say that the kind of innovation going on in Israel is critical to the future of the technology business"

> Bill Gates, Microsoft founder, 2005

"The quantity and quality of software engineers in Israel made it logical that we would open a R&D center here at some point"

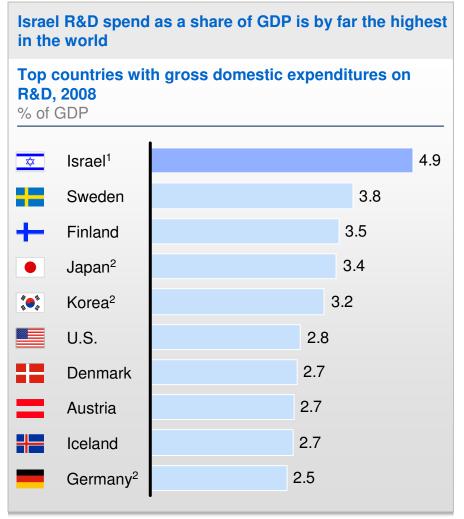
> David Woodside, EMEA manager, Google February 2006

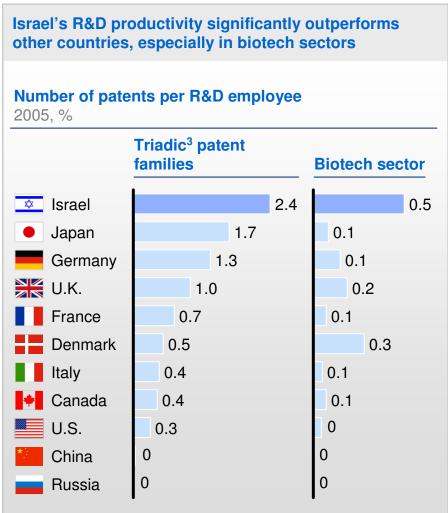
1 Multinational giants have recognized Israel's innovative environment and established their R&D centers there¹

1990-1995 1995-2000 2000-2010 Microsoft* CISCO SYSTEMS Google ORACLE SanDisk 22 invent APPLIED MATERIALS. **SIEMENS Juniper**® **Lucent Technologies** Bell Labs Innovations SAMSUNG EMC² 'intel') **VISHAY** Kodak where information lives®

¹ In some cases by M&A of Israeli companies

1 Israel has become world-leading on R&D investments and productivity



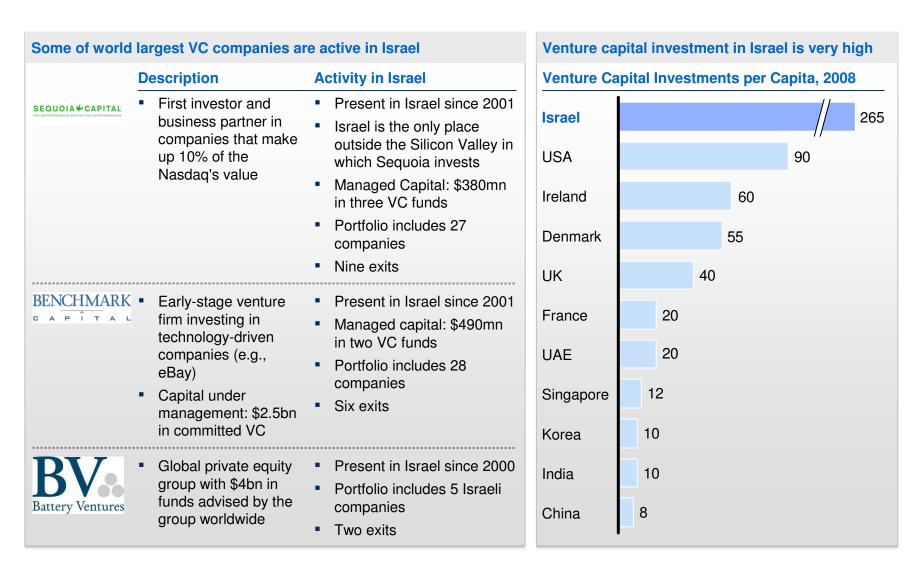


¹ Exclude defense spending

² R&D spend for the year 2007

³ Patent field simultaneously in Europe, Japan, and the U.S.

1 R&D productivity has been supported by a very intensive venture capital industry with strong international presence ...



1 ... and by strong support from the Israeli government

R&D incentive programs **Program Description** Designed to encourage and support individual entrepreneurs Pre seed Grants are up to 85% of the approved expenses for building prototypes, registering patents, designing business plans Supports the formation of consortia Generic comprised of industrial firms and R&D academic institutions, to jointly develop generic, pre-competitive technologies Grants are up to 66% of the approved budget No royalty payments Overall budget: ~ \$60mn/yr Grants are on a sliding scale from Competitive 20% to 50% of R&D budget R&D Royalty payment is 3% to 5% of future product sales Supports more than 1,000 projects/yr from more than 500 companies Overall budget: ~ \$300mn/yr

Tax incentive program

Program

Description

Grants programs

 Foreign investor investing more than 140mn NIS will enjoy a grant of 20% of the investment and a reduced tax rate for an eight-year period

Priority area programs

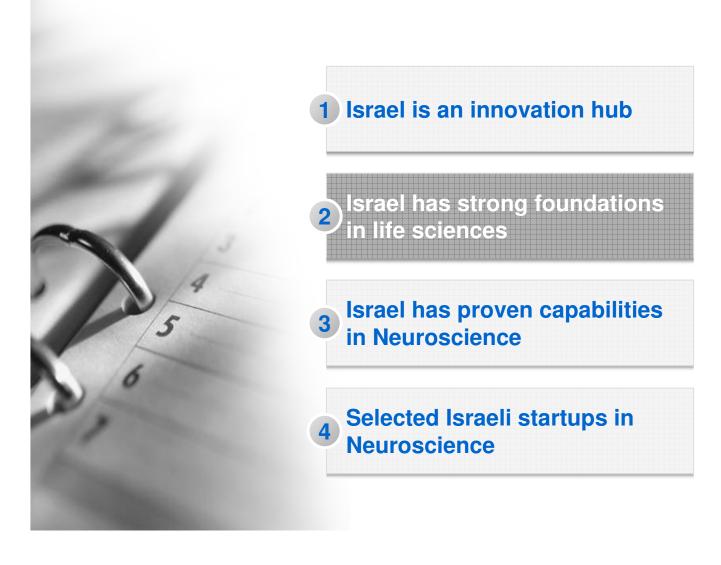
- For a foreign investor, the dividend tax rate is 4% and a total corporate tax rate is 11.5%
- Time: If at least 25% of the company is foreign owned, then the benefit period is 10 years

