THIRTY-SIXTH ANNUAL REPORT

of the

RESEARCH ADVISORY PANEL OF CALIFORNIA

2006



Prepared for the

LEGISLATURE AND GOVERNOR

RESEARCH ADVISORY PANEL OF CALIFORNIA

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This report represents a consensus among Panel members acting as individual experts. It does not represent policies or positions of the appointing agencies nor have those agencies been consulted by the Panel during its function or during the preparation of this report.

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SUMMARY OF 2006 PANEL ACTIVITIES

During 2006 the Panel reviewed fifty-two new research study submissions. Forty-six were approved by the Panel, including nineteen Academic research studies, and twenty-seven Multicenter Clinical Drug Trial protocols. Eight of the approved studies were Substance Abuse Treatment research protocols.

Forty-seven research studies were completed (or in a few cases - terminated) in 2006, upon which Panel approval was withdrawn and they were closed on the Panel's records.

At the end of 2006 the Panel was monitoring 151 active research projects. Note Appendices A, B, and C for specific listings.

As part of the Panel's supervisory responsibility, ongoing projects are monitored by means of annual reports, AE reports and site visits; and approval may be withdrawn if activities deviate significantly from the approved protocol.

Table 1 is a list of the studies approved by the Panel in 2006 and Table 2 is a list of the studies closed by the Panel in 2006.

SELECTED RESEARCH FINDINGS

Below are brief summary reports of several Panel approved projects which are of interest and indicative of the types of controlled substance and substance abuse treatment research projects currently ongoing in California:

<u>Dr. Donald Abrams</u> and colleagues at the UCSF Community Consortium in San Francisco have completed a study titled "The Effects of Marijuana on Neuropathic Pain in HIV-Related Peripheral Neuropathy". This study was supported by the University of California Center for Medicinal Cannabis Research. The results of this study were recently published and summarized with the following abstract:

Objective: To determine the effect of smoked cannabis on the neuropathic pain of HIV-associated sensory neuropathy and an experimental pain model. *Methods:* Prospective randomized placebo-controlled trial conducted in the inpatient General Clinical Research Center between May 2003 and May 2005 involving adults with painful HIV-associated sensory neuropathy. Patients were randomly assigned to smoke either cannabis (3.56% tetrahydrocannabinol) or identical placebo cigarettes (with the cannabinoids extracted) three times daily for 5 days. Primary outcome measures included ratings of chronic pain and the percentage achieving greater than 30% reduction in pain intensity. Acute analgesic and anti-hyperalgesic effects of smoked cannabis were assessed using

a cutaneous heat stimulation procedure and the heat/capsaicin sensitization model. *Results*: Fifty patients completed the entire trial. Smoked cannabis reduced daily pain by 34% vs 17%with placebo (p = 0.03). Greater than 30% reduction in pain was reported by 52% in the cannabis group and by 24% in the placebo group (p = 0.04). The first cannabis cigarette reduced chronic pain by a median of 72% vs 15% with placebo (p < 0.001). Cannabis reduced experimentally induced hyperalgesia to both brush and von Frey hair stimuli (p < 0.05) but appeared to have little effect on the painfulness of noxious heat stimulation. No serious adverse effects were reported. *Conclusion*: Smoked cannabis was well tolerated and effectively relieved chronic neuropathic pain from HIV-associated sensory neuropathy. The findings are comparable to oral drugs used for chronic neuropathic pain.

Thomas King, CEO of Alexza Pharmaceuticals Inc., has provided the Panel with the following summary on work this company is doing in developing a pharmaceutically active THC aerosol product for inhalation delivery.:

A thermally-lablile prodrug of dronabinol (Δ^9 -tetrahydrocannabinol, THC) has been identified that meets the requirements for a chemically and physically stable and coatable solid drug form. Conditions have been established for optimal conversion of the prodrug to pharmaceutically active THC aerosol using Alexza's Staccato® system. These conditions have been used to design and prepare several device configurations that could be used in clinical trials. Pulmonary delivery of the thermal condensation aerosols of THC have been shown to provide rapid *in vivo* absorption and high Bioavailability in dogs. Although we do not currently have plans to develop this product alone, we have engaged in conversations with entities that could be potential partners in developing the product or licensees of the relevant technology.

