Rethinking Opportunity Risk in Neurodegeneration:
New Pathways to Treatment

Ginger Johnson, PhD
Rethinking Opportunity Risk in Neurodegeneration: New Pathways to Treatment
A Focus Neurodegenerative Disorders

Level of unmet need

Competitive environment

AD  PD  MS

Schizophrenia  Epilepsy  Migraine  Depression

1  2  3  4  5  6  7  8  9  10  11  12  13
The Opportunities in Neurodegenerative Disease are Centered Around a Few Disease Areas

From a Market Standpoint:

*WW Market for Neurodegenerative Disorders, $8+ billion*

- Multiple Sclerosis
- Alzheimer’s Disease
- Parkinson’s Disease

Huntingtons, ALS, Pick’s, Lewy Body Dementia...
Neurodegenerative Disease ≠ CNS (for the purposes of this presentation)

Bubble size represents equals total revenue.

Source: Evaluate Pharma, 01/04
Neurodegenerative Disease = 4 Buckets of Opportunity

- Enormous Untapped Opportunity
  - Alzheimer's Disease
- Major Untapped Opportunity
  - Parkinson's Disease
- Smaller opportunity, but realizing value
  - Multiple Sclerosis
- Untapped Orphan indications
  - ALS, Huntington's, ...
"Everyone is trying to get something for Alzheimer’s”

The story with Tysabri has just started," Ekman said.

Analysts believe that Elan shares have further to rise as Elan and Biogen quantify the amount of revenues as Tysabri is rolled out.

"We won't get a handle on that until the next few months," said Ian Hunter at Goodbody Stockbrokers.

Hunter last moved his 52-week target for the shares last November and has predicted the shares will reach $33.40 by late this year.

"We are not going to see the same level of appreciation as 2004," he said. "You will see solid growth as Tysabri proceeds into the market for MS and as it gets approval for Crohn's."

On the prospects for Alzheimer's, Hunter said that research into the disease was “much more emotive” for investors, and that any news tended to see the share price move.

Alzheimer's research is much bigger, with about 75 drug treatments in research, compared with only 25 potential treatments being explored for MS.

"Everyone is trying to get something for Alzheimer's," said Hunter.
The Untapped Potential

Revenue per Patient

- Alzheimer’s: $217
- Parkinson’s: $1,500
- Multiple Sclerosis: $6,000
And There is MCI ... Not Even a Drop in the Bucket

- The prevalence of MCI was recently estimated at 19% in persons under age 75, 15% in ages 75-79, 23% in ages 80-84, and 29% in the 85 and older group (Lopez O., Archives of Neurology 2003).
Alzheimer’s: A Meteor Heading Our Way

- Affects approximately 4 million people in the US; 15 million people worldwide
- 10% of people age 65 and older; 50% of people 85 and older
- Devastating disease of the elderly, affecting both patients and caregivers
- Direct medical and indirect costs are $80-100 billion annually
- A population that is about to explode
- Global health, economic and social crisis
Expected Growth in AD Patient Population is Tremendous

- If we assume no change in the patient prevalence, the AD patient population will increase dramatically simply as a function of the increase in the number of elderly.
- If, hypothetically, we assume that a disease-delaying drug will command a price per patient similar to that of the MS drugs, the AD market potential could reach more than $40 billion by 2050 (in 2005 dollars).
Rethinking Opportunity Risk in Neurodegeneration: New Pathways to Treatment

= Disease Delay
The Bridge of Peril
Lots of failure in CNS

- CNS has one of the highest pipeline attrition rates in the industry.

- In addition to a higher attrition rate, CNS drugs are the more expensive ($527m) and take longer to develop (114 months) than compounds in any other category.