Strategic program

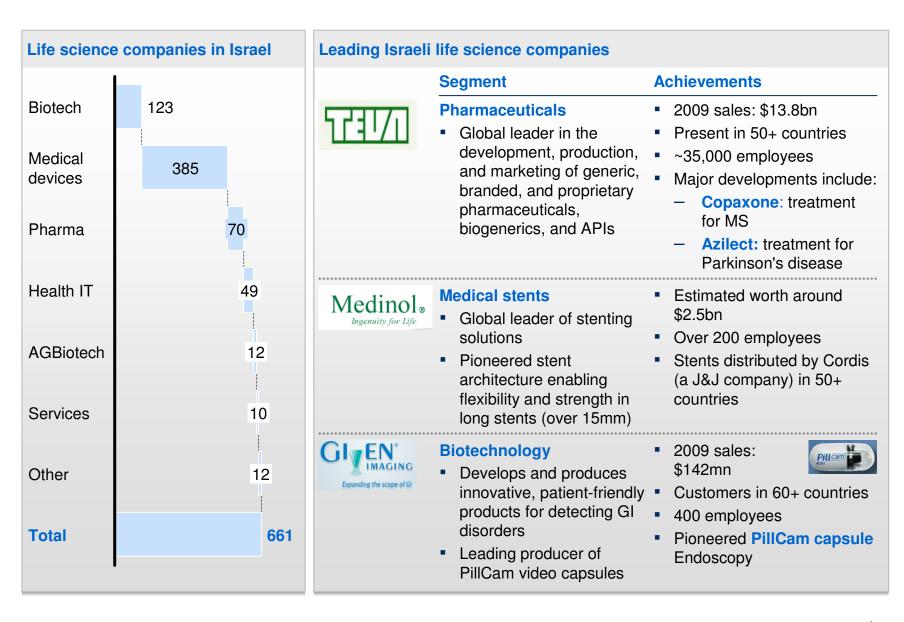
- Intended for large multinational companies meeting the following criteria
- Annual turnover > \$3bn
- Project investment >\$130mn
- Full corporate tax and dividend tax exemptions for 10 years

SOURCE: Team analysis

Israel is the right place to lead in neurotech because of its legacy in innovation, existing excellence in life-sciences, and emerging NS excellence

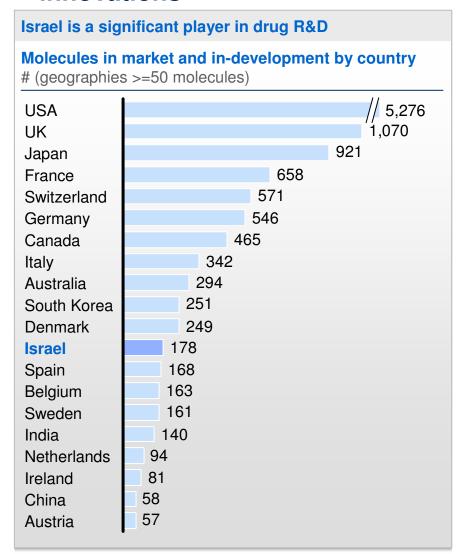


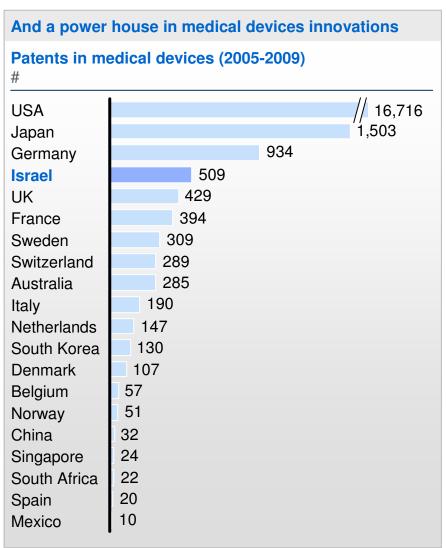
2 Israel enjoys a large and diverse life science ecosystem



SOURCE: ILSI; web

2 This ecosystem has made Israel a world leader in life sciences innovations

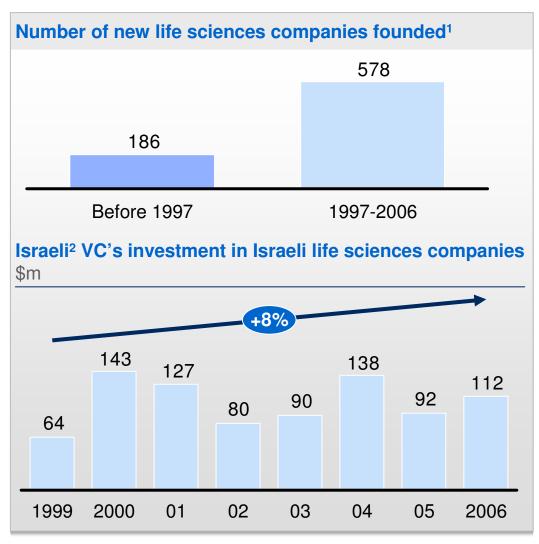




SOURCE: Pharmaprojects (2009)

2 Israel also boasts fast-growing venture capital activity in life sciences ...





^{1 2005} and 2006 figures are incomplete

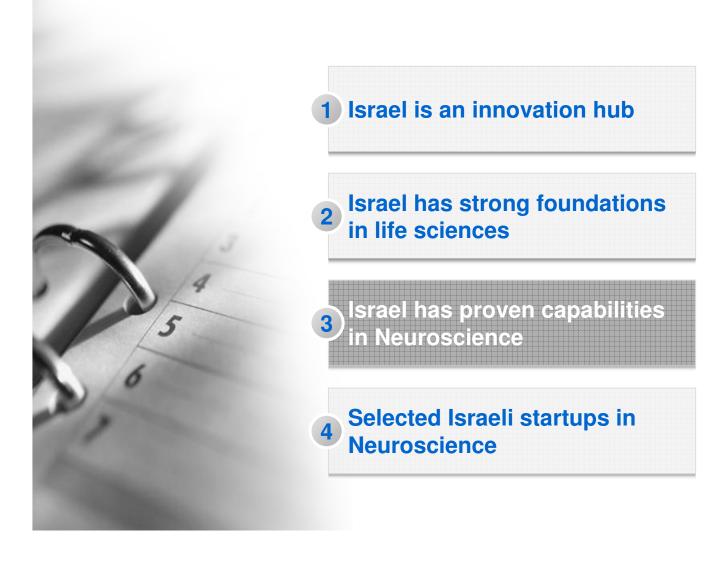
² Not including foreign VC funds

³ Fund not exclusive to life sciences ventures.