Dr. Edward Tung at Innovacon Labs in San Diego has provided the Panel with the following summary of research & development they are doing in their project titled "Development of urine and/or oral-fluid based in-vitro diagnostic tests in the form of lateral flow rapid test format to detect controlled substances commonly abused and misused by individuals":

Development has progressed to the point where a "For Forensic Uses Only" oral fluid-based multi-Drug DOA (drugs of abuse) testing kit (a 6-drug test panel) is now marketed in the United States. This oral fluid-based test panel is less invasive and more convenient to perform for uses such as employment screening, and is beginning to gain popularity in the U.S. market. Research is proceeding to develop and add more drugs to this test panel in the near future. A 12-drug test panel is in the active development stage and an 18-drug panel is in the planning. Thanks to the excellent biotech R&D environments of California,

our company has achieved leading status in the international lateral flow rapid DOA testing market. Our products with either Innovacon/ACON or our OEM brands are now shipped all over the world. We are making strides to play a major role in curbing the use of illegal drugs of abuse. We will continue to strive to develop more innovative DOA test products in the future.

Dr. Walter Ling, and colleagues at the Semel Institute of Neuroscience and Human Behavior at the David Geffen School of Medicine at UCLA, are conducting a study titled "Double-Blind, Placebo-Controlled Trial of Prometa Pharmacotherapy for the Treatment of Methamphetamine Abuse", and have provided the Panel with the following progress report:

This study assesses the efficacy of the PROMETATM (combination of three medications hydroxyzine, gabapentin, and flumazenil) pharmacotherapy compared to placebo for initiating abstinence and for preventing relapse to methamphetamine use in treatment-seeking individuals meeting criteria for methamphetamine abuse. It is hypothesized that individuals assigned to receive the PROMETATM pharmacotherapy, compared to placebo, will demonstrate significantly fewer and less intense withdrawal symptoms, more days abstinent from methamphetamine use, and fewer relapses to methamphetamine use as assessed by self-report of drug use verified by urine samples. A great importance of this study is that it offers a controlled, systematic study of a drug treatment protocol already in use across the United States. Both participants and research staff will be blinded to assignment of treatment condition. The PROMETATM pharmacotherapy is purported to have resulted in successful treatment outcomes for a variety of drug-dependent individuals, however no controlled evaluation has previously been initiated. The current study will test the combination of medications used in the PROMETATM pharmacotherapy (and individually approved by the Food & Drug Administration) for effectiveness in an increasingly growing subgroup of drug dependent individuals - those dependent on methamphetamine.

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TABLE 1

RESEARCH STUDIES APPROVED IN 2006

Sponsor / PI

<u>Title of Study / Clinical Drug</u> Trial Protocol

Donald I. Abrams, M.D. UCSF Community Consortium 3180 18th Street, Suite 201 San Francisco, CA 94110 Opioid & Cannabinoid Pharmacokinetic Interactions: A Pilot Study

Alpharma, Inc. Piscataway, New Jersey A Phase II Multi-dose, Double-blind, Crossover Study to Assess the Safety, Efficacy & PK of Kadian NT in Subjects with Chronic Pain due to Osteoarthritis of the Hip/Knee (Alpharma Protocol ALO-KNT-202)

Archimedes Development Ltd. Nottingham, United Kingdom

A Multicenter, Placebo-Controlled, Double-Blind, Two-Phase Crossover Study of Nasalfent (Fentanyl Citrate Nasal Spray) in the Treatment of Breakthrough Cancer Pain (BTCP) in Subjects Taking Regular Opioid Therapy (CPO43/06/FCNS)

Archimedes Development Ltd. Nottingham, United Kingdom

An Open-Label Study Investigating Long-Term Safety and Tolerability of Nasalfent (Fentanyl Citrate Nasal Spray) in the Treatment of Breakthrough Cancer Pain (BTCP) in Subjects Taking Regular Opioid Therapy (CPO45/06/FCNS)

BioDelivery Sciences International Morrisville, North Carolina

A double-blind, placebo controlled, evaluation of the efficacy, safety and tolerability of BEMA Fentanyl in the treatment of breakthrough pain in cancer subjects (BioDelivery Protocol FEN-201)

Cont.