Source: Tufts Center for the Study of Drug Development, April 2004
And a Particularly Poor Showing in Neurodegenerative Diseases

Source: DiMasi and ADIS (1995-present)
Some of the Failure is Pretty Spectacular

• Elan: The Ups and Downs

Historical Stock Price* of Elan

* Stock price adjusted for dividends and splits
Source: Yahoo Finance; Company Website; Defined Health analysis
But We Just Keep Trying

Alzheimer's Payday Eludes Drugmakers
By Robert Steyer
TheStreet.com Staff Reporter
9/30/2004 7:14 AM EDT
URL: http://www.thestreet.com/stocks/robertsteyer/10185381.html

Heroic failures -- that's how medical data firm IMS Health described the quest to find a cure for Alzheimer's disease. That was four years ago, when there were two drugs available in the U.S. and another was about to reach the market. Now there are five drugs, including one that is rarely used because of its troublesome side effects. But none of these drugs cure or halt the disease in which brain cells deteriorate and die, robbing people of their memory, their ability to function and eventually their lives. 

Although research failures keep coming, companies keep trying.
Everyone is Going for the Gold

**Big Pharma**
BMS  
Eli Lilly  
Pfizer  
Roche  
AstraZeneca  
Novartis  
Wyeth  
Abbott  
Sanofi-Aventis  
GSK  
Merck  
Pfizer  
Amgen

**Mid-Cap & Specialty**
Lundbeck  
Kyowa  
Forest Labs  
Biogen-Idec  
Chiron  
Serono  
Elan  
Elan  
Schwarz  
Somerset

**Emerging Biotech**
Saegis Pharmaceuticals  
Axonyx  
Memory Pharmaceuticals  
Neurochem  
Myriad Genetics  
Praecis  
Migenix (MitoKor)  
Cortex  
Prana Biologics  
NeuroSearch  
Targacept  
Rinat Neuroscience

*DefinedHealth
unconventional insight*
In AD, Biotech is Primarily Targeting the Accomplices to the Crime

- Ca++ channel modulators
- Anti-inflammatory
- Glutamate antagonists
- Nicotinic receptor modulators
- Acetylcholinesterase inhibitors
- Estrogen
- Metal Toxicity
While Pharma Goes After the Prime Suspect
(or, at least what we think is the Prime Suspect)
Pharma Shoots for the Moon

Some ... Opportunistically

Some ... With Dedication
The Few, The Dedicated … The Crazy?

With Dedication

Wyeth

Bristol-Myers Squibb Company
50/50 development and commercialization partnership with Elan for AN-1792

Completed initial 100-patient trial with AN-1792; well tolerated

Terminated Phase IIa AN-1792 program due to CNS inflammation

Filed IND for a monoclonal antibody, AAB-001, against beta amyloid

IND for conjugate formulation of peptide fragment of beta amyloid

Wyeth (with Elan): Takes a Licking, but Keeps on Ticking
Wyeth (with Elan): In For the Long Haul

Elan continues its bid for Alzheimer's breakthrough

The Sunday Business Post, Ireland; Jan, 16, 2005

Lars Ekman, Elan's head of research and development: “The first drug we had was – AN1792. What happened was that in Phase II we had a small number of patients who had a transitory inflammation of the brain they had it for 10 days, and then it went away.

“Because of that, we decided not to continue to dose patients. We decided it was not worth the risk,” Ekman said.

“What the market did not understand is that we continued to monitor those patients, and what we found was that they had an improved quality of life and brain function. We got what is called the ‘truth of principle’ for the drug, and what we had to find was a safer mechanism.”

Elan and pharmaceutical giant Wyeth are betting that their new AAB-001 is that safer drug. The antibody treatment has been in clinical trials for 18 months, and no side effects have been reported.

Additional data from the trials will be published in the next three months, potentially bringing investor focus back to Elan's work on Alzheimer's this year.

The company plans to start testing 180 patients with AAB-001 in trials in the US this year. A small trial is also planned for Britain and Finland, with 30 patients. This will get under way in the next three months.
BMS: Shooting for the Moon

Theme borrowed from BMS presentation at Defined Health’s Therapeutic Insight 2004 Conference
And With a Single Arrow

A Beta gamma/beta secretase
Plaque polymerization inhibitors
APP deposition inhibitors
Vaccines
Gene Therapy

Theme borrowed from BMS presentation at Defined Health’s 2004 Therapeutic Insight Conference
## Sanofi-Aventis: Multiple Shots on Goal

<table>
<thead>
<tr>
<th>Product</th>
<th>Originator</th>
<th>Pharmacological Class</th>
<th>Stage</th>
<th>Indication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1726</td>
<td>Aventis</td>
<td>Pyrimidine synthesis inhibitor</td>
<td>Phase III</td>
<td>MS</td>
<td>Oral immuno-modulator that blocks pyrimidine synthesis.</td>
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<tr>
<td>Xaliproden</td>
<td>Sanofi</td>
<td>Anti-neurodegeneration agent</td>
<td>Phase III</td>
<td>AD</td>
<td>Orally-active neurotrophic agent. Originally investigated in ALS. However, EU filing withdrawn in 2002.</td>
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<td>SL 65.0155</td>
<td>Sanofi</td>
<td>5HT4 partial agonist</td>
<td>Phase II</td>
<td>AD</td>
<td>Partial 5HT4 agonist which is thought to improve neural repair and prevent memory loss.</td>
</tr>
<tr>
<td>SR 57667</td>
<td>Sanofi</td>
<td>Anti-neurodegeneration agent</td>
<td>Phase II</td>
<td>AD</td>
<td>Non-peptidic compound similar to Xaliproden. Phase IIb studies are ongoing in Alzheimer’s and Parkinson’s disease</td>
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<tr>
<td>Beta Amyloid Inhibitor</td>
<td>Sanofi</td>
<td>Gamma secretase inhibitor</td>
<td>Preclinical</td>
<td>AD</td>
<td></td>
</tr>
</tbody>
</table>
Pharma Cocktail Party – Neurodegenerative Chatter

“Let’s try everything and see what happens.” Sanofi-Aventis

“I’m there or I’m nowhere.” BMS

“Wait and see, then come to me.” Pfizer

“I’m in for the long haul.” Wyeth
Pharma Repurposes

- Repurposing
  - Statins
  - Diabetes Agents
Why Repurpose

• One step ahead of the game
  – History of safety
  – Doctors comfortable with use
  – Eliminates NCE risk
Others Ride the Repurposing Wave

- **Clioquinol** (Prana Biotechnology)
- **Rifampicin** (University of California, Santa Cruz)
- **Ceftriaxone** (joint project of ALSA, NINDS, HDF and HDSA).
- **Cannabis Extract** (GW Pharmaceuticals, Pharmos)
- **R-flurbiprofen** (*Flurizan*, Myriad Genetics)
Will Repurposing Lead Myriad to Success?

Alzheimer's Drug on the Horizon?

By Charly Travers
January 12, 2005

Today, Myriad Genetics (Nasdaq: MYGN) announced that it was moving its drug Flurizan into phase 3 trials for the treatment of Alzheimer's disease. I found this announcement to be a pleasant surprise. Flurizan is now in a phase 2 trial that will conclude in March. I was originally expecting the results from the phase 2 trial to either propel the stock or cause it to crash, depending on the outcome.

Now that the drug has moved into phase 3, it appears that the phase 2 data will be positive -- good news for both patients and investors. Surely Myriad Genetics believes there is enough evidence to think that will be the case if it is willing to jump into phase 3 before phase 2 is over.

Preclinical studies demonstrated that the drug can lower levels of beta amyloid protein in mice, an important result because beta amyloid plaques are the hallmark characteristic of the disease. Not everyone agrees that the formation of these plaques causes Alzheimer's disease, but many people think that is the case.

Flurizan is an interesting drug that appears to have a lot of potential for Alzheimer's disease. This is why Flurizan's clinical development is so interesting. These studies should provide an answer to the question about whether lowering the levels of beta amyloid in Alzheimer's patients will improve their cognitive and behavioral functions. If it does, then that's a very big deal, which could make Myriad Genetics a very well-known company as a leader in treating Alzheimer's disease.

Developing drugs for Alzheimer's is not easy. This is certainly a high-risk situation that isn't appropriate for all investors. But identifying potential future market leaders such as Myriad Genetics can be very rewarding.
And at What Cost?

“But for all the money Myriad has spent on research--nearly $11 million in the last year alone--its only drug in clinical trials, R-flurbiprofen, did not come from Myriad's genetic databases. Instead, the company bought the drug two years ago from Riverside, CA based Encore Pharmaceuticals, a privately held biotechnology firm.”

Forbes.com Aug. 2002
And for What Reward?

• Myriad up as Alzheimer's trial enrollment starts.

• Wed Jan 12, 2005 (Reuters) - Shares of Myriad Genetics Inc. on Wednesday rose 14 percent to their highest price in almost 2-1/2 years after the company said it began enrolling patients in a late-stage clinical trial to evaluate its lead drug Flurizan in patients with Alzheimer's disease.
Compare that to the Increase Generated by the Avastin Data

- At ASCO 2003, Genentech (DNA) presented overwhelmingly positive results for its pioneering colorectal cancer drug Avastin.
- That data sent Genentech stock climbing, also lifting the broader biotech market.

Source: Yahoo Finance, Genentech’s website
Other High Profile Companies in Neurodegenerative Disease: Axonyx

- Dec. 2004: Axonyx completes Phase III trials for phenserine, a potential symptomatic and disease modifying treatment for AD.
- But still no pharma partner?

Source: Yahoo Finance, Axonyx’s website
Other High Profile Companies in Neurodegenerative Disease: Memory Pharmaceuticals

- August 2002: Roche received an exclusive worldwide license to Memory’s preclinical Alzheimer’s compounds; potential for Memory to receive $150 million in upfront payments, R&D funding and milestones. Memory also is eligible for royalties.
- March 2004: Memory raised $35 million, a significant haircut from the $87 million hoped with the original filing in Dec 2003.
- The stock is now way under water.

Source: Yahoo Finance, Memory's website
What Does it Take to Win?

= \textit{Disease Delay}
What Does it Take to Win in Neurodegenerative Disease?

• Dedication, or the Opportunistic Approach?
• Spreading Bets, or A Moon Shot?
• Multiple Shots on Goal, or A Focused Approach?

• Or, do you wait for the science to catch up…
**Drawing Parallels from the Oncology Market**

1992: Taxol first approved

The Discovery of Taxol
NCI

Advancing the Basic Science
NCI, Academia

A Few Big Pharma Players Enter
BMS, Aventis

Biotech & Pharma Partner

1960’s: NCI collected plant specimens from around the world

Biotech Jumps on Board

Biotech Tries to Go-it-Alone
In neurodegenerative disease, are we still in the “Advancing the Science” stage?
What Can We Do Besides Wait?

Things to do when you are bored:

- Wax the ceiling.
- Clean and polish your belly button.
- Wash a tree.
- Flash your goldfish.
- Sharpen your sleeping skills.
- Count to a million...fast.
- Think shallow thoughts.
- Interview a cloud.
What Can We Do Besides Wait?

Are there ways to speed, or circumvent, the process?

- Predictive Biomarkers
- Animal Models
- QoL Measurements
- Reaching the Target
Lessons from Success Stories in Degenerative Disease

- Multiple Sclerosis
- Macular Degeneration
Multiple Sclerosis: Disease Modifying Agents

- Although there is no cure for MS, disease-modifying drugs are available that can help reduce the frequency and severity of exacerbations.
These Agents Have a Practical Impact on Quality of Life

- Reduce the number of exacerbations
- Reduce the severity of exacerbations
- Improve ability to walk
- Delay or prevent secondary progressive disease
Not Necessarily So with Alzheimer’s Disease

Who wants to be a little less demented?
Is the Only Point of Intervention an *Early* Intervention?

### Stage of Alzheimer’s Disease

- **FAST (Functional Assessment Staging)** is a scale that allows professionals and caregivers to chart the decline of people with Alzheimer’s disease. The FAST scale has 16 stages and sub-stages.

#### FAST Stage 1
- Normal Adult
- No Decline in Function

#### FAST Stage 2
- Deficits Noticed in Demanding Employment Situations

#### FAST Stage 3
- Requires Assistance with Complicated Tasks (i.e., handling finances)

#### FAST Stage 4
- Requires Assistance in Choosing Proper Attire

#### FAST Stage 5
- Moderate to Moderately Severe AD
- Average Duration is 3-10 years

#### FAST Stage 6
- Requires Assistance with Complicated Tasks (i.e., handling finances)
- Sub-Stages within Stage 6
  - Assistance w/Dressing
  - Assistance w/Bathing
  - Assistance w/Toileting
  - Urinary Incontinence
  - Fecal Incontinence

#### FAST Stage 7
- Severe AD
- Average Duration is 1-3 years
- Sub-Stages within Stage 7
  - Speech Ability Limited
  - Unintelligible Vocabulary
  - Ambulatory Ability Lost
  - Ability to Sit Up Lost
  - Ability to Smile Lost
  - Ability to Hold Up Head Lost

*Source: Alzheimer’s Association*
Will Statins be the Answer?

- "Our current situation with regard to statins and Alzheimer's disease prevention is a classic 'open question' moment in science," says William H. Thies, Ph.D., Alzheimer's Association Vice President, Medical & Scientific Affairs.

- "The question to be resolved is: Do statins reduce an individual's risk of developing Alzheimer's disease if you prescribe them specifically for that purpose before a person shows any detectable symptoms of dementia?"

- "Although current data are mixed, there has been promising evidence of some biological mechanisms that may account for the preventive benefit. Almost everyone agrees that the data are good enough to justify large-scale trials.

Source: The 9th International Conference on Alzheimer's Disease and Related Disorders (ICAD), presented by the Alzheimer's Association
Multiple Sclerosis: A Predictive Biomarker

- As MS develops, it leaves lesions - signs of inflammation on the brain and spinal cord that appear as white spots on MRIs. Even if a person is not experiencing any symptoms, MS can still be active, and the presence, size, and extent of lesions indicate how much "silent" damage MS is doing to the central nervous system.

- MRI is used to help diagnose MS at an early stage, so treatment can begin immediately, rather than waiting for continued flare-ups to confirm a diagnosis.

**Mechanism Precedented by Antegren™**

- Antegren is given by intravenous infusion
- Excellent efficacy in reducing new brain lesions
- 66% reduction in relapse rate
- Use of imaging as surrogate for registration

Source: GlaxoSmithKline Neurology Pipeline Update, Jackie Hunter, SVP, Neurology and GI CEDD,
GSK’s Orally Available Anti-adhesion Drug: Moving Forward Based on Biomarker Activity

683699 Phase 1: Equivalent Biomarker Activity to Antegren

Oral 683699 matches i.v. Antegren pharmacodynamic effects even during troughs of activity

Source: GlaxoSmithKline Neurology Pipeline Update, Jackie Hunter, SVP, Neurology and GI CEDD,

DefinedHealth unconventional insight
No Generally Accepted Biomarker for AD (or PD)

- The National Institute on Aging's Biological Markers Working Group, part of the NIH’s Alzheimer's Disease Prevention Initiative.
- Looking for a way to diagnose AD in the prodromal, or presymptomatic, phase, where intervention will have the greatest benefit.
- The Biological Markers Working Group recently released a discussion of the status of biomarker research in AD.
  - Beta amyloid CSF or Plasma Test
  - Brain Imaging
    - Magnetic resonance imaging (MRI) and functional MRI
    - Positron emission topography (PET)
- None of these new imaging techniques or biomarkers is likely to become a stand-alone method of diagnosing AD. Instead, they will complement existing clinical tests and criteria to help patients obtain earlier and more accurate diagnoses.
...doctors don’t agree yet, but four out of five mice recommend this stuff.
Beta interferon: anti-inflammatory agent is thought to alter cell trafficking of the T-cell through the blood-brain barrier by their effects on proteases released by the T-cell.

MS Agents Reach the Target
MS Agents Reach the Target

*TYSABRI* ("Tie - SAB – ree"), natalizumab, Biogen Idec/Elan

...”the first humanized monoclonal antibody approved for the treatment of MS, inhibits adhesion molecules on the surface of immune cells. Research suggests *TYSABRI* works by preventing immune cells from migrating from the bloodstream into the brain, where they can cause inflammation and potentially damage nerve fibers and their insulation.”
“Given the choice, most would rather receive medicine orally or through an injection over a hole drilled in the skull. Unfortunately, many of the new therapies developed for brain ailments cannot be administered in these ways because they are barred from crossing into the brain. “
Lessons Learned from Other Degenerative Disease

- Age-Related Macular Degeneration

Retina No AMD  
Dry AMD  
Wet AMD

Photograph courtesy of the AROS Research Group
December 17, 2004 – Eyetech and Pfizer Announce FDA Approval of Macugen for Treatment of Neovascular (Wet) Age-Related Macular Degeneration

First treatment that helps preserve vision by targeting an underlying cause of disease.

Eyetech Pharmaceuticals, Inc. (Nasdaq: EYET) and Pfizer Inc (NYSE: PFE) announced today that the U.S. FDA approved Macugen(R) (pegaptanib sodium injection) for the treatment of neovascular (wet) age-related macular degeneration (AMD), an eye disease associated with aging that destroys central vision. AMD is the leading cause of irreversible severe vision loss in patients older than 50 years of age in developed countries. Macugen helps preserve vision and helps limit progression to legal blindness. … Macugen is the first in a new class of ophthalmic drugs to specifically target vascular endothelial growth factor (VEGF), a protein which acts as a signal in triggering the abnormal blood vessel growth and leakage that is the hallmark of neovascular AMD. … The anti-angiogenic approach specifically addresses, for the first time, an underlying cause of blindness in age-related macular degeneration. Anti-angiogenesis has evolved from theory to therapy," said Judah Folkman, M.D., Julia Andrus Dyckman Professor of Pediatric Surgery at Children’s Hospital in Boston and Harvard Medical School. … Until now, the only FDA-approved treatment was limited to the predominantly classic subtype of neovascular AMD, which accounts for up to 25 percent of the neovascular AMD patient population. … "Preserving vision will make a significant difference to AMD patients, since AMD can severely compromise a patient's ability to function independently. Neovascular AMD can lead to a rapid loss of central vision that impairs activities such as recognizing faces, reading, driving a car, crossing streets and basic tasks. … There are 15 million people in the United States living with some form of AMD, with more than 1.6 million experiencing the active blood vessel growth and blood vessel leakage associated with neovascular AMD. There are over 200,000 new cases of neovascular AMD each year and this number is expected to increase significantly as the baby boom generation ages and overall life expectancy increases. … Macugen is a pegylated anti-VEGF aptamer, a single strand of nucleic acid that binds with specificity to a particular target. Macugen specifically binds to VEGF 165, a protein that plays a critical role in angiogenesis (the formation of new blood vessels) and increased permeability (leakage from blood vessels), two of the primary pathological processes responsible for the vision loss associated with neovascular AMD. Macugen is administered in a 0.3 mg dose once every six weeks by intravitreal injection. …
## Eyetech: The Shining Star of the Class of ‘04

<table>
<thead>
<tr>
<th>Company</th>
<th>Gross Proceeds (IPO Date)*</th>
<th>IPO Price Per Share</th>
<th>Share Price On 12/31/04</th>
<th>Percent Change From IPO Price</th>
<th>Business Focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corgentech (CGTK)</td>
<td>$110.4M (2/11/04)</td>
<td>$16.00</td>
<td>$8.28</td>
<td>-48%</td>
<td>Cancer, cardiovascular &amp; inflammatory diseases</td>
</tr>
<tr>
<td>CoTherix (CTRX)</td>
<td>$30.0M (10/15/04)</td>
<td>$6.00</td>
<td>$11.92</td>
<td>+99%</td>
<td>Cardiopulmonary &amp; infectious diseases</td>
</tr>
<tr>
<td>Critical Therapeutics (CRTX)</td>
<td>$42.8M (5/26/04)</td>
<td>$7.00</td>
<td>$8.00</td>
<td>+14%</td>
<td>Respiratory, inflammatory &amp; critical care diseases</td>
</tr>
<tr>
<td>Cytokinetics (CYTK)</td>
<td>$103.2M (5/26/04)</td>
<td>$13.00</td>
<td>$10.25</td>
<td>-21%</td>
<td>Cancer &amp; cardiovascular disease</td>
</tr>
<tr>
<td>Dynavax (DVAX)</td>
<td>$51.8M (2/18/04)</td>
<td>$7.50</td>
<td>$8.00</td>
<td>+7%</td>
<td>Allergies, infectious diseases &amp; chronic inflammatory diseases</td>
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<tr>
<td>Eyetech (EYET)</td>
<td>$157.0M (1/29/04)</td>
<td>$21.00</td>
<td>$45.50</td>
<td>+117%</td>
<td>Ocular diseases</td>
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<tr>
<td>Genitope (GTOP)</td>
<td>$37.6M (10/30/03)</td>
<td>$9.00</td>
<td>$17.04</td>
<td>+89%</td>
<td>Cancer</td>
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<td>GTx (GTXI)</td>
<td>$78.3M (2/2/04)</td>
<td>$14.50</td>
<td>$13.49</td>
<td>-7%</td>
<td>Men's health conditions</td>
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<td>Idenix (IDIX)</td>
<td>$64.4M (7/21/04)</td>
<td>$14.00</td>
<td>$17.15</td>
<td>+23%</td>
<td>Viral diseases</td>
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<tr>
<td>Immunicon (IMMC)</td>
<td>$55.2M (4/15/04)</td>
<td>$8.00</td>
<td>$6.98</td>
<td>-13%</td>
<td>Cancer diagnostics</td>
</tr>
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</table>
Perhaps Pharma Can’t do it Alone

- Should we take a multimodality, franchise approach?
J&J Sees Rx Synergies in Guidant Deal

“...the potential synergies from combining different therapeutic technologies goes way beyond the stents, J&J expects to see a continual convergence on the businesses that goes into other areas that we can take advantage of.”

- William Weldon, J&J Chief Executive
Convergence Opportunities?

Deep Brain Stimulator (DBS, Medtronic)
- Deep Stimulation (DBS) vs. Best Medical Therapy (BMT) Trial
Convergence Opportunities?

VNS (Cyberonics)
- $60 billion pharmacoresistant depression market
- 2006 will invest aggressively in VNS for AD

COGNIShunt system (Eunoe)
- Completes initial closing of $40 Million Private Placement
- Investments led by Domain Associates.
  - CHL Medical Partners
  - Schroder Venture Life Sciences
  - BA Venture Life Partners & Affinity Ventures
  - Piper Jaffray Ventures
  - Vanguard Venture Partners
Key Takeaways:

• In neurodegenerative disease, the holy grail is “Delay.”
  – AD stands out as the enormous, untapped opportunity … and it’s getting bigger.
  – MCI could be the mother lode.

• This is not a therapeutic area for the “chicken.” (Sir Robin is a chicken!)
  – The failures are many.
  – The fall is hard.
Key Takeaways:

- Everyone is going for the gold.
  - Biotech is targeting the *accomplices*.
  - While pharma goes after the prime suspect.
    - Some opportunistically and some with dedication.
    - Some spreading bets and some shooting for the moon.
    - Some taking multiple shots on goal and some taking a focused approach.
Key Takeaways:

• Is any of this “responsible business”?  
  – Or is the science just too far behind and the risk too much to justify the cost?

• Can we advance the cause?  
  – Predictive Biomarkers
  – Better Animal Models
  – Practical QoL Measurements
  – Multi-Modal Approach
Thanks

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