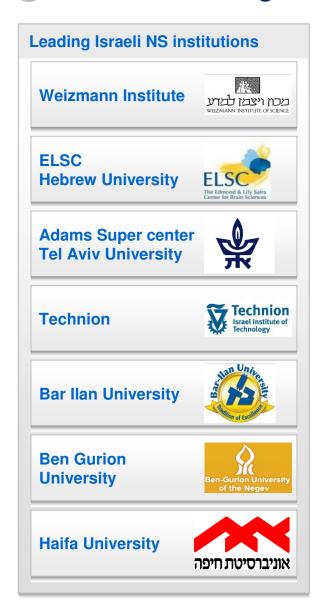
2 ... and government has started encouraging activities in the life sciences space

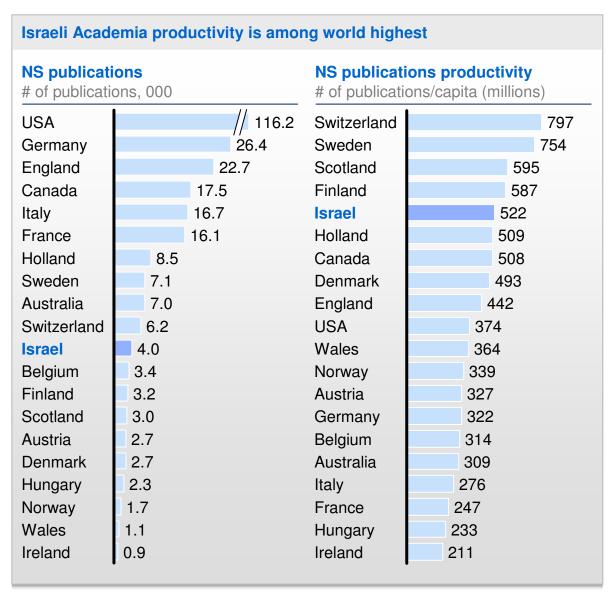
Life science **Descriptions** programs Government Endeavour to advance infrastructure in selected fields of science. Committee was able to raise **TELEM** over \$250m for investments in Nanotechnology and is now reviewing options in Neuroscience A \$340m program initiated by the Council of Higher Education to create centers of research excellence in I-CORE multiple academic fields, including Cognitive Sciences Government sponsored \$250m capital fund launched in **BIOTECH** mid 2009 to finance biotechnology start-up companies **FUND** Under the Ministry of Trade and Industry, chief scientist **CHIEF** office spends \$150m a year supporting start up R&D and **SCIENTIST** academic programs

Israel is the right place to lead in neurotech because of its legacy in innovation, existing excellence in life-sciences, and emerging NS excellence



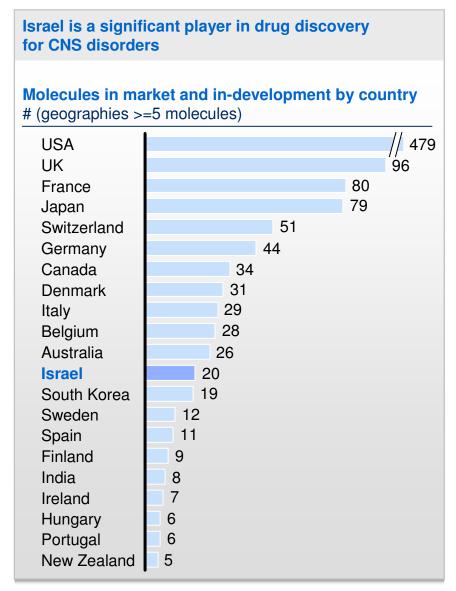
3 Israel has a strong neuroscience cluster supported by 9 Institutes

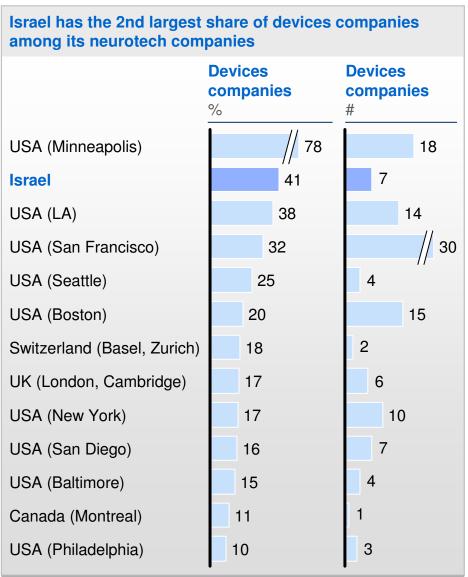




SOURCE: Neuroinsights, PubMed

3 Research excellence has made Israel a prominent neurotech cluster





Israel is the right place to lead in neurotech because of its legacy in innovation, existing excellence in life-sciences, and emerging NS excellence



Israeli start-ups table of contents

| Company | Description | Main contact |
|---|--|-----------------------------|
| ALPHA Alpha — Defining Resusciones Producing Omega | Devices for deep brain stimulation implanting surgery | i.younis@alphaomega-eng.com |
| ARGO ARGO | Walk restoration devices for people with lower limb disabilities | amit@argomedtec.com |
| BIO BioControl | Neurostimulation devices for treating autonomic disorder | udi@biocontrol-medical.com |
| BioLert BioLert | Wireless device providing real time alert of epileptic seizure | Amos@biolertsys.com |
| BIOLINERX BioLineRx | Biopharmaceutical therapeutic for schizophrenia | kinnerets@BioLineRx.com |
| BrainsGate BrainsGate | Miniature electrode increasing blood flow to the brain | dayan@brainsgate.com |
| BrainStorm | Stem cell therapy for ALS and PD | efrati@brainstorm-cell.com |
| @Brainsway Brainsway | Electromagnetic brain stimulation | uzis@brainsway.com |
| CerebralRx | Vagus nerve stimulation to treat drug refractory epilepsy | tamir@cerebralrx.com |
| PHARM D-Pharm | Biopharmaceutical therapeutic for acute stroke | akozak@dpharm.com |
| ElMindA ElMindA | Diagnostic device based on mapping brain activity network | ronen@elminda.com |
| Motorika Motorika | Robotic rehab products for neuromuscular training | yuris@medinvestgroup.com |
| Naleetina Nano Retina | Ultra small artificial retina | gefen@nano-retina.com |
| NEURONIX Neuronix | Magnetic stimulation and cognitive training for treatment of Alzheimer's disease | eyal@neuronixmedical.com |
| Prnim Ornim | Non-invasive monitor for brain oximetry and blood flow | Yitzhak.zilberman@ornim.com |
| RIMED ::: Rimed | Non-invasive measure of blood flow in brain | jadlin@rimed.com |
| Surpas Medical Medical | Non-invasive measure of blood flow in brain | ygael@surpass-med.com |

4 Leading the Way in Technologies for Neurosurgery and Neuroscience



Who we are

- Developing technologies for treatment of neurological and psychiatric disorders (Parkinson, Epilepsy, Depression)
- Market potential of over US\$2 Billion and growing. Annual global economic cost of diseases in hundreds of billions
- We are a unique company in the Galilee, employing people from all different religions and ethnicities from the area with one goal in mind the advancement of human health and improvement of quality of life

Our product

- FDA and CE approved devices for surgery in the implanting of deep brain stimulators. Products considered best in their field by top doctors, hospitals, and universities worldwide (Mayo Clinic, John Hopkins, UCLA, Oxford, etc.)
- Installed base of more than 500 clients
- Soon to be released products offering end-to-end solutions for hospitals and research centers

Our innovation

- Multi-channel recording and sophisticated stimulation paradigms, combined with accurate and safe implantation of electrodes in the brain, using wireless and tethered technologies
- Deep understanding of the industry and applications allows continuous development of pioneering products

NeurNav -Recording and Stimulation System



MicroGuide – DBS Implantation System



Our partners

- Hebrew University
- Weizmann Institute
- Hadassah Hospital
- Axion Inc.

Our future

- Series of new and innovative miniature devices implantable in the brain
- We are searching for partners with access to new markets and complimentary technologies

CEO contact information

Imad Younis

+972 (4) 656-3327

i.younis@alphaomega-eng.com

www.alphaomega-eng.com

4 ReWalk[™] – Enabling Wheelchair Users to Walk



Who we are

- Argo's mission is to become a leader in the research, development and marketing of walk restoration devices for people with lower limb disabilities. Specifically, we offer an ambulation alternative to the wheelchair users community that counts 5 million people in the USA & EU, a market size of \$60 billion.
- Our team is a group of leading experts in ambulation and medical technologies, robotics, algorithms and software

Our product

- The ReWalk has already gone through clinical trials and proved its ability to restore upright mobility and to enable paraplegics to stand, walk, use stairs and more
- 'ReWalk™-I' is available for institutional use and 'ReWalk™-P' will be introduced later this year for a personal use

Our innovation

- ReWalk[™] is based on a man-machine interaction that utilizes sophisticated control methods
- Argo found the way of assimilating technology with human abilities for restoring mobility

From Wheelchair



To Rewalk



Our partners

 Argo collaborates with leading USA and Italian university hospitals, e.g., MossRehab, PA; VA-Bronx, NYC

Our future

- Adapt the ReWalk to suit more disabilities
- Integrate BCI-based ambulation control with ReWalk
- Develop ReWalk for children
- Collaborate with leading R&D institutions in the field
- Team up with strategic partners

CEO contact information

Dr. Amit Goffer amit@argomedtec.com

+972 (4) 959-0123 www.argomedtec.com

4 BioControl - Therapeutic Devices for Autonomic Disorders



Who we are

- BioControl develops unique neurostimulation technology to treat a variety of indications.
- Current focus is Heart Failure, which affects 14 million patients world-wide, with over \$30 billion annual cost

Our product

- The CardioFit®, currently in the world's largest FDA approved phase III study in HF (INOVATE-HF)
- Next products will treat Atrial Fibrillation and additional neurocardiology applications.

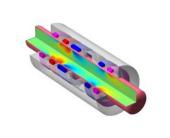
Our innovation

- Unidirectional neurostimulation enables focused treatment of autonomic disorders.
- Technology backed by over 35 issued patents worldwide and 20 additional applications

The cardiofit® System



BioControl's neurostimulation electrode



Our partners

Medtronic Inc.

- Cleveland Clinic.
- Heidelberg Univ.

Our future

 Following successful completion of the current study, the CardioFit® system will become a standard of care in HF

CEO contact information

Ehud Cohen
udi@biocontrol-medical.com

+972 (3) 632-2126 www.biocontrol-medical.com

4 Epilepsy Alert Devices



Who we are

- We are a medical device company, headed by epilepsy-expert doctors and experienced engineers
- Our team has received international citations and recognition for its innovative technology
- We address the millions of epilepsy patients and their caregivers by providing seizure alerts which can save the lives of thousands of patients; prevent brain damage; give peace of mind to families and support medical treatment

Our product

- 'EpiLert' is a wireless, watch-like device providing real-time ALERT to caregivers of an on-going epileptic seizure
- Pre-clinical trials conducted at NYU and Tel Aviv Epilepsy Centers have proven our product's technology accurate detection of seizures with minimal false alerts
- 'EpiLert' is an affordable, easy to use product for the use of infants, adults and the elderly

Our innovation

Our breakthrough algorithm distinguishes epileptic seizure-movements from ordinary daily-movements. It is based on thousands of hours of epilepsy patient monitoring and provides almost-instant alert with virtually no false alarms. (Study will be published in The Journal of Clinical Neurophysiology, Feb. 2011). Existing alert devices are confined to the bed and suffer from frequent false alarms



'EpiLert' accurately identifies epileptic seizures within seconds and notifies caregivers and physicians.

Our partners







Our future

We are looking for additional sources of funding as well as international partners for strategic collaboration in order to bring the 'EpiLert' to the world markets within 18 months

CEO contact information

Amos Shaham

E-mail: Amos@biolertsys.com

Who we are

- Biopharmaceutical development company identifying, in-licensing and developing therapeutic candidates for unmet medical needs or with advantages over currently available therapies
- Current pipeline -3 clinical stage candidates and 8 pre-clinical candidates for various indications, including neurological.
- Lead candidate- BL-1020 for schizophrenia, a severe mental disorder affecting ~1% of population

Our product

BL-1020 is a novel, first-in-class, oral therapeutic for schizophrenia. Clinical trials have shown that BL-1020 is highly efficacious with a
good safety profile. Moreover, our studies have shown that BL-1020 has positive effects on cognition, an unmet medical need in
schizophrenia. BL-1020 was out-licensed to a company specializing in the CNS field- Cypress Bioscience Inc. in June 2010 for
continuation of development and commercialization in N. America

Our innovation

BL-1020 has a dual mode of action: antagonism of the neurotransmitter dopamine and enhancement of the activity of another neurotransmitter, GABA. This unique combination of features contributes to BL-1020's anti-psychotic activity, enhanced safety profile and pro-cognitive effect. BL-1020's profile has been demonstrated in pre-clinical and clinical trials, particularly the recently completed Phase 2b EAGLE trial



Our partners

- Cypress Bioscience Inc.
- Bar Ilan Research & Development BIRAD, Ramot

Our future

- Continuation of BL-1020 development and commercialization by our partner
- Partnerships to develop new compounds and partnerships to conduct advanced clinical trials and commercialize candidates from pipeline

CEO contact information

Dr. Kinneret Savitsky kinnerets@BioLineRx.com +972 (2) 5489100 www.BioLlneRx.com



4 "A new hope to treat brain disorders"



Who we are

- Our vision is to treat a variety of brain disorders using a unique technology for controlling brain blood flow
- We are focusing on Acute Ischemic Stroke, the leading cause of long term disability, with over 5 million victims each year (800K in the US, 1.1M in Europe), costing over \$100s of billions worldwide

Our product

- BrainsGate's product is currently in a Pivotal II (last stage) study. Pilot & Pivotal I results on 394 patients were very promising
- Future applications include chronic treatment of Vascular Dementia (promising results in a small feasibility study)

Our innovation

A miniature electrode, with a minimal invasive implantation, when externally activated, increases blood flow to the brain. and can be used to treat a variety of brain disorders

Electrode implantation



External activation



Our partners

Johnson & Johnson

Our future

- Complete the Pivotal II study and get FDA approval, then launch commercial operations for stroke
- Move ahead with the vascular dementia program and other diseases

CEO contact information

Avinoam Dayan dayan@brainsgate.com +972 (4) 637-7774 www.brainsgate.com

4 BrainStorm Cell Therapeutics: Regenerating the mind



Who we are

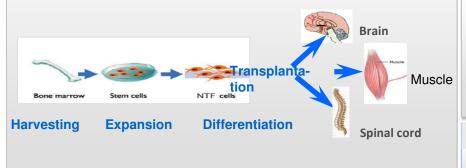
- A biotech company developing innovative adult stem cell therapies for highly debilitating neurodegenerative disorders such as ALS and PD, areas of currently unmet clinical need
- Currently more than million people diagnosed with PD in the Western world; 100,000 suffer from ALS.
- Addressable market for BrainStorm: ALS 50,000 patients, PD 400,000 patients

Our product

- The NurOwn technology: Adult bone marrow-derived stem cell therapy
- Clearance granted by the Israeli Ministry of Health for Phase I/II Clinical trial for ALS beginning Q1 2011
- Clinical trials in additional countries planned

Our innovation

- Bone marrow derived adult human Mesenchymal Stem Cells (MSC), expanded ex-vivo and induced to differentiate into astrocyte-like cells secreting Neurotrophic factors, including GDNF and BDNF for treating neurodegenerative diseases.
- No other MSC secreting Neurotrophic factors currently in clinical development.



Our partners

- Tel-Aviv University
- Hadassah Medical Center

Our future

- Clinical Trials for in several medical centers worldwide
- We are seeking collaborations with big Pharmaceutical companies for the development of the NurOwn technology for additional neurodegenerative indications

CEO contact information

Rami Efrati +972 (3) 923-6384 efrati@brainstorm-cell.com www.brainstorm-cell.com

4 DEEP TMS – Non-invasive activation of deep brain structures



Who we are

- Electromagnetic Brain Stimulation for Psychiatric and Neurological Disorders (NIH & Weizmann Inst. based Technology)
- Huge market (>30B\$/Y) of Depression, Alzheimer and Parkinson Disease in the growing elderly population and many other disorders
 involving impaired electrical activity of neurons, not responding to current medications.

Our product

Helmets containing electromagnetic coils that can induce immediate, visible non-voluntary motor activation and proved to be effective
in several clinical trials in Israel and abroad. Received CE approval for marketing in Europe for Depression, bi-polar disorder and
schizophrenia. Additional coil shapes and indications in development

Our innovation

- Electromagnetic coils are placed over the head and connected to capacitors discharged to induce facilitation or inhibition of specific deep brain regions
- The innovation is unique with no competition based on established patents of our investigators in the NIH and the Weizmann Inst. allowing non-surgical deep brain stimulation

An example of a coil design

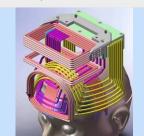


Illustration of the full patented system



Our partners

- The Weizmann Institute of Science
- Jones Hopkins Hospital
- Harvard Medical School
- The National Institute of Health (NIH)
- UCLA-university of California
- Columbia University New York

Our future

- Collaboration with local distributors for the marketing of our CEapproved systems in Europe and other regions
- Completion (during 2011) of the multi-center study in depression
 the last stage for achieving FDA approval
- Develop products for treating various devastating psychiatric and neurological disorders

CEO contact information

Uzi Sofer uzis@brainsway.com +972 (2) 581-3140 www.brainsway.com

4 "CerebralRx delivers neurostimulation therapy for Neurological disorders"



Who we are

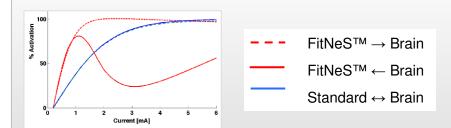
- Manufacture a unique implantable device that utilizes directional Vagus nerve stimulation to treat drugs refractory epilepsy
- Epilepsy is a serious neurological condition affecting up to 50 million people worldwide, where 15% are refractory to drugs

Our product

- FitNeS™ is an implantable device that sends pulses to the brain via the Vagus nerve, using a nerve electrode that generates directional nerve activation. The device is CE mark approved and will be available on the market during the coming year
- Future pipeline products include: implementing Vagus nerve stimulation to other neurological dysfunctions including Depression and Parkinson

Our innovation

FitNeS™ unidirectional selective stimulation is a result of a proprietary cuff electrode that enables effective activation of brain centers while minimize inappropriate activation of other nerve fibers



- More effective activation of the brain
- Less unwanted activation in the other direction
- Less current in needed for effective stimulation

Our partners

- AMS Group
- Univ. of Gothenburg

Our future

- CerebralRx is starting sales in Europe followed by WW expansion
- CerebralRx is looking for strategic partners that will help its expansion into new territories

CEO contact information

Dr. Tamir Ben David tamir@cerebralrx.com

+972 (3) 536-3556 www.Cerebralrx.com

4 "D-Pharm designs and develops innovative drugs for the most devastating brain disorders"



Who we are

- A technology-driven clinical stage biopharmaceutical company focused on the discovery and development of innovative proprietary drugs for the treatment of central nervous system disorders
- DP-b99, is currently the most advanced clinical stage neuroprotectant in development to treat acute stroke

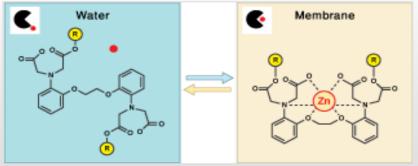
Our product

- DP-b99 is being studied in a multi-national Phase III trial (MACSI) under IND and according to the FDA's Special Protocol Assessment (SPA) program. DP-b99 increases by 2-fold full recovery following stroke
- DP-VPA is a Phase II clinical product for epilepsy, migraine and bipolar disorder

Our innovation

- Membrane Activated Chelators (MACs)
- MACs have a in-built switch on/off mechanism which limits their activity to where it is needed and makes them safe

Inactive Active



Our partners

- Yungjin Pharmaceutical Co.
- Wangbang Biopharmaceuticals

Our future

- Develop MAC treatment for Alzheimer's Disease
- Partner DP-b99 for global marketing
- Advance DP-VPA's clinical development
- Expand IP portfolio

CEO contact information

Alex Kozak +972 (8) 9385100 akozak@dpharm.com www.dpharm.com

4) "The Brain – as never seen before"



Who we are

- One in 3 people suffers from a brain disorder (Alzheimer's, Stroke, Depression, ADHD, pain, Parkinson's, etc ...)
- Due to the brain's complexity, the current diagnostic tools are insufficient to make accurate and objective treatment decisions, leading to significant guesswork & poor outcomes with large societal and financial impacts
- We address this unmet need with a novel diagnostic & treatment management tool for neurologists & psychiatrists

Our product

- ADHD diagnosis & treatment: ElMindA's Brain Network Activation (BNA) technology was validated in 2 independent clinical studies as an accurate and objective diagnosis & treatment management tool, with high specificity and sensitivity
- Brain Pharmaco-Imaging: BNA is commercially available and adopted by several of the world's top pharmaceutical companies to accelerate, enrich, and improve success rate of drug development for brain disorders

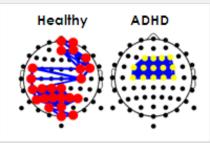
Our innovation

- The only available practical, objective tool for capturing the brain's complex interconnections associated with brain function, dysfunction and response to treatment
- Based on non-invasive, easy-to-use electro-physiological data acquisition and patented signal processing & algorithms

Brain activity recording



BNA differential signatures



Our partners

- Kendle CRO
- Harvard Medical School
- Mass General Hospital
- UC Berkeley and San Francisco

Our future

- Change the practice of medicine for the diagnosis & treatment of numerous neuro-psychiatric disorders, starting with ADHD, followed with Alzheimer's and Pain
- Target an existing market of millions procedures annually
- Accelerate adoption of pharmaco-imaging commercial activity by top pharmaceutical companies

CEO contact information

Ronen Gadot +972 (9) 951-6476 ronen@elminda.com www.elminda.com

4 Motorika – Setting the Standard for Neurorecovery



Who we are

- A leader in the development and marketing of innovative, cutting-edge robotic rehab products for upper & lower extremities
- 700K new stroke patients annually, 80% require rehab, no accepted standard of care

Our product

- ReoGo Robotic arm for passive & active upper limb neuromuscular training
- ReoAmbulator Robotic gait training integrating Body Weight-Support Treadmill Training
- Both products commercially available (CE and FDA clearance), with over 200 installations in major over 300,000 therapy sessions to date



hospitals worldwide and

Our innovation

- Easy to use robotic-based rehabilitation systems increasing efficiency & outcome improvement
- Increases patients' motivation & improves cognitive and motor skills

ReoGo System



ReoAmbulator System



Our partners

- HealthSouth USA
- Teijin Pharma Japan

Our future

- ReoHome designed specifically for placement in the home and is currently in the prototype stage
- Strategic partnerships and distributors in the neurostimulation and rehabilitation

CEO contact information

Yuri Shoshan yuris@medinvestgroup.com +972 (4) 627-5559 www.motorika.com



4) "Nano Retina will restore sight for the blind"



Who we are

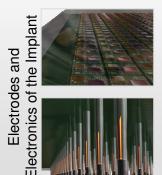
- Nano Retina, Inc. is developing an ultra small, easy to implant, artificial retina designed to restore sight.
- There are currently about 10 million people worldwide aged 40 and older who are legally blind, most of them due to degenerative blindness condition like AMD.
- Nano Retina will bring millions of the blind into the light to experience the splendors of life.

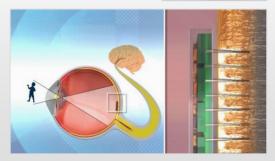
Our product

- This bionic retina incorporates various nano-size components in one tiny, flat implant, approximating the size of a child's fingernail bed.
- This implant transforms naturally received light into an electrical signal that stimulates the neurons, which send the pictures to the brain

Our innovation

Our nanotechnology base implant enclose in one package ten time better vision perception in tenth of the size of similar developments





Implant function and interface with human retina

Our partners

- Zyvex Labs LLC, Texas
- CSEM, Switzerland
- Tel Aviv University

Our future

- First clinical studies in human are planned for 2013
- Strategic partnership with leading player in the field is being assess

CEO contact information

Ra'anan Gefen gefen@nano-retina.com +972 (52) 334-9161 www.nano-retina.com

4) "A promising new treatment for Alzheimer's disease"



Who we are

- Neuronix has developed a unique Medical Device technology for the treatment of Alzheimer's Disease (AD)
- AD is currently an incurable disease, progressively leading to the loss of all cognitive functions of the patient
- AD prevalence increases dramatically with age, currently affecting about 26 million people worldwide, but expected to reach over 100 million by 2050

Our product

- Neuronix NICE™ system employs a unique and accurate combination of Magnetic Stimulation on affected brain regions, concurrently with tailor-made cognitive training, targeted at the same regions
- The system has been clinically proven in two separate clinical trials. It is currently undergoing additional trials both in Germany and in the USA

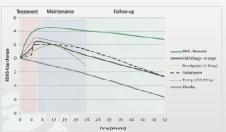
Our innovation

- Concurrent combination of Magnetic Stimulation and Cognitive
- Technology is clinically proven not only to stop deterioration but also to regenerate lost cognitive functions

The NICE system



12 month results



Our partners

- Harvard University, USA
- Tubingen University, Germany

Our future

- Obtain CE mark for NICE and initiate commercial operations
- Conduct additional trials targeting FDA approval
- Demonstrate efficacy at prevention of Alzheimer

CEO contact information

Eyal Baror

+972 (4) 903-8600

eyal@neuronixmedical.com

www.neuronixmedical.com

4) "Vital Signs for Vital OrgansTM"



Who we are

- Ornim provides physicians with the most advanced monitoring tools to direct safe and decisive patient care when perfusion of most vital tissue, the brain, is at stake
- Brain monitoring is vital to manage cardiovascular surgery, stroke, and traumatic brain injury patients, and valuable during resuscitation. With a WW market potential of \$2-3B, it is emerging as standard of care in high-risk surgeries

Our product

- Ornim's CerOx is a continuous and non-invasive monitor of both regional oximetry and blood flow, a combination which provides the best indication of brain perfusion
- CerOx may help physicians titrate blood pressure, ventilation, sedation, and temperature to customize patient care
- CerOx 3210 is FDA cleared, and carries the CE mark

Our innovation

- A patented combination of near infrared light technology and ultrasound to isolate brain tissue oxygenation, and uniquely track blood flow
- Available monitors offer partial or sporadic information, but the CerOx can trigger differential diagnoses, enhancing patient safety

CerOx 3310 Monitor



Cerebral Probe



Our partners

- Duke University
- UCSF Medical Center
- University of Pennsylvania
- Hadassah Medical Center

Our future

- A new CerOx version is expected mid-2011 with expanded monitoring indications. Ornim plans commercial launch beginning of 2012
- Ornim seeks collaboration with strategic distribution partners to expand CerOx market penetration

CEO contact information

Yitzhak Zilberman Yitzhak.zilberman@ornim.com +972 (8) 928-2801 www.ornim.com

"Detecting brain clots to prevent stroke"



Who we are

Rimed design manufacture & export transcranial Doppler (TCD) medical devices. The company was established in Israel in 1982 and is currently one of the leading players in TCD in the world, selling in over 40 countries worldwide. Our products represent high-end quality and accuracy combined with a young and playful design

Our product

Rimed's main product line is the Digi-LiteTM. This advanced technology TCD, measures non-invasively the blood flow in the main arteries in the brain. In this way any disturbance to flow is detected including emboli (clots) flowing in the blood stream. Rimed's products are mainly used for the diagnosis & treatment of Stroke patients. The new Digi-Lite package featuring a Carotid ultrasound imaging probe provides a complete solution Cerebrovascular diagnosis

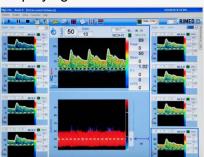
Our innovation

 Rimed's innovative technology is based on Doppler ultrasound & the implementation is done using very advance digital electronics

Digi-Lite ™ system



Displaying blood flow waveforms



Our partners

- Prof. Gaoshan-China
- Prof. Burnstein-Israel
- Prof. Schaafsma-Holland

Our future

- We plan to develop a complete imaging system for the brain arteries which will be based on ultra sound
- The system will be bedside & non-invasive.
- Growing and entering new markets around the world

CEO contact information

Joseph Adlin +972 544-909060

jadlin@rimed.com Web site www.rimed.com

4 Minimally Invasive Technology to Cure Brain Aneurysms



Who we are

- Surpass Medical developed the world's leading flow disruption technology to treat intracranial aneurysms. It's a superior device based upon the strongest & only issued patents in the field. Aimed to replace invasive surgery
- 5% of the world population has intracranial aneurysms, a fast growing market estimated at \$1.2 billion worldwide

Our product

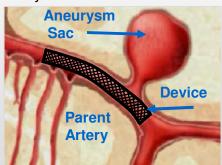
- CE-Marked with positive results from 50 Patients in 7 centers 3 countries
- Occludes brain aneurysms by redirecting blood flow away from the aneurysm, allowing the blood in the aneurysm sac to clot Yields higher safety & efficacy. Published preclinical studies in leading journals. Next: Ischemic stroke

Our innovation

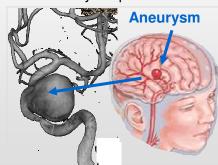
Minimally invasive, easy to use optimized design that:

- Disrupts blood's momentum transfer into aneurysm sac
- Creates a scaffold that produces a healing effect and reconstructs the diseased parent artery's wall

Reconstructs diseased parent artery



Giant Intracranial Aneurysm obliterated by Surpass device



Our partners

- A. K. Wakhloo, M.D. Ph.D. University of Massachusetts
- B. B. Lieber, Ph.D., Stony Brook University, NY

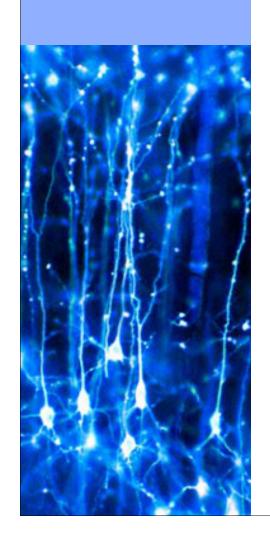
Our future

- 2011: Commence sales outside US
- 2011: Get FDA clearance & commence a US study
- Change the treatment paradigm of hemorrhagic and ischemic stroke through our advanced vascular reconstructive technology

CEO contact information

Ygael Grad, Ph.D. ygael@surpass-med.com

+972 (528) 399-570 www.surpass-med.com



Chapter 2 – Brain communication technology



- Brain Communication technology
 - Brain machine interface (BMI)
 - Therapeutic stimulation devices
- Key success factors in brain communication
- Israel is well positioned to lead in brain communication



Promising technologies allow brain communication by reading and writing information from/to the brain and nervous system

| Invasivo level | e Technology | Description | Applicability |
|-------------------|-------------------------------------|---|--|
| | EEG imaging | Recording of electrical activity along the scalp produced by the firing of neurons within the brain | This non invasive low cost method is the prominent technology to be used for computer interfaces in the near term |
| | fMRI | Measures the change in blood flow related to neural activity in the brain or spinal cord | High resolution imaging promises accurate functionality but cost, size and electromagnetic radiation render it less useful for day-to-day use |
| | Magnetic stimulation | A noninvasive method to cause depolarization in the neurons of the brain using electromagnetic induction to induce weak electric currents | Non invasive advantage, hindered by limited precision which causes side affects. Used mainly for disease treatment |
| | Optogenetics | Using genetics to make neurons react to light, firing and shutting off on command enables bidirectional communication with these neurons | Technology is very premature but could potentially offer first bidirectional communication with the central nervous system |
| | Electro- corticography (ECoG) | Measures the electrical activity of the brain taken from beneath the skull, using electrodes | ECoG is a good compromise between invasiveness level and recording quality & resolution, making the tech applicable for a wider variety of needs |
| | Electrode implant | An implanted electrode array which records/transmits electric signals in the brain and nervous system | High invasiveness level permits use only for severe conditions such as ALS, epilepsy and severe depression |

Two distinct opportunities stem from brain communication technology

Brain machine interface



- Bidirectional communication between the brain and machines/computers
- Reading and interpreting brain activity to allow a user to operate a machine using thought alone
- Building on brain plasticity and adaptability to form complex interactions between the brain and the machine
- Stimulating nerves to send the brain feedback from the machine such as sensory feedback (e.g., heat)

Therapeutic Stimulation



- Using electric or magnetic stimulation, it is possible to manipulate the electromagnetic field generated by neuron electrical activity
- Stimulation devices can activate neurons and modulate the central nervous system
- Manipulation technologies vary by level of invasiveness and ability to target specific brain areas
- Neurostimulation can help treat disorders such as epilepsy, pain, Parkinson's, depression and OCD

Opportunities in brain communication are in early stages on the road to commercialisation

ILLUSTRATIVE

- Scientists are still struggling with interpretation of complex signals
- Accurate comm. still requires high invasiveness levels
- Applied research is still limited to therapeutic benefits
- Low market demand for BMI limits entrepreneurial ventures
- Some stimulation devices are already clinically approved for limited use
- Commercial products are available but scale is still limited

Road to commercial applications

Therapeutic ВМІ stimulation

Description

Basic science

 Basic research of brain comm. technology

Transformational research

- Applied research to create commercial opportunities
- Product prototype / early stage clinical trials

Early commercialization

- Commercial grade product / late stage clinical trials
- Early commercial indications

Commercial product

- Clinically approved product
- Proven commercial potential

1 Brain machine interface (BMI) technology will revolutionize the way we live our lives

PRELIMINARY

Health care

- Prosthetic devices for motor systems
- Sensory implants (e.g. retina, cochlear) communicating with the CNS
- Mobility/Speech aid for paralysis
- Body enhancement





BMI will enable bidirectional communication between the brain and machines/ computers

"Intelligent" devices

- Enhanced communication with high tech devices and software
- Touch free communication with all electrical appliances







Defense

- Advanced weapon control
- Brain inspired computing (e.g. navigation, image recognition)
- Soldier enhancement
- Next generation C4I systems





Entertainment

- Gaming controllers
- Virtual reality
- Outer body experience



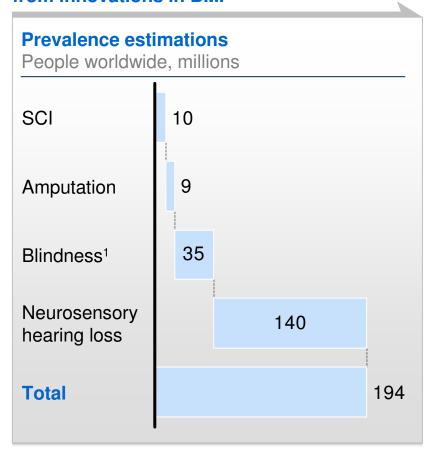


SOURCE: Team 41

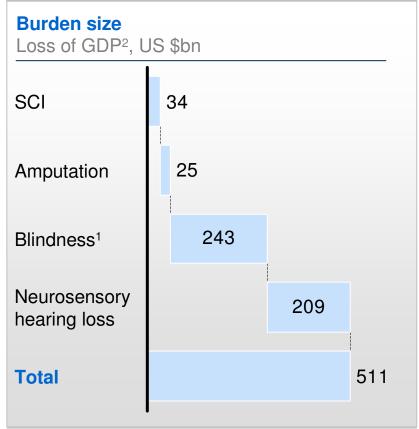
1 BMI application address the needs of over 190m people worldwide, with the potential to relieve a burden of over \$510bn GDP loss

PRELIMINARY

Over 190m people worldwide could benefit from innovations in BMI



Which could help relieve a burden of over \$510bn loss of GDP world wide



¹ Macular degeneration, Diabetic retinopathy and cataract

² Multiplication of DALY (Disability adjusted life years) by world average GDP/capita

Application

Description



- Mind controlled video game
- NeuroSky is developing an EEG based brainwave reader that can detect distinctive emotions and use them to control video games



- Restoring sight
- Second Sight has developed a device which consists of a tiny camera and transmitter mounted in eyeglasses, an implanted receiver and electrode array which together restore eye sight



- Operating a robotic arm with mind
- University of Pittsburgh lab has enabled a monkey to operate a robotic arm processing signals from a Braingate electrode implant in the motor cortex



- Typing with your mind
- Stanford study enables paralyzed patients to type up to 15 words a minute by reading electric activity in the pre-motor cortex using a Utah electrode implant



- Restore speech
- Neural Signals is developing a device which will restore speech using an implanted neurotrophic electrode to detect electrical activity in the Broca's area.



- Brain interface with Humanoid robot
- Honda is developing a brain interface to its ASIMO humanoid robot project

2 Promising technologies allow to stimulate brain and nervous system activity, with remarkable therapeutic capabilities

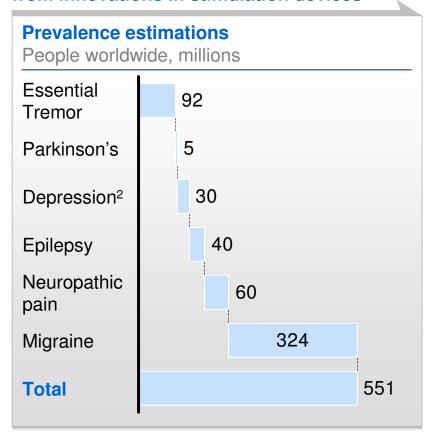
PRELIMINARY

| Technology | Description | Applicability |
|---|--|---|
| Transcranial magnetic Stimulation (TMS) | Noninvasive method to cause depolarization in the neurons of the brain. TMS uses electromagnetic induction to induce weak electric currents using a rapidly changing magnetic field; this can cause activity in specific or general parts of the brain | First non-invasive direct technique for functional mapping of the motor cortex repetitive TMS may help treatment resistant patients suffering from: depression, anxiety, PTSD, OCD, Pain, Parkinson's, migraines, aphasia, stroke, eating disorders, and addiction |
| Spinal cord stimulation (SCS) | A device used to exert pulsed electrical signals to the spinal cord by implementing stimulating electrodes in the epidural space | SCS has notable analgesic properties and, is used mostly in the treatment of chronic pain associated with spinal cord injury |
| Vagus Nerve stimulation (VNS) | VNS uses an implanted stimulator that sends electric impulses to the left vagus nerve in the neck via a lead wire implanted under the skin. The vagus nerve conveys sensory information about the state of the body's organs to the CNS | VNS has been approved to treat epilepsy and treatment resistant depression. Research is being done to determine its usefulness in treating a variety of other illnesses, including anxiety disorders, Alzheimer's disease, migraines and obesity |
| Deep Brain Stimulation (DBS) | A surgical treatment involving the implantation of a medical device called a brain pacemaker, which sends electrical impulses to specific parts of the brain | DBS has provided remarkable therapeutic benefits for otherwise treatment-resistant movement and affective disorders such as chronic pain, Parkinson's disease, tremor and dystonia |

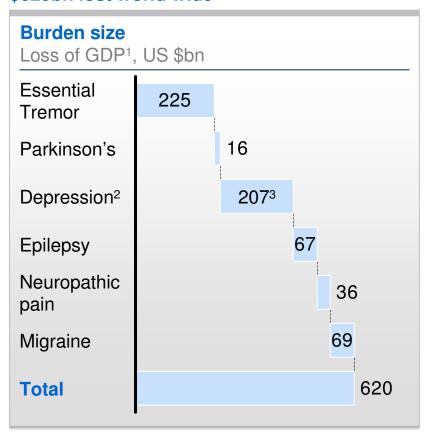
2 Therapeutic stimulation address the needs of ~550m people world wide, with the potential to relieve a burden of \$620bn on HC systems

PRELIMINARY

Over 550m people worldwide could benefit from innovations in stimulation devices



Which could help relieve a burden of over \$620bn lost world wide



¹ Multiplication of DALY (Disability adjusted life years) by world average GDP/capita

² Treatment resistant depression only

³ Using severe depression disability weight (0.76) as proxy

To commercialize brain communication opportunities, excellence in early stage technology is essential



Road to commercial applications

BMI Therapeutic stimulation

Key success factors

Basic science

- Research infrastructure
- Research talent in fields such as signal processing, computer science, nanotechnology and robotics

Transformational research

- Industry driven R&D
- Defense and high tech engineering talent
- Entrepreneurial mindsets and capabilities
- Multidisciplinary approach
- Large scale venture capital

Early commercialization

- Existing industry cluster
- Large scale venture capital
- Government support

Commercial product

- HC managerial experience
- Access to physicians and hospitals
- Proximity to large markets

Key success factors for early stage tech. such as brain communication

Israel is well positioned to succeed in brain communication



Success factors

Description

Research infrastructure

 A new \$130m centre for brain science in the Hebrew University (ELSC) focuses on brain communication research areas such as neural computation, brain stimulation and computational biology

Industry driven R&D

 Israel has established leadership in the fields of nanotechnology, engineering and optics technology in the defence, high-tech and healthcare industries – all key for brain communication

Defense and hitech engineering talent

 Many of the technologies used in the defence and hi-tech sector can potentially be used in Brain communication

Israel has a large talent pool of experienced engineers in these fields

Entrepreneurial mindset & capabilities

 Israel's strong start up legacy created an ecosystem to push forward innovations through an innovative mindset, serial entrepreneurs and large venture capital activity

Israeli entrepreneurs from non HC fields have identified HC as an opportunity for new start-ups

Multidisciplinary approach

 Israeli academia is renowned for its multidisciplinary approach, a vital method to approach BMI research which requires specialty in multiple scientific fields such as biology, physiology, engineering and computer science

Medical devices emerging cluster

- Israel is considered an emerging cluster for medical devices and has dozens of start-ups, success stories such as Medinol & Biosense, and R&D centres of major medical devices multinationals such as J&J and GE Healthcare
- Israel is the 4th largest originator of medical devices IP globally

Large scale venture capital

 Israel attracts one of the world's largest foreign venture capital. Numerous health care venture capital firms are operating in Israel, and over 700 biotech start ups are sustained by the VC industry in Israel