Sponsor / PI

<u>Title of Study / Clinical Drug</u> Trial Proto<u>col</u>

BioDelivery Sciences International Morrisville, North Carolina

An open label, long-term treatment evaluation of the safety of BEMA fentanyl use for breakthrough pain in cancer subjects on chronic opioid therapy (BioDelivery Protocol FEN-202)

Nancy E. Buckley, Ph.D. California State Polytechnic University 3801 W. Temple Ave. Pomona, CA 91768 The cannabinoid system and the modulation of T cell and macrophage Functions

Cephalon, Inc. Frazer, Pennsylvania

A 12-Week Open-Label Study With 3 Within-Patient Double-Blind Placebo-Controlled Periods to Evaluate the Efficacy and Safety of ORAVESCENT® Fentanyl Citrate Treatment for the Management of Breakthrough Pain in Opioid-Tolerant Patients With Noncancer-Related Chronic Pain (Cephalon C25608/3052/BP/US)

Cephalon, Inc. Frazer, Pennsylvania

A 4-Week Open-Label Study to Evaluate the Effect of Treatment With Fentanyl Buccal Tablets on Pain Anxiety Symptoms When Used for the Management of Breakthrough Pain in Opioid-Tolerant Patients With Chronic Pain (C25608/3054/BP/US)

Oliver Civelli, Ph.D. University of California, Irvine Rm 369, Med Surge II Dept of Pharm Irvine, CA 92697-4855 Identify the receptor(s) for gamma-hydroxybutynic acid (GHB)

<u>Title of Study / Clinical Drug</u> Trial Protocol

Ivan Diamond, M.D., Ph.D. CV Therapeutics, Inc. 3172 Porter Drive Palo Alto, CA 94304 Treatment of Experimental Heroin Addiction in Rats

Robert Edwards, M.D. Dept. of Neurology & Physiology UCSF School of Medicine 600 16th St. GH-N272B San Francisco, CA 94158-2517 Role of glutamate release by monoamine neurons

Endo Pharmaceuticals Chadds Ford, Pennsylvania A Double-Blind, Randomized, Placebo-Controlled, multicenter Study to Evaluate the Efficacy and safety of EN3267 for the Treatment of Breakthrough Pain in Opioid Tolerant Cancer Patients Followed by a 12-Month Non-Randomized, Open-label Extension to Assess Long-Term Safety (Endo Protocol EN3267-005)

Endo Pharmaceuticals Chadds Ford, Pennsylvania A Multiple-Dose, Non Randomized, Open-Label, Multicenter Study to Evaluate the Long-Term Safety and Effectiveness of EN3267 in the Treatment of Breakthrough Pain in Cancer Pts (Endo Protocol EN3267-007)

Gantt P. Galloway, Pharm.D. Addict'n Pharmacology Research Lab California Pacific Medical Center St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 A Pilot Trial of Dextroamphetamine for Treatment of Methamphetamine Dependence Cont.

Sponsor / PI

<u>Title of Study / Clinical Drug</u> Trial Protocol

Alan Gevins, D.Sc. SAM Technology 425 Bush Street San Francisco, CA 94108 Realtime Neural Monitor for Drug Abuse Research

GW Pharmaceuticals Wiltshire, United Kingdom **GW Protocol GWCA0501**

Javelin Pharmaceuticals Cambridge, Massachussets

A Randomized, Double-Blind, Active- and Placebo-Controlled, Study of the Analgesic Efficacy & Safety of Repeated Dosing of MNS075 (Intranasal Morphine), IV Morphine and Placebo in Patients with Acute Post-Operative Pain after Elective Orthopedic Surgery (Javelin MOR-003)

Johnson & Johnson Pharmaceuticals Titusville, New Jersey

A Randomized, Double-Blind, Active- and Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy and Safety of Multiple Doses of CG5503 Immediate-Release (IR) Formulation in the Treatment of Acute Pain From Total Hip Replacement Surgery Followed by a Voluntary Open-Label Extension (R331333-PAI-3001)

Johnson & Johnson Pharmaceuticals Titusville, New Jersey A Randomized, Double-Blind, Active-Control, Parallel Arm, 90 Day Safety Study of CG5503 Immediate Release or Oxycodone Immediate Release in Subjects With Chronic Pain From Low Back Pain or Osteoarthritis of the Hip or Knee (R331333-PAI-3004)

<u>Title of Study / Clinical Drug</u> <u>Trial Protocol</u>

Johnson & Johnson Pharmaceuticals Titusville, New Jersey A Randomized, Double-blind, Active- and Placebo-Controlled, Parallel Group, Multicenter Study to Evaluate the Efficacy and Safety of Multiple Doses of CG5503 Immediate-Release (IR) Formulation In Subjects Awaiting Primary Joint Replacement Surgery for End-Stage Joint Disease (R331333-PAI-3002)

Johnson & Johnson Pharmaceuticals Titusville, New Jersey A One-Year, Randomized, Open-Label; Parallel-Arm, Phase III Long-Term Safety Trial, with Controlled Adjustment of Dose, of Multiple Doses of CG5503 PR* and Oxycodone in Subjects with Chronic Pain (R331333-PAI-3007)

Lorrin Koran, M.D. Stanford University School of Med 401 Quarry Road Stanford, CA 94305 Double-Blind Trial of Acute and Intermediate-Term Dextro-Amphetamine versus Caffeine Augmentation in Treatment-Resistant Obsessive-Compulsive Disorder

Walter Ling, M.D. UCLA ISAP 11075 Santa Monica Blvd., Suite 200 Los Angeles, CA 90025-7539 Double-Blind, Placebo-Controlled Trial of Prometa Pharmacotherapy for the Treatment of Methamphetamine Abuse

Walter Ling, M.D. UCLA ISAP 11075 Santa Monica Blvd., Suite 200 Los Angeles, CA 90025-7539 Optimizing Outcomes Using Suboxone for Opiate Dependence

Cont.

Sponsor / PI

<u>Title of Study / Clinical Drug</u> <u>Trial Protocol</u>

James T. McCracken, M.D. UCLA Neuropsychiatric Institute 300 UCLA Medical Plaza, Suite 1534 Los Angeles, CA 90095-7057 An Eight-Week, Randomized, Double-Blind Comparison of Twice-Daily Guanfacine, Once-Daily d-Methylphenidate Extended Release (Focalin XR) and the Combination, with a Twelve Month Open-Label Extension for the Treatment of Attention Deficit/Hyperactivity Disorder in Pediatric Subjects Aged 7 to 14 years.

McNeil Pharmaceuticals
Fort Washington, Pennsylvania

A Placebo-controlled, Double-blind, Parallel-group, Dose Titration Study to Evaluate the Efficacy & Safety of CONCERTA in Adults with Attention Deficit Hyperactivity Disorder at Doses of 36mg, 54mg, 72mg, 90mg, or 108mg per day (McNeil #02-159)

McNeil Pharmaceuticals
Fort Washington, Pennsylvania

An Open-label, Dose-Titration, Long-Term Safety to Evaluate CONCERTA at Doses of 36mg, 54mg, 72mg, 90mg and 108mg per day in Adults with Attention Deficit Hyperactivity Disorder (McNeil #12-304)

John E. Mendelson, M.D. Addict'n Pharmacology Research Lab California Pacific Medical Center St. Luke's Hospital, 7th Flóor 3555 Cesar Chavez Street San Francisco, CA 94110 Interactions of Prazosin and MDMA

<u>Title of Study / Clinical Drug</u> Trial Protocol

John E. Mendelson, M.D. Addict'n Pharmacology Research Lab California Pacific Medical Center St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Is There an Acute MDMA Single Dose Withdrawal Syndrome?

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024

An evaluation of the presence of psychotic symptoms in response to experimental administration of methamphetamine or placebo in the laboratory

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024

Methamphetamine Dependence: A Novel Laboratory Model

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024

The Dual Deficit Hypothesis of Stimulant Dependence: An Experiment Assessment in Human Volunteers

National Institute on Drug Abuse (NIDA) Bethesda, Maryland Phase 2, Double-Blind, Placebo-Controlled Trial of Topiramate for the Treatment of Methamphetamine Dependence (NIDA-MDS-Topiramate/meth0001)

National Instituté on Drug Abuse (NIDA) Bethesda, Maryland Starting Treatment with Agonist Replacement Therapies (START) (NIDA CTN Protocol 0027) Cont.

Sponsor / PI

<u>Title of Study / Clinical Drug</u> Trial Protocol

National Institute on Drug Abuse (NIDA)
Bethesda, Maryland

A Two-Phase Randomized Controlled Clinical Trial of Buprenorphine/Naloxone Treatment Plus Individual Drug Counseling for Opiod Analgesic Dependence

(NIDA CTN Protocol 0030)

Novartis Pharmaceuticals Corporation East Hanover, New Jersey A 5-week treatment, multi-center, double-blind, randomized, placebo-controlled, parallel-group, fixed-dose study of the efficacy, tolerability and safety of dexmethylphenidate HCl extended-release capsules (Focalin XR) administered once daily in pediatric patients 6-12 years of age with Attention-Deficit/Hyperactivity Disorder (Novartis CRIT124E2305)

Novartis Pharmaceuticals Corporation East Hanover, New Jersey

An open-label, behavioral-treatment-controlled evaluation of the effects of extended release methylphenidate (Ritalin LA) on the frequency of cytogenetic abnormalities in children 6-12 year of age with ADHD (Novartis Protocol: CRIT 124D2201)

Scott J. Novick, Ph.D.

Panel Approved Research Project

Pain Therapeutics, Inc. 416 Browning Way South San Francisco, CA 94080 A Long-Term, Open-Label, Safety Study of PTI-821 in Patients with Moderate to Severe Chronic Low Back Pain or with Moderate to Severe Chronic Pain Due to Osteoarthritis of the Hip or Knee (Pain Therapeutics Protocol PTI-821-CM)

<u>Title of Study / Clinical Drug</u> Trial Protocol

Pain Therapeutics, Inc. South San Francisco, California A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase III, Efficacy & Safety Study of PTI-821 in Patients with Moderate to Severe Chronic Pain Due to Osteoarthritis of the Hip or Knee (Pain Therapeutics PTI-821-CO)

PriCara, Unit of Ortho-McNeil, Inc. Raritan, New Jersey Time to Onset of Pain Relief Using a Standard Regimen of IV PCA Morphine Following Total Abdominal Hysterectomy (PriCara Protocol No. FENHYDPAI4003)

Purdue Pharma, L.P. Stamford, Connecticut

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Pilot Study to Evaluate the Analgesic Efficacy of BTDS on Postoperative Pain During Rehabilitation Following Total Knee Arthroplasty (Purdue Pharma Protocol BUP2003)

Gary Scott, M.D. Childrens Hospital Los Angeles 4650 Sunset Blvd. MS #3 Los Angeles, CA 90027

Comparison of On-Q PainBuster with Intrathecal Opioids for Postoperative Analgesia after Posterior Spinal Fusion SkyePharma, Inc. San Diego, California A Phase 2/3, Multicenter, Randomized, Double-Blind, Dose-Finding and Dose-Confirmations Study to Evaluate the Safety and Efficacy of a Single Epidural Dose of SKY-0401 (Morphine Sulfate Extended-Release Liposome Injection) in the Management of Post-Operative Pain in Pediatric Subjects Undergoing Lower Abdominal (Below the Diaphragm), Genitourinary, or Lower Extremity Orthopedic Surgery (SkyePharma SKY0401-C2-021)

Barth Wilsey, M.D. UC Davis Medical Center 4860 Y Street, Suite 3020 Sacramento, CA 95817 The Analgesic Effect of Vaporized Cannabis on Neuropathic Pain

TABLE 2

RESEARCH STUDIES CLOSED OR DISCONTINUED IN 2006

Sponsor / PI

<u>Title of Study / Clinical Drug</u> Trial Protocol

Donald I. Abrams, M.D. UCSF Community Consortium 3180 18th Street, Suite 201 San Francisco, CA 94110-2042 Vaporization as a Smokeless Cannabis Delivery System - A Pilot Study

Donald I. Abrams, M.D. UCSF Community Consortium 3180 18th Street, Suite 201 San Francisco, CA 94110-2042 The Effect of Marijuana on Neuropathic Pain in HIV-Related Peripheral Neuropathy

Alpharma, Inc. Piscataway, New Jersey A Phase II Multi-dose, Double-blind, Crossover Study to Assess the Safety, Efficacy, and Pharmacokinetics of Kadian NT (morphine sulfate plus naltrexone hydrochloride extended-release capsules) in Subjects with Chronic Pain due to Osteoarthritis of the Hip or Knee (Alpharma Protocol ALO-KNT-202)

Martin Angst, M.D. Stanford Univ. School of Medicine 300 Pasteur Drive, Grant Bldg, S-276 Stanford, CA 94305-5117

Differential Rate for Development of Acute Tolerance to Opioid Induced Analgesia, Respiratory Depression, and Sedation

Martin Angst, M.D. Stanford Univ. School of Medicine 300 Pasteur Drive, Grant Bldg, S-276 Stanford, CA 94305-5117 Opioid Induced Hyperalgesia and Central Noxious Inhibitory Control

<u>Title of Study / Clinical Drug</u> Trial Protocol

Teresa Bennett, Ph.D. Novasite Pharmaceuticals 11095 Flintkote Ave. San Diego, CA 92121 Development of Selective Ligands for 5HT2 and Cannabinoid G protein-Coupled Receptors

David Braff, M.D. University of California at San Diego 9500 Gilman Drive La Jolla, CA 92093-0804 The Effects of Stimulants on Psychophysiological Measures in Normal Subjects

Nancy Buckley, Ph.D. California State Polytechnic Univ. 3801 W. Temple Ave. Pomona, CA 91768 The Role of the Peripheral Cannabinoid (CB2) Receptor Activation in Immune Function

Cephalon, Inc. Frazer, Pennsylvania A Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of ORAVESCENT Fentanyl Citrate in Opioid-Tolerant Patients With Cancer and Breakthrough Pain (Cephalon Protocol C25608/3039/BP/US)

Cephalon, Inc. Frazer, Pennsylvania A 4-Week, Open-Label Extension Study of ACTIQ (Oral Transmucosal Fentanyl Citrate [OTFC ®] Treatment for Opioid-Tolerant Children and Adolescents with Breakthrough Pain (Cephalon Protocol C8278/2022/BP/US-CA)

<u>Title of Study / Clinical Drug</u> Trial Protocol

Cephalon, Inc. Frazer, Pennsylvania

A Double-Blind, Placebo-Comparison Study to Evaluate the Efficacy and Safety of ACTIQ® (Oral Transmucosal Fentanyl Citrate[OTFC®]) Treatment for Opioid-Tolerant Children and Adolescents with Breakthrough Pain (Cephalon Protocol C8278b/202/BP/US-CA)

Lin Chang, M.D. UCLA Digestive Disease Research Center 100 UCLA Medical Plaza Suite 255 Los Angeles, CA 90095 Neuroendocrine Alterations in Fibromyalgia and IBS

Jody Corey-Bloom, M.D. UCSD Clinical Research Ctr. 9500 Gilman Drive La Jolla, CA 92093-0620 Short-Term Effects of Cannabis Therapy on Spasticity in MS

Elan Pharmaceuticals Inc. San Diego, California

Elan Protocol ELN92045-205

Ronald J. