Neurotech Insights™

THE NEUROTECHNOLOGY INDUSTRY NEWSLETTER

MARKET HIGHLIGHTS: NEUROCHEM CONCEDES DEFEAT IN ALZHEIMER'S TRIAL

By Casey Crawford Lynch

After meeting with the FDA to discuss alternative statistical models for analyzing their Phase III data, **Neurochem (NRMX)** finally announced that their Alzheimer's lead, *Alzhemed,* failed to provide significant improvement on the primary endpoint of the trial, improvement on the ADAS-Cog *(see story, page 6)*. The stock lost almost two thirds of its value in August. The company says it has enough cash to get back on its feet, with $80 million projected to last 18 months.

Top Gainers	Symbol	1 mo. return	3 mo. return	1 yr. return
Questcor Pharmaceuticals	QSC	+46%	-5%	-67%
Corcept Therapeutics	CORT	+43%	+131%	+165%
Neuralstem, Inc.	CUR	+38%	-7%	n/a
Somaxon Pharmaceuticals	SOMX	+25%	-18%	-12%
Javelin Pharmaceuticals	JAV	+20%	-26%	+52%

See more Neurotech Stocks, page 18

A new report from Friedman, Billings, Ramsay confirmed what investors already knew - the FDA has tightened its reigns in the wake of *Vioxx*, approving only 61% of drugs this year compared to 73% last year. Only seven of the 38 drugs approved were new molecular entities. Neurotech companies seem to be taking the brunt of conservative decisions. Last month **Biovail** was hammered when its follow-on to *Wellbutrin*, a once daily formulation of the active ingredient, was controversially rejected due to the design of a pharmacokinetic study.

This month **Wyeth/Solvay's** bifepunox for schizophrenia was deemed nonapprovable based on a single complex patient death during the trial. The FDA also delayed action or requested more information on **Endo's** *Fovra*, **GSK's** *Requip CR* and **POZEN's** *Trexima*. Not to mention the rejection of **Sanofi's** *Acomplia* and **Cephalon's** *Sparlon* over suspect safety concerns. Undoubtly, the current trend will be reversed eventually. Limiting treatment options in the name of public safety simply can't last while other countries continue to bring to market the latest treatments.

The Neurotechnology Industry Organization (NIO) announced the launch of a new industry job board. Access is free for employers and job seekers. There are over 150 jobs posted over 3 continents including research, regulatory, and management positions at drug, device and diagnostic companies for the brain and nervous system.

HEARING LOSS: ONE OF THE GREATEST UNMET MARKETS IN THE INDUSTRY

By Frank Eeckman, MD, PhD

Hearing loss is extremely common, especially in the elderly. The NIH estimates that 33% of older Americans, age 65 to 74, and nearly half of those 75 and older, have some hearing loss. There are many types of hearing loss and a variety of different causes, including genetic defects, infectious disease, and drug exposure. But the overwhelming majority of cases are due to exposure to loud noise.

Humans are sensitive to sounds with frequencies ranging from 20 to about 20,000 cycles per second (Hz). Most mammals can hear even lower frequencies which allows them to respond to earthquakes and other natural disasters faster than humans. Most everyday sounds are in the 300-5,000 Hz range. The average male voice peaks near 500 Hz, while the average female peaks near 700 Hz. The top end of the hearing range is very sensitive to aging and even young adults cannot hear sounds higher than 16,000 Hz. Hence the recent popularity among teens of cell phone ring tones adults cannot detect.

The second property of sound is volume, or amplitude. It is expressed as sound pressure levels (SPL) and the unit is the decibel (dB). Decibels are logarithmic measurements so a 10dB difference equals a subjective doubling of volume. Human hearing runs from 0 dB to 120-140 dB, the threshold of pain. Long term exposure to sound levels as low as 85 dB, or the inside of a commercial plane during flight, can cause permanent damage to the auditory system. Most damage is irreversible and progressive even after the offending stimulus has stopped.

Our auditory system is typically divided into three parts, the outer, middle and inner ear. The outer or external ear, includes the ear proper (pinna), the ear canal, and the ear drum. It is responsible for directing sound to the sensors deep in the ear via air conduction. Occasionally hearing loss can occur due to plugs of waxy material in the ear canal which is easily fixed by lavage.

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Where Is The NeuroInsights® Neurotech Index? Our new Neurotech Index will be launching very soon. Please stay tuned...

Product & Clinical Trial Updates

LEXICON'S COGNITIVE DISORDERS LEAD SAFE IN PHASE I

August 1, 2007

Lexicon Pharmaceutical's (LXRX) lead for cognitive disorders, *LX6171*, successfully completed a Phase I clinical trial. *LX6171* was well-tolerated at all dose levels and showed excellent systemic exposure. Over the seven day trial, no dose-limiting toxicities were observed and exposure levels supported a once daily dosing regimen. *LX6171* is being developed under a product development collaboration with **Symphony Capital Partners** and its co-investors.

The Phase Ib was a randomized, double-blind, placebo-controlled, multiple ascending-dose study to evaluate safety, tolerability and pharmacokinetics over seven days of dosing in normal healthy young (age 18-50) and elderly (age 65-80) volunteers. Lexicon expects to receive full audited results of its Phase I trials in the third quarter of 2007 and anticipates filing with European regulatory authorities for approval of its Phase II plans in the fourth quarter.

LX6171 is an oral drug candidate that was generated by Lexicon's small molecule drug discovery team and is being developed to treat disorders characterized by cognitive impairment, such as Alzheimer's disease, schizophrenia or vascular dementia. Its target, a membrane protein that is expressed exclusively in the central nervous system, was identified through *Lexicon's Genome 5000* program through the study of mouse knockouts that showed enhanced learning and memory. *LX6171* is a potent oral inhibitor of its target and reproduces these effects in animal models.

Lexicon entered into a product development collaboration with Symphony in June 2007. $45 million was provided to **Symphony Icon, Inc.,** a newly-created company established to fund and accelerate development of Lexicon's first three product candidates and hold the license to the intellectual property of *LX6171*, *LX1031* and *LX1032*. An additional $15 million of equity capital was provided directly to Lexicon for general corporate purposes.

EV3 GETS CE MARK FOR AXIUM COIL SYSTEM

August 1, 2007

ev3 Inc. (EVVV) has announced that it received CE Mark approval for its *Axium Detachable Coil System*. *Axium* was approved for the endovascular embolization of intracranial aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae. It is also intended for use in the European Union for the treatment of peripheral vascular abnormalities.

Axium incorporates several innovative technologies designed to meet the performance "wish list" of a diverse group of leading neurosurgeons and interventional neuroradiologists, including:

1) A high degree of coil conformability, which facilitates the physician's goal of more easily and completely filling and packing the aneurysm, regardless of its shape or size.
2) Coil softness combined with stretch resistance, which allows the coil to be positioned or re-positioned within the aneurysm without adding to the risk of bleeding or hemorrhagic stroke.
3) Ease of coil placement through the microcatheter, providing the physician with enhanced control and deliverability.
4) Rapid, safe and simple detachment of the coil through a proprietary *Instantaneous Detacher (I.D.)* device that offers instantaneous coil detachment without the use of wires or syringes.

PRANA'S AD LEAD PASSES PHASE IIA SAFETY REVIEW

August 6, 2007

Prana Biotechnology (PRAN) announced an update on the progress of its Phase IIa clinical trial of PBT2 in patients with early Alzheimer's disease. The independent Drug Safety Monitoring Board has reviewed blinded data of over 50 patients and as there have been no treatment-related serious adverse events or withdrawals, the trial will continue as per the original protocol. Seventy percent of the planned 80 patients have been randomized and patient dosing is expected to be completed by the end of 2007. Outcomes of the trial will include measures of cerebrospinal fluid A-beta and tau levels, as well as neurocognitive and behavioral changes.

INDEVUS' SANCTURA APPROVED FOR OVERACTIVE BLADDER, COMPANY GETS $50 MILLION MILESTONE

August 6, 2007

Indevus Pharmaceuticals, Inc. (IDEV) announced that *Sanctura XR* (trospium chloride extended release) has been approved by the FDA. *Sanctura XR* is indicated for the once-daily treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency. *Sanctura XR*, the once-daily formulation of *Sanctura*, is a quaternary ammonium compound and belongs to a class of anticholinergic compounds known as muscarinic receptor antagonists. These compounds relax smooth muscle tissue found in the bladder, thus decreasing bladder contractions. Indevus received a $49.9 million milestone payment from **Esprit Pharma**, the company's partner in the U.S. for *Sanctura* and *Sanctura XR*. The milestone payment was based on the total costs to develop the drug, including clinical and manufacturing development.

INTELLECT TO HUMANIZE ANTIBODIES FOR ALZHEIMER'S

August 6, 2007

Intellect Neurosciences (ILNS.OB) and **Medical Research Council Technology (MRCT)** entered into an agreement under which MRCT will use its proprietary technology to humanize Intellect's beta-amyloid specific, monoclonal antibodies for the treatment of Alzheimer's disease. Intellect will pay MRCT milestone payments related to the development and commercialization of the humanized antibodies and a royalty based on sales of any resulting products

The antibodies are intended as a form of passive immunization to promote clearance from the brain of the endogenous soluble Alzheimer's toxin, beta-amyloid. Humanization is an essential step in making antibodies safe for use in humans..

ALLON ADDS IMAGING BIOMARKER TO PHASE II

August 7, 2007

Allon Therapeutics Inc. (TSX:NPC) announced that in collaboration with TURNS (Treatment Units for Research on Neurocognition and Schizophrenia) and with support from the **National Association for Research in Schizophrenia and Affective Disorders (NARSAD)** they will add an imaging-biomarker component to the current Phase II efficacy trial evaluating *AL-108* as a treatment for schizophrenia-related cognitive impairment.

Three different imaging techniques will be used to investigate whether *AL-108* treatment results in a change in the brain structures affected by schizophrenia. TURNS believes that based on the mechanism of action of *AL-108*, structural changes in the brain should correlate with an improvement in cognitive function. The company expects to begin dosing shortly.

MERCK AND NEUROMED ABANDON PHASE II PAINKILLER

August 8, 2007

Merck & Co (MRK) and **Neuromed** have discontinued development of *NMED-160* (also known as *MK-6721*), a Phase II compound for the treatment of chronic pain. A joint research collaboration will continue to evaluate alternate, earlier stage, N-type calcium channel blocker candidates. N-type calcium channel blockers represent a novel class of analgesics that are selective for calcium channels involved in pain signal transmission.

The companies determined that *MK-6721* "does not demonstrate the ideal pharmaceutical characteristics considered necessary to advance the compound further in development." No serious adverse events with *MK-6721* were observed in clinical trials in which up to a 1,600 mg single dose was administered.

BIOVAIL ACQUIRES TREATMENT FOR SEXUAL DYSFUNCTION

August 8, 2007

Biovail Laboratories (BVF) entered into a license and development agreement with an undisclosed, privately held, drug-development company for the exclusive global rights to *BVF-324*, a novel product for the treatment of a prevalent sexual dysfunction. For competitive reasons Biovail did not disclose the nature of the compound or name of the other company.

The agreement allows for the licensing of clinical data, intellectual property and the rights to develop, manufacture and market *BVF-324* globally. In return, Biovail has paid an upfront fee and will make milestone payments, including upon the initiation of the first Phase III trial for the product and upon the first commercial sale of the product in the U.S. Biovail will also make tiered, single-digit royalty payments on net commercial sales of the product.

A meeting with the FDA to discuss the development program for *BVF-324* is scheduled for the fall. Biovail anticipates initiating Phase III studies for the product in the first half of 2008, which could lead to a New Drug Application filing in mid-2009.

GENAERA REVEALS DATA FROM PHASE I OBESITY TRIAL

August 8, 2007

Genaera Corporation announced interim data from the first Phase I clinical study of *MSI-1436* (trodusquemine) for the treatment of obesity. *MSI-1436* is the first drug candidate that acts both centrally and peripherally to selectively inhibit the established and validated enzyme target, protein tyrosine phosphatase 1B (PTP-1B). The dual locations of *MSI-1436* action make the drug a promising candidate for both obesity and type 2 diabetes. By inhibiting PTP-1B, trodusquemine is expected to decrease appetite and normalize blood sugar as PTB-1B is central to both the insulin and leptin pathways.

According to the company, preclinical testing shows that trodusquemine suppresses appetite, causes differential weight loss, reduces adipocyte size, reduces body fat (with no reduction of lean mass), and improves glucose tolerance via inhibition of a unique combination of signaling pathways in a mouse model of diet induced obesity.

Interim data from the initial cohorts in the placebo-controlled trial which included safety and pharmacokinetic (PK) data from 20 treated subjects and eight vehicle controls in four sequential dose groups showed a predictable pattern with minimal subject-to-subject variability and linearity across the range of doses studied. To date, no serious adverse events have been reported. Further study will be needed to establish dose limiting toxicity and proof-of-concept in humans.

DOV GETS POSITIVE PHASE IB FOR ANTIDEPRESSANT

August 9, 2007

DOV Pharmaceutical, Inc. (DOVP.OB) announced Phase Ib results for *DOV 21,947*, its lead triple reuptake inhibitor ("TRIP") for the treatment of depression and obesity. Preliminary analysis of the study results indicates *DOV 21,947* was safe and well-tolerated at the doses examined over an eight week period and produced a significant decline in plasma triglyceride levels.

DOV 21,947 treated subjects had lowered plasma triglyceride levels compared to placebo treated subjects ($p<0.015$). This reduction in mean triglyceride levels was noted following two weeks of treatment (23% reduction), was maintained at the end of the *DOV 21,947* treatment period (29% reduction) and was reversed after the one-week washout period at the end of the study. These results are consistent with preclinical evidence that *DOV 21,947* is able to produce a significant and sustained reduction in both triglyceride levels and body weight in animal models of obesity.

The double-blind, Phase II study scheduled for initiation later this year will compare up to 100 mg per day of *DOV 21,947* versus placebo in approximately 200 patients with major depressive disorder over a six-week treatment period. The company expects the results from this Phase II study will be available in the fourth quarter of 2008.

SOVAY AND WYETH'S BIFEPRUNOX NOT APPROVABLE

August 10, 2007

Solvay Pharmaceuticals (SOLB.BE) and **Wyeth (WYE)** announced that the FDA issued a not approvable letter for bifeprunox, an atypical antipsychotic that was reviewed for the acute treatment of schizophrenia, as well as the maintenance of stable adult patients.

The FDA said that bifeprunox demonstrated effectiveness in the long-term maintenance study and indicated that a second positive maintenance study could be sufficient to support a maintenance claim for bifeprunox. The companies believe that bifeprunox offers distinct benefits for the long-term maintenance of patients with schizophrenia and will meet with the FDA to discuss the study design and to assess how this additional study combined with ongoing and planned studies can support a maintenance indication.

Although the FDA acknowledged that bifeprunox separated from placebo in two short-term studies in the acute setting, the Agency concluded that the efficacy data, when compared to reference drugs, were not sufficient for approval. The Agency also requested further information regarding human metabolism of bifeprunox, and information regarding a complex case of a patient who died while participating in one of the trials.

AVIGEN TO BEGIN CLINICAL TESTING OF AV411 IN THE US

August 13, 2007

Neuropharmaceutical company **Avigen (AVGN)** received approval from the FDA to proceed with the U.S. clinical development of *AV411* (ibudilast). The initial trial for *AV411* will be a Phase I maximum tolerated dose study that is designed to build on data from Avigen's Phase I and exploratory Phase IIa studies in Australia and assess the safety and tolerability of the drug. The trial will also assess the effect of food on *AV411* pharmacokinetics and tolerability. In parallel, Avigen's Australian Phase IIa trial will provide safety and initial efficacy data of *AV411* in patients with neuropathic pain and is expected to report by the end of 2007.

AV411 is a first-in-class orally bioavailable small molecule glial cell attenuator. It down regulates neurological inflammation potentially via suppressing pro-inflammatory cytokines IL-1 beta, TNF alpha, and IL-6. It has other activities that are still being validated. The compound is approved in Asia at doses up to 30 mg per day, according the company. The Phase I trial will create a clear path towards further development of AV411 at higher doses.

While considered a New Chemical Entity in the U.S. and Europe, the drug was first approved in Japan for bronchial asthma over 15 years ago. The drug has been prescribed to over a million patients and has a good post-marketing safety profile in nearly 15,000 patients.

NEURAXON GETS POSITIVE PHASE I MIGRAINE DATA

August 14, 2007

NeurAxon, Inc., a developer of pain therapeutics targeting neuronal nitric oxide synthase (nNOS), announced positive data from its Phase I trial assessing the safety and pharmacokinetic profile for *NXN-188*. *NXN-188* is small molecule being developed for acute migraine which incorporates both 5-HT agonism (the mechanism of action of triptans, the current standard of care in migraine therapy) and nNOS inhibition.

Migraine models indicate that nNOS inhibition can relieve pain. Additionally, nitric oxide induces migraines in migraineurs, while the inhibition of NOS has been demonstrated to relieve migraine pain.

In the study, nine dose levels were evaluated with subjects receiving single oral doses of either *NXN-188* or placebo. Subjects were monitored for adverse events and pharmacokinetic parameters. Results from the trial indicate that *NXN-188* was well tolerated, with no drug-related adverse events reported. The company plans to advance *NXN-188* into a Phase IIa clinical proof-of-concept study.

CEPHALON GETS POSITIVE PHASE III RESULTS TO EXTEND PAIN INDICATIONS FOR FENTORA

August 16, 2007

Cephalon, Inc. (CEPH) announced positive results from a 12-week, Phase III trial of *Fentora* (fentanyl buccal tablet) in patients with breakthrough pain associated with a broad range of chronic non-cancer pain conditions. Results across the 12 weeks of treatment showed both statistically significant and clinically relevant outcomes for patients with breakthrough pain who were already receiving and who were tolerant to opioid therapy for their underlying persistent pain. *Fentora* is currently approved only for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.

ANESIVA'S ZINGO APPROVED BY FDA FOR LOCAL PAIN

August 17, 2007

The FDA approved **Anesiva's (ANSV)** *Zingo* (lidocaine hydrochloride monohydrate) powder intradermal injection system, which provides rapid, topical, local analgesia to reduce the pain associated with venous access procedures, such as IV insertions or blood draws, in children. *Zingo* is an easy-to-administer, single-use, needle-free system containing 0.5 mg sterile lidocaine powder. It provides a rapid onset of action, allowing intravenous line placement or venipuncture to begin one to three minutes after administration.

Anesiva is now studying *Zingo* in a large Phase III trial in adults. There may be opportunities to use the needle-free delivery technology employed in *Zingo* for the delivery of drugs other than lidocaine. Possible drug candidates include insulin, human growth hormone, erythropoietin, calcitonin, and other medications, excluding vaccines. The company may license the rights to the use of this technology for such other medications to third parties.

ELI LILLY SEEKS FIBROMYALGIA INDICATION FOR CYMBALTA

August 21, 2007

New data suggest that patients with fibromyalgia treated with 60mg or 120mg of *Cymbalta* (duloxetine HCl) experienced greater reduction in pain severity beginning one week after starting treatment than those taking placebo, as measured by the Brief Pain Inventory Average Pain Score (BPI). The study, which included patients with and without depression, also showed greater improvements in patients taking duloxetine in scores on the Patient's Global Impression of Improvement questionnaire (PGI- I), which measures how the patient has felt overall since starting the medication.

At three months, more patients treated with either 60mg or 120mg of duloxetine showed significantly greater reduction in pain as measured by a 30% improvement in baseline BPI scores (50.7% and 52.1%, respectively) compared with patients taking placebo (36%). Eli Lilly recently submitted a supplemental new drug application to the FDA for *Cymbalta* for the management of fibromyalgia. The sNDA submission is based on data from approximately 1,400 patients in five clinical trials.

NEWRON PHASE III PARKINSON'S ENDPOINT NOT MET

August 22, 2007

Newron Pharmaceuticals (SWX: NWRN), a company focused on novel CNS and pain therapies, and its partner **Merck Serono (MRK)** announced preliminary results of a 12-month extension study of a 6-month Phase III trial of safinamide as an add-on to dopamine agonist therapy in patients with early stage Parkinson's disease.

Patients were randomized to one of the three arms of the study to receive either safinamide at a dose of 50 to 100 mg once daily, safinamide at a dose of 150 to 200 mg once daily, or matching placebo tablets, as an add-on treatment to dopamine agonist therapy. Of the 270 patients originally enrolled in the trial, 227 entered the 12-month extension; 187 patients completed the 12-month extension period.

The primary efficacy endpoint of the 18-month trial was time from baseline to intervention (ie: increase in dose of dopamine agonist; or addition of another dopamine agonist, levodopa or another Parkinson's disease therapy; or discontinuation due to lack of efficacy). Analysis of the primary efficacy measure indicated that safinamide treatment delayed the onset of the above events by 93 days (3 months) as measured by the median time to event (559 days versus 466 days; p=0.334, not statistically significant).

A post-hoc analysis of the mean change in motor symptoms, as measured by the Unified Parkinson's Disease Rating Scale Part III Motor Score (UPDRS III) (secondary efficacy endpoint) demonstrated that the addition of safinamide resulted in a statistically significant improvement in motor symptoms over the 18-month treatment period (minus 4.7±9.34 versus minus 1.95±7.41; p=0.019). This improvement in motor symptoms was also accompanied by a statistically significant improvement in quality of life as measured by the Euro quality of life 2 scale (tertiary endpoint). As observed in the initial 6-month trial, the higher safinamide dose-range of 150 to 200 mg per day did not offer any incremental advantage over placebo.

A Phase III evaluating safinamide at the 50 to 100 mg once daily dose-range as add-on to levodopa therapy is ongoing in patients with mid-to-late stage Parkinson's disease. Additional Phase III trials evaluating this safinamide dose-range either as add-on to dopamine agonist or as add-on to levodopa therapy are expected to be initiated in 2007 in early and mid-to-late stage Parkinson's disease respectively.

JAPAN APPROVES EISAI'S ARICEPT FOR SEVERE ALZHEIMER'S

August 23, 2007

Eisai's (ESALY) Alzheimer's drug *Aricept* has been approved to treat the late stage of the disease in Japan, the world's second-biggest drug market.

NEUROCHEM'S ALZHEMED FAILS PHASE III TRIAL

August 26, 2007

Neurochem Inc. (NRMX) announced top-line results from the North American Phase III clinical trial assessing the safety, efficacy and disease modification effect of *Alzhemed* (tramiprosate) for the treatment of Alzheimer's disease (AD). Following a recent meeting with the FDA and subsequent statistical analyses, the company announced that there was descriptive data showing numerical differences but the treatment did not demonstrate a statistically significant difference in favor of *Alzhemed* with respect to the primary endpoints over 18 months of treatment. A substantial difference observed in hippocampal volume did approach statistical significance. Due to significant interference from high between-site variations that complicated the statistical analyses beyond expectations, it is not possible to draw definitive conclusions about the efficacy of *Alzhemed*. *Alzhemed* was generally safe and well tolerated.

At the recent FDA meeting, Neurochem sought feedback on appropriate next steps, especially with respect to the statistical models and the detailed analysis of potential confounding factors. The agency recognized the difficult issues surrounding a trial of this magnitude, with its significant site effect and the large number of covariates identified during the modeling process, and advised that neither the proposed adjusted models nor any further adjustments could be used for this trial to provide results in support of a claim of clinical efficacy.

Neurochem will continue to evaluate the treatment effect of *Alzhemed* with post-hoc evaluations to facilitate its understanding of the data and assess any treatment effect from the North American trial. Neurochem has established a Special Advisory Board which will comprise regulatory, medical and statistical experts from the fields of AD, therapeutics for the central nervous system, functional assessments, imaging, biomarkers, and clinical trial design. The purpose of the Advisory Board will be to assist Neurochem over the coming months in reviewing and analyzing the data and in designing future trials.

The study was a double-blind, placebo-controlled, three-armed and parallel-designed, 18-month Phase III clinical trial. The study included 1,052 patients with mild-to-moderate AD recruited across 67 sites in Canada and the U.S. who were randomized to receive either placebo or one of two doses (100mg or 150mg twice daily) of *Alzhemed*. All patients were required to be on a stable does of conventional symptomatic AD therapies for at least four months prior to the trial and continuing throughout the clinical trial.

Neurochem is also currently conducting a European Phase III clinical trial for *Alzhemed*. To date, 966 mild-to-moderate AD patients are enrolled at 69 clinical centers in 10 European countries. Neurochem is presently considering potential modifications to the European study to take best advantage of the experience gained from the recently completed North American Phase III clinical trial.

Alzhemed is a small, orally-administered molecule known as an amyloid B antagonist. *Alzhemed* crosses the blood-brain-barrier, binds to soluble AB peptide and interferes with the amyloid cascade that is associated with amyloid deposition and the toxic effects of AB peptide in the brain. The presence of amyloid in the brain is one of the major histopathological characteristics of AD. *Alzhemed* has Fast Track designation from the FDA for the treatment of mild-to-moderate Alzheimer's disease.

BRAINSWAY TO DEVELOP TMS FOR RARE BRAIN DISORDERS

August 28, 2007

Brainsway Ltd. (TASE:BRIN) will conduct human clinical trials of its Deep TMS transcranial magnetic stimulation device in the UK in partnership with the **National Institute of Neurological Disorders and Stroke (NINDS)**, a branch of Britain's National Institutes of Health (NIH), for the treatment of Blepharospasm (BSP) and Tourette's syndrome. In the case of BSP, a condition causing eyelid spasms, the research will seek to achieve a better understanding of the internal mechanism of the disease and test the effectiveness of Brainsway's methodology of external brain stimulation using TMS to treat it. 23 patients will participate in the trial.

ACCERA'S KETASYN POSITIVE IN AAMI PHASE II

August 29, 2007

Accera, Inc. announced that recent data from a Phase II study of its lead compound *Ketasyn* (AC-1202) in age-associated memory impairment (AAMI) showed that *Ketasyn* has a positive and clinically meaningful effect on memory in older adults.

AAMI symptoms may be related to declines in glucose metabolism in the brain that are also associated with aging. Glucose is the brain's primary fuel source, so aging brains with impaired glucose metabolism require an alternative energy source. *Ketasyn* is an orally available compound metabolized into ketone bodies, which the brain can use for energy even when its ability to process glucose is impaired.

The randomized, double-blind, placebo-controlled, parallel, multi-center trial was conducted at six centers in the

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U.S. One hundred fifty-nine subjects diagnosed with AAMI received either *Ketasyn* or placebo for 90 days followed by a two-week washout period. Mean age in this study was 65. Subjects were tested for apolipoprotein E gene (APOE) variants, a known genetic risk factor for Alzheimer's disease (AD) that occurs in 15-20% of the general population. On days 0, 30, 60, 90 and 104, subjects were evaluated through a battery of neuropsychometric tests that measure various aspects of memory and cognition.

Ketasyn showed significant efficacy in tests of memory. On average, subjects taking Ketasyn performed significantly better on the 'First-Last Name Association' test (FLN) than subjects taking placebo (p=0.042). In another memory test called Name-Face Recognition (NFA), which associates a person's name and face, Ketasyn subjects under age 59 improved significantly more than placebo subjects at Day 90 (p=0.0217). The efficacy in the NFA test observed with Ketasyn in subjects under age 59 captures a large portion of the AAMI population.

Consistent with the findings of Accera's Phase IIa and IIb AD studies, subjects who did not have the APOE4 genotype (E4(-)) responded particularly well to treatment: E4(-) subjects showed a further significant treatment effect of Ketasyn in FLN at Day 90 (p=0.012). In contrast, and also consistent with the AD trial results, APOE4(+) subjects showed no difference between *Ketasyn* and placebo for FLN scores at Day 90 (p=0.4639). The safety profile of *Ketasyn* was excellent, as shown in the previous AD trials with *Ketasyn*. The incidence of adverse events was low and similar between *Ketasyn* and placebo groups.

Accera recently completed a Phase IIb clinical trial in AD patients that confirmed *Ketasyn's* safety and efficacy as measured by improvement in ADAS-Cog scores, the gold standard measure for efficacy in cognition and short-term memory. Accera plans to initiate a pivotal, Phase III multi-center clinical trial in early 2008 in mild-to-moderate AD patients.

PALATIN AND KING DELAY BREMELANOTIDE PHASE III

August 30, 2007

Palatin Technologies (PTN) and **King Pharmaceuticals (KG)** delayed plans for the initiation of Phase III clinical trials with bremelanotide, a first in class melanocortin agonist drug candidate, for the treatment of male erectile dysfunction (ED). The decision follows responses from representatives of the FDA, which raised serious concerns about the acceptable benefit/risk ratio to support the progression of the drug into Phase III.

After reviewing the data generated in the Phase I and II studies, the FDA questioned the overall efficacy results and the clinical benefit of this product in both the general and diabetic ED populations, and cited blood pressure increases as its greatest safety concern. Though not supportive of the proposed Phase III studies for ED with bremelanotide, the FDA stated that it was amenable to proposals for a different drug development pathway, such as for a second-line therapy in non-responders to currently approved PDE-5 inhibitors.

Palatin and King plan to review the FDA comments in the overall context of the program in order to determine next steps related to the further development of bremelanotide for the treatment of ED.

NEURALSTEM ENTERS ALS COLLABORATION

August 30, 2007

Stem cell company, **Neuralstem, Inc. (CUR)** entered into a collaborative agreement with the ALS Clinic at University of Michigan Health System. The goal of the collaboration is to provide further proof-of-principle data to move Neuralstem's spinal cord stem cells into patients with Amyotrophic Lateral Sclerosis (ALS), or Lou Gehrig's disease. Neuralstem expects to submit its first Investigational New Drug application for the treatment of Ischemic Paraplegia shortly and begin its first human trial during 2007.

ALZHEIMER'S DRUG GALANTAMINE GOING GENERIC

August 30, 2007

Ranbaxy Laboratories Limited (RLL) and **Sun Pharmaceuticals** received tentative approval from the FDA to manufacture and market Galantamine Hydrobromide Tablets for mild to moderate Alzheimer's disease. Total annual sales for **Ortho McNeil's** *Razadyne* are approximately $130.0 million according to IMS Health.

BRAINZ & GE LAUNCH INFANT BRAIN MONITOR IN EUROPE

August 31, 2007

BrainZ Instruments will launch its upgraded bedside infant brain monitor *BRM3* in Europe next month with immediate sales expected. Brainz has received confirmation that the *BRM3 Brain Monitor* meets all requirements of the European Union Medical Devices Directive. The Certificate of Conformance to these requirements allows application of the CE mark and distribution in Europe. The product will be launched into Europe and the Middle East through BrainZ Instruments' distribution partner **GE Healthcare** at the beginning of September 2007.

Deals, Alliances, and Financings

MICRUS TO ENTER CHINA NEUROVASCULAR MARKET

August 1, 2007

Micrus Endovascular Corporation (MEND) signed a five-year, exclusive agreement with **Beijing Tian Xin Fu Medical Appliances Co. (TXF Medical)**, for the distribution in China of Micrus' implantable and disposable medical devices used in the treatment of neurovascular diseases. Micrus expects to begin distributing its products through TXF Medical in the Chinese market upon receiving regulatory approval. According to the company, China is the worlds fastest growing neurointerventional market with 7,500 endovascular procedures last year and 25 to 30% growth in the number of procedures.

NEURONETRIX TO DEVELOP ALZHEIMER'S DIAGNOSTIC

August 1, 2007

Neuronetrix, Inc. and **Rowan University** have entered a research agreement to jointly develop methods for the early diagnosis of Alzheimer's disease. The goal is to integrate a novel analysis technology developed by Dr. Robi Polikar of Rowan into Neuronetrix' *Cognision ERP System*. Neuronetrix, recently recruited a new CEO, Mike Reid, to raise venture funding for developing the product.

This diagnostic technology uses electroencephalograph (EEG) measurements to record brain activity as a patient listens to auditory stimuli. These "event-related potentials" (ERP) can then be compared to a database of normal subjects and subjects with Alzheimer's disease and the system will automatically classify the patient as being normal or showing early signs of Alzheimer's. The method was tested on 52 patients and demonstrated that this simple, non-invasive test could identify patients with Alzheimer's disease more accurately than most community physicians.

The first phase of the 18-month agreement is to implement the analysis method in the current generation *Cognision System*. Neuronetrix plans to use Dr. Polikar's method and protocols in a recently approved clinical study at the University of Kentucky. In follow on phases, Polikar and Neuronetrix will optimize the approach to increase the diagnostic accuracy of the *Cognision ERP System*.

CYBERKINETICS TO BENEFIT FROM $6.5 MILLION NIH GRANT

August 2, 2007

Cyberkinetics Neurotechnology Systems (CYKN.OB), Brown University, and the Cleveland FES (Functional Electrical Stimulation) Center at the Case Western Reserve University announced that they will act as a consortium benefiting from a five-year, $6.5 million grant from the National Institutes of Health (NIH) to support the development of Cyberkinetics' *BrainGate Neural Interface System (BrainGate System)*. The goal of the *BrainGate System* is to provide a reliable, fully implantable and wireless neuroprosthesis that enables paralyzed people to use their own limbs to perform tasks such as eating, drinking, and controlled breathing, as well as to regain bowel and bladder function.

Cyberkinetics may receive up to $2.5 million of the total grant award during the five-year period covered by the agreement.

KINEMED RAISES $15 MIL BRIDGE TO SERIES D

August 3, 2007

KineMed, a pathway-based drug discovery and development company, completed a $15 million convertible notes offering. The offering was led by a direct investment from **Stanford Financial Group**, joined by existing investors from previous financing rounds. The funding will convert at the next financing which is likely to be a Series D.

The funds will be used to advance KineMed's lead compound, *KM-801*, into clinical studies in 2008 for the treatment of Amyotrophic Lateral Sclerosis (ALS, or Lou Gehrig's disease). *KM-801* is a small-molecule agent, which has been shown to alter microtubule dynamics in nerve cells in preclinical studies.

CENES LICENCES ANESTHETIC TO ONO PHARMACEUTICAL

August 6, 2007

CeNeS Pharmaceuticals (LSE: CEN), a Cambridge based company focused on CNS disorders, licensed exclusive rights to **Ono Pharmaceutical** to develop and commercialize *CNS-7056*, a general anesthetic and short-acting sedative, in Japan. Under this agreement, Ono will pay to CeNeS upfront and milestone payments as well as royalties on sales of *CNS-7056*.

CNS-7056 is a new short-acting general anesthetic and sedative that acts on GABA-A receptors. Pre-clinical studies demonstrate that, after intravenous administration, the compound rapidly induces deep sedation which is maintained during continuous administration. Importantly the sedative effects rapidly disappear after cessation of administration. The rapid offset of effect of the compound is due to its metabolism by esterase enzymes that are widely distributed throughout the body.

CeNeS plans to start a Phase I study in the U.S. in the first half of 2008 and Ono plans to start a Phase I study in Japan as early as the second half of 2008.

TIKVAH LICENSES ORAL FORMULATION FROM NAVINTA FOR NEURODEGENERATIVE DISEASE LEAD

August 7, 2007

Neuropharmaceutical company, **Tikvah Therapeutics**, and New Jersey-based **Navinta** entered into an exclusive worldwide licensing agreement that encompasses unique solution formulations, including a proprietary formulation of sodium phenylbutyrate, and methods of use and treatments of a variety of neurodegenerative disorders including, amongst others, spinal muscular atrophy, amyotrophic lateral sclerosis and multiple sclerosis, and certain metabolic disorders.

Navinta's proprietary formulation of sodium phenylbutyrate overcomes the unpleasant taste, unpleasant smell, and lack of solubility of existing oral products being explored for the treatment of various neurodegenerative diseases. Clinical studies have often been hampered by lack of availability of formulations optimized for use in infants, children, and older individuals with difficulties swallowing.

Tikvah will pay a licensing fee, potential milestones, and royalty payments in exchange for an exclusive worldwide license to pursue the commercial development of the technology for the treatment of SMA and other neurodegenerative diseases.

ENCORE GETS $500K SEED ROUND FOR STROKE DEVICE

August 8, 2007

Encore Path also known as **Newregen,** a company developing stroke rehabilitation devices, has raised $500,000 in seed financing, according to VentureWire. **The Maryland Venture Fund and Maryland Technology Development Corp.** provided the financing, along with angel investors and friends and family. The company's first product will be a training device for restoring arm movement.

PALADIN AND SHIRE EXPAND MARKETING AGREEMENT

August 8, 2007

Paladin Labs (PLB.TO) expanded its current exclusive Canadian distribution agreement with **Shire Human Genetic Therapies (SHPGY)**. Under the new agreement, Paladin will be distributing *Elaprase* (idursulfase) for Hunter syndrome in addition to *Replagal* (agalsidase alfa) for Fabry disease. Health Canada recently granted Shire HGT regulatory approval for *Elaprase*, indicated for enzyme replacement therapy in patients with Hunter syndrome.

Hunter syndrome is an X-linked recessive disorder caused by a deficiency or absence of iduronate-2-sulfatase (I2S). Its absence results in a deleterious accumulation of cellular waste products (GAG) in cells throughout the body and results in mental retardation and aggressive behavior.

BOSTON SCIENTIFIC TO UNDO MERGER WITH ADV. BIONICS

August 10, 2007

Boston Scientific Corporation (BSX) is amending its merger agreement with **Advanced Bionics**, which it acquired in 2004, eliminating shared management provisions and modifying the schedule of earnout payments. The amendment grants Boston Scientific sole management and control of the Pain Management business, including the emerging indications program. The company has agreed to sell the auditory business and drug pump development program to principals of Advanced Bionics. The transactions must be approved by former Advanced Bionics shareholders who are entitled to earnout payments under the original merger agreement. The transactions are expected to close in January 2008.

Following the closing of the transactions, the parties have agreed to dismiss currently pending litigation between Boston Scientific and former Advanced Bionics shareholders.

The Pain Management business Boston Scientific will retain includes spinal cord stimulation technologies, as well as emerging technologies such as the *bion microstimulator*; a very small injectable stimulator, that will position the company well in the broader neuromodulation field. Boston Scientific currently has the number two overall market position in pain management. The transaction provides a new schedule of consolidated, fixed earnout payments by Boston Scientific to former Advanced Bionics shareholders, consisting of $650 million payable upon closing in January 2008 and $500 million payable in March 2009. The Advanced Bionics principals will acquire a controlling interest in the auditory and drug pump businesses for an aggregate payment of $150 million at closing. The company expects to record an estimated after-tax charge, primarily non-cash, of $360 million related to the transactions.

"We are excited about the immediate and long-term growth opportunities presented by neuromodulation," said Jim Tobin, President and CEO of Boston Scientific. "We hope to replicate the success of the pain management technologies across a wide spectrum of indications, expanding our microelectronic capabilities and strengthening our leadership in neuromodulation and cardiac rhythm management. The sale of the Auditory business and drug pump program is consistent with our previously announced objective of selling assets we do not consider core to our long-term strategy."

The Pain Management business and emerging indications program will operate as Boston Scientific Neuromodulation under the leadership of Michael Onuscheck, currently head of the Pain Management business. The Auditory business and drug pump program will operate as Advanced Bionics under the leadership of Jeff Greiner.

MINDWEAVERS GETS $1 M SERIES A FOR NEUROSOFTWARE

August 10, 2007

Privately owned neurosoftware company, **MindWeavers,** raised $1.1 million from **City and Merchant Group PLC** according to VentureWire. Prior to this funding, MindWeavers was funded through its founders and friends.

The company's first product, *Phonomena*, uses software-based activities to improve children's language skills. MindWeavers is scheduled to launch its second product, *MindFit*, in September, which provides brain exercises for baby boomers. The company is also working with **CogniFit** to develop a third product, targeted at elderly patients with more advanced brain conditions, including early Alzheimer's disease and mild cognitive impairment.

FOLDRX TO RECEIVE UP TO $22 MILLION IN FUNDING FROM CYSTIC FIBROSIS FOUNDATION

August 13, 2007

FoldRx Pharmaceuticals, Inc. (FoldRx) will receive up to $22 million from Cystic Fibrosis Foundation Therapeutics over five years to discover and develop new compounds aimed at treating a core defect in cystic fibrosis. The research, development and commercialization agreement - one of the largest of its kind for CFFT - calls for FoldRx to use its novel yeast-based, high throughput screening platform to detect new compounds that could improve the function of a misfolded protein associated with cystic fibrosis, thus helping treat the disease. FoldRx Pharmaceuticals is developing small molecules to treat diseases of protein misfolding and aggregation (amyloidosis), including Alzheimer's and Parkinson's.

OPHTHOTECH RAISES $36 MILLION SERIES A; INLICENSES POTENTIAL TREATMENTS FOR MACULAR DEGENERATION

August 13, 2007

Ophthotech Corporation closed a Series A financing of $36 million and announced two in-licensing deals for compounds to treat age-related macular degeneration (AMD). With this financing, Ophthotech management which includes the co-founders of Eyetech, expects to have sufficient resources to execute its strategy. Participants in the round include **SV Life Sciences, HBM BioVentures** and **Novo A/S.**

The company obtained an exclusive, worldwide license from **Archemix Corp.** for the treatment of the wet and dry forms of AMD. The deal encompasses worldwide rights to all ophthalmic uses of Archemix's proprietary aptamers targeting the C5 component of the complement cascade. Specific terms of the agreement were not disclosed.

OSI Pharmaceuticals (OSIP) recently announced that its subsidiary, **Eyetech,** entered into an agreement with Ophthotech to divest its anti-platelet derived growth factor (PDGF) aptamer program. OSI plans to transfer to Ophthotech all rights in the PDGF aptamer program, including rights to its pre-clinical compound *E10030*, in exchange for an up-front cash payment, an equity interest in Ophthotech and potential future milestones and royalties. Financial terms were not disclosed.

In pre-clinical studies, *E10030* demonstrated the potential to regress neovascularization when used in combination with a vascular endothelial growth factor (VEGF) inhibitor. Anti-VEGF agents alone have shown the ability to slow or halt, but do not regress choroidal neovascularization. OSI elected to suspend further research on this compound in connection with its decision to divest its eye disease business.

ICAGEN AND PFIZER ENTER PAIN AGREEMENT

August 14, 2007

Icagen (ICGN) entered into a worldwide collaboration and licensing agreement with **Pfizer (PFE)** for the discovery, development and commercialization of compounds which modulate three specific sodium ion channels as new potential treatments for pain and related disorders.

Pfizer will provide $38.0 million in committed funding over the first two years of the collaboration including an initial upfront license fee of $12.0 million, up to $15.0 million through an equity commitment, and research and development funding. The equity commitment is comprised of an initial investment in Icagen common stock in the amount of $5.0 million at fair market value on the effective date of the agreement and an equity put option, exercisable by Icagen, to sell to Pfizer at fair market value up to $10.0 million of common stock, subject to certain terms and conditions, at any time during the first eighteen months following the signing of the agreement. Additionally, Icagen is eligible to receive $359 million in research, development, regulatory and commercialization milestones for each product. Icagen is also eligible to receive tiered royalties, against which the commercialization milestones are creditable, depending upon sales achieved. Pfizer will have exclusive worldwide rights to commercialize resulting products.

The ion channel targets included in the collaboration are important in the generation of electrical signals in nerve fibers that mediate the initiation, transmission and sensation of pain. In preclinical studies, compounds identified by Icagen have demonstrated efficacy in pain models.

Based upon the financial terms of the collaboration, the company now expects to end the third quarter of 2007 with approximately $46.0 million in cash, and approximately an additional $20.0 million in committed funding.

EPIX HITS $3 MILLION MILESTONE IN GSK COLLABORATION

August 14, 2007

EPIX Pharmaceuticals, Inc. (EPIX) achieved an initial milestone under its collaboration with **GlaxoSmithKline (GSK)** related to the first of three discovery stage programs. EPIX has identified three lead candidates that will move forward into lead optimization in this first collaborative G-protein coupled receptor (GPCR) discovery program. EPIX is entitled to receive a $3 million milestone payment from GSK in the next 30 days.

In December 2006, EPIX and GSK announced a worldwide multi-target strategic collaboration targeting four G-protein coupled receptors (GPCRs) for the treatment of a variety of diseases, including EPIX's novel 5-HT4 partial agonist program, *PRX-03140*, which is in early-stage clinical development for the treatment of Alzheimer's disease. As part of the collaboration, EPIX received total initial payments of $35 million, including $17.5 million through the purchase of its common stock at a premium, and may be eligible to earn up to $1.2 billion in milestones across the four GPCR programs. Under the collaboration, EPIX is also entitled to receive tiered double-digit royalties of sales by GSK on all collaboration-developed product sales.

ALSERES EXTENDING LOAN FOR ADDITIONAL $10 MILLION

August 14, 2007

Alseres Pharmaceuticals (ALSE) plans to borrow up to $10 million from a new purchaser, **Ingalls & Snyder Value Partners**, in an extension to the Convertible Promissory Note Purchase Agreement dated May 1, 2007. According to the company, the additional funds will enable them to continue to advance clinical programs and on-going partnering activities for their molecular imaging assets.

Alseres, formerly **Boston Life Sciences**, is developing diagnostic and therapeutic products for central nervous system (CNS) disorders including *Cethrin*, a recombinant-protein-based drug to promote nerve repair after acute spinal cord injury (Phase I/IIa) and *Altropane*, a molecular imaging agent for the diagnosis of Parkinson's Disease (Phase III).

OBESITY NEUROSTIM COMPANY LEPTOS CLOSES $20 MIL

August 15, 2007

Leptos Biomedical, a neurostimulation company focused on treating obesity, has raised $20 million in Series C funding according to VentureWire. The deal includes a pair of $10 million tranches, with the first called down in April and the rest dependent on the achievement of certain milestones. **Latterell Venture Partners** led the deal, and was joined by return backers **Spray Venture Partners, Technology Partners** and **Thomas McNerney & Partners**. Leptos previously raised $6 million in 2004.

TRANSITION THERAPEUTICS TO LIST ON NASDAQ

August 16, 2007

Common shares of **Transition Therapeutics (TSX: TTH)** began trading on the NASDAQ Capital Market on August 20, 2007, under the symbol "TTHI". The company's common shares will continue to trade on the Toronto Stock Exchange under "TTH" in addition to NASDAQ. Transition's lead products include AZD-103/ELND005 for the treatment of Alzheimer's disease and regenerative therapies E1-I.N.T.(TM) and GLP1-I.N.T.(TM) for the treatment of diabetes. Transition has an emerging pipeline of preclinical drug candidates developed using its proprietary drug discovery engine.

CORCEPT RAISES $10 MILION IN PRIVATE PLACEMENT

August 20, 2007

Corcept Therapeutics (CORT) announced a private placement of approximately 4.8 million shares of its common stock at a price of $2.10 per share, for proceeds of $10.1 million. The investors were led by **Paperboy Ventures LLC,** who is currently the largest shareholder of Corcept. Other investors participating in this financing round included **Sutter Hill Ventures** and **Alta Partners, LLP**, venture capital firms that are currently significant shareholders in Corcept, and various entities and individuals related to these firms.

Corcept intends to use the proceeds of the financing to conduct a new Phase III clinical trial evaluating *Corlux* for the treatment of the psychotic features of psychotic depression, to conduct studies to extend and confirm the results of its recent study of *Corlux* for the prevention of antipsychotic-induced weight gain, to continue development of its new chemical entities and for general corporate purposes, including working capital.

CONCENTRIC FILES FOR IPO; LAUNCHES NEW RETRIEVER

August 17, 2007; August 29, 2007

Neurovascular-device maker **Concentric Medical** registered an initial public offering of up to $69 million in common stock. The number of shares and estimated price range were not disclosed. The company previously raised $14 million from **H&Q Capital Management, NeuroVentures Capital, New Enterprise Associates, New Venture Partners,** and **ProQuest Investments.** Merrill Lynch & Co., Lehman Brothers and Thomas Weisel Partners LLC are listed as underwriters for the IPO

Concentric also obtained regulatory clearance for its *Merci L6 Retriever* in the U.S. This new Retriever, designed to target larger vessels, joins four other *Merci Retrievers* on the market, and incorporates filaments which help to secure a clot during retrieval for treatment of an ischemic stroke.

NEURAXON CLOSES $32 MILLION SERIES B

August 20, 2007

NeurAxon Inc., a developer of next generation pain therapeutics targeting neuronal nitric oxide synthase (nNOS), closed a $32 million Series B Financing. The financing was led by new investors, **Delphi Ventures** and **OrbiMed Advisors**,. Also participating in the round were Series A investors **BDC Venture Capital, Genesys Capital Partners, H.I.G. Ventures, NeuroVentures Fund, Ventures West Capital Ltd**. and new Lawrence E. Bloch, M.D., J.D., CEO of NeurAxon. Concurrent with the financing, Deepa Pakianathan general partner of Delphi and Samuel P. Wertheimer, principal of OrbiMed will join the NeurAxon Board of Directors.

NEUROMED RAISES $53 MILLION SERIES E FOR PAIN

August 21, 2007

Neuromed Pharmaceuticals, a biopharmaceutical company developing improved chronic pain drugs, completed a Series E financing of $53.3 million. This brings Neuromed's cumulative financing to $126 million. The financing was comprised of new investors and significant participation from existing investors including **MPM Capital, James Richardson & Sons, Neuro Discovery LP, GrowthWorks Capital (Working Opportunity Fund), BDC Venture Capital, CMDF,** and the **Royal Bank of Canada.**

Neuromed plans to use the financing to advance *NMED-1077*, an extended release formulation of hydromorphone, recently acquired from **ALZA Corporation**. Hydromorphone is a Schedule II opioid that has been widely used for many years under the brand name *DILAUDID* and is also available from various generic manufacturers. Current formulations of hydromorphone marketed in the U.S. are immediate release, requiring dosing several times per day. *NMED-1077* employs the *OROS® PUSH-PULL* osmotic delivery system to release hydromorphone at a controlled rate over an extended period.

Neuromed is also evaluating two pathways for the development of new classes of oral pain drugs. In collaboration with Merck, Neuromed is researching compounds designed to block the N-type calcium channel, a target linked to pain signal transmission. Separately, Neuromed is also developing T-type calcium channel blockers for the treatment of acute and chronic pain as well as other potential disorders such as hypertension and epilepsy.

MEDTRONIC NEUROMODULATION BUSINESS GROWS 5%

August 21, 2007

Medtronic, Inc. (MDT) announced financial results for its first quarter of fiscal year 2008, which ended July 27, 2007. Medtronic recorded first quarter revenue of $3.127 billion, an 8 percent increase over the $2.897 billion reported in the first quarter of fiscal year 2007. Non-U.S. revenue of $1.179 billion grew 16 percent, driven by double digit revenue growth in all major geographic areas. For the quarter, 38% of Medtronic's revenue was from outside the U.S. Neuromodulation revenue of $289 million grew 5%. The segment's largest product lines, which include implantable neurostimulation and drug-delivery systems used in the treatment of chronic pain, movement disorders and spasticity, generated first quarter revenue of $237 million, increasing 5%. Revenue from the *InterStim* neurostimulators for the treatment of overactive bladder grew 26%.

CEPHALON GETS RIGHTS TO MUSCLE SPASM TREATMENT

August 23, 2007

Cephalon, Inc. (CEPH) signed an agreement to acquire the North American rights to *Amrix* (cyclobenzaprine hydrochloride extended-release capsules) from **ECR Pharmaceuticals**, a privately held company. Two dosage strengths of *Amrix* (15 mg and 30 mg) were approved in February 2007 by the FDA for short-term use as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute, painful musculoskeletal conditions. The product is not yet available commercially in the United States; however, Cephalon expects to launch the product early in the fourth quarter.

Amrix is a once-a-day, extended-release version of cyclobenzaprine hydrochloride, the active ingredient in the brand *Flexeril*. With once-daily dosing, AMRIX provides relief from muscle spasm comparable to that with *Flexeril* taken three times daily. In Phase 3 clinical trials, once daily dosing of AMRIX at 15 mg and 30 mg resulted in somnolence rates of one and two percent respectively.

Cephalon will pay ECR $100 million in cash and may make future cash payments upon achievement of certain sales milestones. The company anticipates that the transaction will be modestly dilutive in the fourth quarter due to product launch costs; despite this, the company is reaffirming its existing 2007 sales and adjusted income per common share guidance.

PRESTWICK RAISES $20 MIL, SEEKS TO EXPAND PIPELINE

August 27, 2007

Prestwick Pharmaceuticals Inc., raised $20 million financing from existing investors, including Atlas Venture, Sofinnova Ventures, Vivo Ventures, Scale Venture Partners, Warburg Pincus and Pequot Ventures according to VentureWire. The company is looking to acquire additional products which could solidify a future attempt to go public. Prestwick filed to go public in 2005, but withdrew its registration in December of that year, citing market conditions. Last week Prestwick announced that it had strengthened its management team by hiring Robert S. Radie as executive vice president and chief business officer.

INFLAZYME PASSES ON OPTION FOR ALZHEIMER'S TREATMENT; SEEKS MERGER TO AVOID LIQUIDATION

August 27, 2007

Inflazyme Pharmaceuticals Ltd. (Toronto:IZP.TO) will not exercise their option to *IPL455,903*, a PDE4 inhibitor discovered and patented by the company. Under the limited license granted to **Helicon** in January 2003, Inflazyme had 90 days to exercise its option after receiving certain information from Helicon which included the results of the first Phase IIa study.

Inflazyme reported on the results of this study for Age Associated Memory Impairment in June and stated that the data may support further clinical studies with *IPL455,903*, as well as the development of Inflazyme's other PDE4 inhibitors. However, Inflazyme has insufficient cash to exercise the option which is estimated to be in the range of CDN$3-$4 million based on limited information provided by Helicon. Under the terms of the limited license with Helicon, by not proceeding with the option, Inflazyme will receive certain royalties on any product commercialized. Helicon has rights in the field of learning and memory disorders, while Inflazyme retained rights to this compound for all other uses.

Inflazyme is currently seeking to sell or license its assets or seek a merger or acquisition with another company. Outside of *IPL455,903*, Inflazyme has other assets that could be of significant value to third parties. These consist of the LSAID portfolio comprising several compounds targeting respiratory disease, two of which have completed Phase II clinical studies in asthma.

Other assets include its pre-clinical portfolio of PDE4 inhibitors that have shown efficacy in models of respiratory disease, and models of depression, as well as clinical stage protein therapeutics which are targeted towards inflammatory diseases. Inflazyme continues to work towards completing a transaction in the very near term to realize value for its shareholders. Alternatively, the company may need to terminate operations and liquidate its assets.

TIKVAH ACQUIRES CNS LEAD FROM PHASE 2 DISCOVERY

August 29, 2007

Neuropharmaceutical company **Tikvah Therapeutics** signed a licensing agreement with **Phase 2 Discovery**, a drug development company affiliated with researchers at the University of Cincinnati School of Medicine, for worldwide rights to develop and commercialize *LY156735* for the treatment of circadian rhythm, sleep disorders and depression. Tikvah will also explore additional indications for *LY156735* through its own research and development efforts in special subpopulations, and other general conditions of sleep deprivation and/or insomnia, among others.

Phase 2 Discovery (P2D) acquired *LY156735* from Eli Lilly in 2001. Under their own IND, P2D has already generated substantial Phase II clinical data demonstrating statistically significant improvement in both objective and subjective sleep measures. Pilot clinical studies, conducted by P2D in response to the unique receptor binding profile of *LY156735*, suggest that improved efficacy in standard measures of sleep may be possible compared to another melatonin agonist. Further, in patients with severe insomnia, *LY156735* significantly decreased latency to persistent sleep compared to placebo. Efficacious results were also obtained in pilot clinical studies where jet lag was induced by a time shift in an aerospace temporal isolation clinical laboratory unit.

In receptor binding studies, *LY156735* has equal or better affinity for 5-HT2c receptors as agomelatine, a molecule which acts as an antidepressant, in part, through interaction with melatonin receptors and 5-HT2 receptors. The potential antidepressant actions of *LY156735* have been shown in a preclinical rodent model of antidepressant activity.

P2D will be transferring its open IND for *LY156735* to Tikvah which will then assume responsibility for the further clinical development and commercialization of the compound, which will be known as *TIK-301*.

FOREST PULLS OUT OF STROKE PARTNERSHIP WITH PAION

August 30, 2007

Forest Laboratories, Inc. (FRX) terminated the co-development partnership with **PAION AG (FSE: PA8)** for the compound *Desmoteplase,* a thrombolytic for acute stroke. Based on the results of the Phase III study DIAS-2 (Desmoteplase in Acute Ischemic Stroke) and the anticipated delay in development as well as the additional investments necessary, Forest has decided to return all rights to *Desmoteplase* for North America to PAION.

As recently reported the DIAS-2 study was not sucessful due to a lack of improvement in the *Desmoteplase* groups over placebo while observing an unexpectedly high response rate in the placebo group. Since the presentation of top-line results in late May this year, the partners have been conducting an in-depth analysis of the available study data.

In a joint effort, PAION and its other licensee, **H. Lundbeck A/S** are currently finalizing the analysis in order to discuss further steps and their commercial implication. Lundbeck has not yet made a decision on the partnership and PAION is evaluating additional options to proceed with the program. The termination of the cooperation by Forest leads to a one-time profit in the amount of $5.9 million which includes, the derecognition of the provision for the repayment obligation towards Forest resulting from the reimbursement of development expenses.

Featured Company

SOUND PHARMACEUTICALS: RISING ABOVE THE NOISE

Sound Pharmaceuticals was founded in July of 2001 in Seattle, WA to focus on hearing loss and specifically neurosensory hearing loss. Several of the founders were involved in an earlier venture, called **Otogene**, based in Germany. Otogene attempted to block the effects of a protein that prevents inner ear hair cell regeneration. If the protein can be silenced, hair cells in the inner ear responsible for transmitting auditory information, could regrow after being damaged by noise or other insults.

Otogene was focused on developing a peptide inhibitor of the protein, known as p27Kip1, but several people on the management team, including Jonathan Kil, Eric Lynch and Glenn Kawasaki believed that the approach was flawed. They left Otogene and co-founded SPI, eventually acquiring the assets of Otogene when the company went under. They received some institutional funding, and a lot of support from the Department of Defense (DoD) and the Veterans Administration (VA). Now the company has one lead compound in the clinic and through Phase I and a robust research effort into using RNAi to block p27Kip1.

SPI's lead compound, ebselen, is a small molecule that mimics glutathione peroxidase, a key enzyme in the cochlea. It is a scavenger of free radicals and inhibits cyclooxygenases (COX enzymes) and lipoxygenase enzymes. Ebselen was in clinical studies in Japan for stroke but the compound failed to achieve significance there. Although Ebselen did not make it for stroke, its prospects for hearing loss are much better according to SPI's CEO, Jonathan Kil.

SPI was able to show that ebselen could help prevent neurosensory hearing loss, and managed to get patent protection on that discovery. Ebselen is a new medical entity (NME) in the US so SPI has to run a complete series of trials. The company's Phase I clinical trials showed that the compound is safe in humans and they are now awaiting FDA approval to start a Phase II trial.

The Phase II trial will involve 80 volunteers, in a double blind, placebo-controlled, four arm study to prevent hearing loss. There are three dose levels of compound in the study in addition to placebo. The volunteers, who are military recruits, will undergo a 300 round rifle training course and will take the compound or placebo orally, starting one day prior to exposure and continuing for 14 days afterward.

DoD studies have shown that a 300 round rifle training can cause extensive and permanent hearing loss. That is true even if precautions are taken. All subjects will be tested before the study, and immediately after exposure to detect temporary hearing loss and then again at 15 and 30 days post-exposure. OSHA, which monitors hearing loss in the workplace, established through other studies that hearing loss at 30 days is permanent. It is also known that all permanent hearing loss is preceded by a temporary hearing loss immediately after exposure. The trial will take approximately 8 weeks from enrollment to final results. It will be mostly paid for by DoD and the VA.

If the Phase II study is successful, SPI may do a second study to refine the results, or move directly into a multi-center Phase III trial. Either way the design will be very similar. If all goes well, and results are positive, the compound could be on the market by the end of 2008. As for sales, Kil points out that the DoD and the VA have some of the largest formularies in the country. "We could sell directly to them, without the need for a partner," he says. As for the general market, "we will need a partner there to reach general practitioners."

SPI also plans to develop ebselen in combination with allopurinol for chemotherapy induced hearing loss. "It is a smaller market but very well defined," says Kil. "In North America there are about half a million adults that get a platinum agent each year and the side-effect profile is pretty substantial. There are agents to help reduce kidney and bone marrow damage, but there is nothing available for ototoxicity or neurotoxicity."

SPI has 10 employees, most of whom are in R&D. The company operates its own laboratories and animal testing facilities. "It is highly specialized work," says Kil, "and we need to do it in-house." SPI plans to close a financing of approximately $10 million in the next quarter. That would be enough cash for five Phase II studies and will allow for substantial expansion in personnel and new laboratory space. One year from now, Dr. Kil expects the company will have about three times as many FTE's and a new facility to work in.

Apart from ebselen, SPI also has an active RNAi program focused on p27Kip1. The current lead compound is a naked double helix. As with all RNAi therapeutics, there is still much work to be done. The company is working to optimize the delivery and cellular uptake and Dr. Kil is optimistic that they will be ready to advance a formulation to toxicology in about one year.

There are surprisingly few pharmaceutical companies working on hearing loss. It is an enormous problem affecting many adults and elderly, and a very large unmet medical need. With a little bit of luck and continued perseverence, this small Seattle startup could make a big difference in many people's lives, and provide a good return to its investors in the process.

HEARING, Continued from page 1

The external ear aids in sound localization. Many mammals can move their ears to better pinpoint sounds but most humans cannot. Even so, humans are quite good at localizing sounds. The shadow effect of the head plays an important role in localization. At 500 Hz, humans can localize a sound to within 1 to 2 degrees on the horizontal plane. For sounds below 500 Hz, where the shadow effect is nil due to the long wavelength, the auditory system uses intra-aural phase differences to localize the source. Very low sounds cannot easily be localized, which is why subwoofer placement is easy. Despite good accuracy horizontally, human performance in the vertical plane is very poor.

The second part of the auditory system is the middle ear. It consists of an enclosed air filled chamber, between the ear drum and the cochlea, that contains three tiny bones. The bones conduct the vibrations of the drum to the inner ear. The pressure in the chamber is equalized via a small tube that leads into the throat, called the Eustachian tube. Equalization requires swallowing or a forced exhalation with the nostrils closed. Whenever the outside pressure changes, due to a change in altitude, underwater diving, or sometimes a sudden drop in air-pressure in a storm, hearing is affected and equalization is needed to regain sensitivity.

Prolonged unequal pressure can lead to edema, fluid accumulation, and pain. Pressure changes are especially rapid underwater and divers learn to equalize by pressing their noses and exhaling against a closed airway. In air, changes are less rapid and most people equilibrate without conscious intervention. Little children often have problems with equilibration in planes. The resulting discomfort leads to crying, which tends to equalize pressures rapidly. Equilibration can be difficult when infection clogs up the pharynx or the ear.

The middle ear is a frequent site of infections, especially in small children. Otitis media, as it is called, results in a temporary hearing loss and acute pain. Any form of excess pressure in the middle ear is extremely painful as the lining (mucosa) is tightly adherent to the bone, leaving little room for fluid buildup. Repeat infections may lead to hearing loss due to damage to the drum or the conducting bones.

A hereditary disease, called otosclerosis, affecting mostly young women, results in abnormal bone growth that fixates the small bones in the middle ear. That causes a hearing loss of about 30dB. A similar loss can occur due a large hole in the drum, or a fracture of any of the bones. These conditions can be surgically repaired in many cases.

Damage limited to the outer and middle ear results in loss of air-conduction. Sound is still transmitted to the sensors via the skull or bone conduction but a loss of about 30 dB is seen. Bone conduction, which is the way people hear underwater, may be less effective but it still offers the full spectral range of hearing. Some sports companies market mp3 players for swimmers that use bone conduction exclusively. Some hearing aids work the same way.

Hearing loss is typically divided into five broad categories. Normal is 0 to 20 dB loss, mild is 20-40 dB, moderate 40-60 dB, severe 60-80 dB, and profound, anything over 80 dB. Disability payments usually start at bilateral moderate hearing loss. Hearing loss is often non-uniform across the spectrum and noise-induced losses primarily affect high frequencies. Noise losses often start with a pronounced dip at 4,000 Hz, the origin of which is not well understood. Over time, the gap widens especially at the high frequency end, and a total loss above 2-3 KHz may result.

The third part of the auditory system, the inner ear, is a two part organ. One part senses gravity and acceleration and the other part, known as the cochlea, senses sounds. Both use hair cells to detect fine changes in the environment. The auditory part of the inner ear is a small complex structure, known as the organ of Corti, deeply embedded into the skull. It consists of several fluid filled cavities separated by membranes. The main basilar membrane holds the sensory cells, which are modified hair cells. Their hairs are embedded in a fixed membrane, called the tectorial membrane.

The basilar membrane vibrates in response to sounds. The stiffness of the membrane is not uniform and a frequency spectrum is laid out along its length. Movement causes the inner hair cells to move with respect to their fixed hairs and opens ion channels generating electrical signals. Those signals are then transmitted via the auditory nerve to the brainstem and the brain. Humans have between 15,000 and 20,000 hair cells. Hair cells are very fragile and can easily be damaged by excessive movement (sound). No stem cells are found in the cochlea and any hair cell loss is permanent.

Not all hair cells are passive detectors. There are several rows of hair cells and only the ones in the inner row are detectors and connected to the auditory nerve. Outer hair cells are not connected to the auditory processing centers in the CNS. Instead they receive outgoing innervation from the CNS and are thought to actively move the membrane, thus generating sounds. Their function is not well understood but it is believed to be key to hearing in many situations. It is thought these cells selectively amplify certain sounds and help in frequency focusing.

The role of outer hair cells is demonstrated in pathology. Most hair cell losses due to noise damage are in the outer hair cells. Such hearing loss is characterized by two important phenomena. One is called recruitment or loudness hyperacusis. It happens when the intensity of a sound is

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above the threshold for detection and then quickly "recruits" all remaining capacity to produce a sensation of maximum loudness. That effectively reduces the dynamic range of hearing. Either sounds cannot be heard at all, or they immediately become maximal intensity.

People suffering from recruitment are very difficult to treat. Hearing aids usually do not do much good as they tend to make every sound too loud or even painful, while doing little to improve hearing. Additionally, these people tend to lose certain frequencies that are hard to correct.

Another phenomenon associated with outer hair cell loss is the so-called cocktail party effect. The cocktail party effect refers to the ability to focus one's listening attention to one speaker among a mixture of background sounds and voices. It was described by Colin Cherry in 1953. Although the exact mechanism underlying this phenomenon is unknown, and most of it is thought to reside within the auditory cortex, the evidence for a peripheral filter is quite strong also. Patients with outer hair cell loss quickly lose the cocktail party effect and their hearing is more affected when background noises are present.

Tinnitus or ringing in the ears is another phenomenon that has been linked to outer hair cell damage. There are many causes for tinnitus but in some cases actual sounds have been recorded in the cochlea of tinnitus sufferers. That means the outer hair cells are producing sounds that are then registered by the inner hair cells and processed in the CNS. Tinnitus is hard to treat and can be quite disturbing in some patients, occasionally leading to suicide.

Sensorineural loss is considered permanent and no treatment exists. The most common cause is excessive noise. The auditory system has only one defense mechanism against excessive noise. It consists of a reflex contraction of a middle ear muscle that prevents effective sound transmission into the cochlea and reduces sound pressure levels by about 30 dB. Known as the stapedius reflex or acoustic reflex, it is only active at high sound levels after a short delay. The reflex is also active during speech.

Short impulses such as gun shots, jet plane blasts, and jackhammers do not evoke a stapedius reflex and are therefore more harmful than steady high intensity noise. Exposures as brief as 1 minute can cause hair cell losses. At 110 dB, a level not uncommon in rock concerts, damage can occur within 15 minutes.

Damage is preceded by a temporary threshold shift (TTS) or a temporary hearing loss that may persist for hours or days. Some recovery occurs in most cases but in general, the longer the TTS, the more permanent damage there is. Apart from outright physical shear due to sudden high sound pressure levels, as in explosions, hair cells are thought to succumb to metabolic and biochemical changes that involve reactive oxygen species (ROS).

Several drugs are also known to be highly ototoxic. Probably the most famous are streptomycin and the aminoglycoside antibiotics. A course of treatment often causes extensive permanent damage. Other drugs known to induce hearing loss are macrolide antibiotics (erythromycin), loop diuretics, salicylates, quinine, and Pt-containing chemotherapy agents. The most common severe damage in the Western World is caused by chemotherapy with cisplatin and its derivatives.

Hearing losses due to outer and middle ear problems are, as a rule, amenable to medical and surgical therapy and failing those, good candidates for hearing aids. Inner ear damage is generally considered permanent and no good treatments exist. Hearing aids can help, but they are most useful in the outer-middle ear group where conduction is the issue. They can be of some help in the mixed group where conduction and sensorineural loss co-exist. Sensorineural or inner ear damage tends to include recruitment, selective frequency losses, tinnitus and other symptoms that make the tuning of an effective hearing aid very problematic.

Several companies are developing therapies for hearing loss. **Sound Pharmaceuticals**, our featured company this month, is working with ebselen, a hair cell protectant *(see story, page 14)*. **Auris Medical** has a Phase I/II selective NMDA receptor blocker that is aimed at tinnitus. The compound was developed at INSERM in Montpellier France and is currently in trials in Germany.

Device companies like **Otologics** and **Envoy Medical** have fully implantable prostheses that allow the user to swim and participate in other activities where normal hearing aids fail. Once implanted, the devices are invisible and leave the ear canal open. Envoy's device is called *Esteem*. **Cochlear Corporation** offers the *Baha (Bone Anchored Hearing Aid)* system, a prosthesis that uses bone conduction and bypasses the middle ear completely. It is the only one of its kind approved by FDA.

More than 40,000 people in the US and 100,000 worldwide have their hearing enabled by cochlear implants. Cochlear implants transduce sound from an external microphone and relay the signal to electrode arrays that directly stimulate nerve fibers in the inner ear. The devices sort incoming sound into different frequency ranges that are passed down the wires. While implants are still relatively crude devices, they work remarkably well in patients with congenital hearing loss who are born deaf, providing them with ability to hear and understand speech.

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Australia's **Cochlear Corporation** is the market leader with approximately 70% market share. **Boston Scientific's Advanced Bionics** offers an array and auditory products including cochlear implants. The company has announced that Boston Scientific will be divesting the auditory portion of the business after a dispute with founder Al Mann *(see story, page 9)*. Austria's **Med-El** manufactures the other implant available in the U.S.

Advanced Cochlear Systems is developing an advanced device using MEMS manufacturing techniques for enhancing frequency resolution to allow for more natural mapping to the cochlea. This device uses 72 electrical contacts compared to 22 channels found in the best systems today.

Newer experimental therapies include the use of stem cells, selective growth factors, inhibitors of hair cell death, and gene therapies. **GenVec** has *TherAtor*, a preclinical-stage gene-therapy method that delivers human atonal gene (Hath1), a gene shown to produce a protein that promotes hair cell growth. The therapy may also be effective for hair cell loss in the balance organs. It is delivered using an adenovirus vector.

NEUROTECH STOCKS

Company	Symbol	1 mo return (%)	3 mo return (%)	1 yr return (%)	Market Cap. ($M)	30 day Ave Volume	Last Price	52 Week Low	52 Week High
ACADIA Pharmaceuticals	ACAD	2%	13%	66%	531	519,508	14.39	6.63	17.33
Adolor Corporation	ADLR	4%	-1%	-85%	172	715,493	3.74	3.09	25.26
Alseres Pharmaceuticals	ALSE	-19%	-18%	-39%	49	4,091	2.39	1.95	4.23
Amarin Corporation plc (ADR)	AMRN	6%	-15%	-81%	49	400,605	0.51	0.35	4.32
Arena Pharmaceuticals, Inc.	ARNA	17%	-4%	9%	818	1,001,349	13.40	9.96	17.69
Aspect Medical Systems	ASPM	-8%	-22%	-35%	213	247,639	12.58	12.30	21.35
Cephalon, Inc.	CEPH	0%	-10%	32%	5,018	1,899,818	75.05	55.15	84.83
Cortex Pharmaceuticals	COR	-29%	-36%	-36%	76	316,135	1.90	1.03	3.81
Cyberkinetics Neurotechnology	CYKN	-26%	0%	-69%	19	69,045	0.50	0.35	1.80
Cyberonics, Inc.	CYBX	8%	-20%	-7%	406	349,021	15.09	12.95	27.55
Cypress Bioscience, Inc.	CYPB	15%	-12%	84%	495	516,553	13.26	6.69	18.20
Elan Corporation, plc (ADR)	ELN	3%	-2%	17%	9,060	3,945,748	19.38	11.70	23.11
Endo Pharmaceuticals	ENDP	-6%	-10%	-3%	4,272	1,393,208	31.88	26.68	35.85
Integra LifeSciences Holdings Corp.	IART	-2%	-5%	26%	1,275	381,825	48.57	36.36	52.85
Memory Pharmaceuticals Corp.	MEMY	8%	-24%	116%	158	95,712	2.18	0.94	4.94
Micrus Endovascular Corporation	MEND	1%	11%	72%	365	167,027	23.82	11.62	25.78
Neurobiological Tech.	NTII	-33%	-57%	-71%	28	87,031	0.86	0.81	3.22
Neurochem Inc. (USA)	NRMX	-63%	-60%	-87%	105	1,219,051	2.36	2.12	26.51
Neurocrine Biosciences, Inc.	NBIX	-2%	-14%	-14%	378	719,553	9.97	7.51	14.88
Neurogen Corporation	NRGN	17%	-36%	-12%	207	149,529	4.94	4.04	8.75
NeuroMetrix, Inc.	NURO	-8%	-14%	-71%	98	150,508	7.77	7.06	27.55
Northstar Neuroscience	NSTR	11%	-15%	-3%	293	251,239	11.36	9.59	17.50
Pain Therapeutics, Inc.	PTIE	12%	11%	16%	413	288,331	9.38	7.00	9.78
Renovis, Inc.	RNVS	-5%	-5%	-78%	94	359,296	3.18	2.53	15.46
Sepracor Inc.	SEPR	4%	-40%	-38%	3,130	2,608,284	29.17	25.88	63.24
Shire plc (ADR)	SHPGY	7%	13%	54%	14,553	673,610	78.74	46.16	78.83
Somaxon Pharmaceuticals, Inc.	SOMX	25%	-18%	-12%	224	159,572	12.34	8.89	18.57
Targacept , Inc.	TRGT	-3%	4%	76%	197	16,459	9.66	5.26	12.35
Vanda Pharmaceuticals	VNDA	-20%	-25%	58%	397	2,070,222	14.93	8.77	32.00
Xenoport, Inc.	XNPT	-3%	-6%	89%	1,035	241,089	41.53	19.20	47.75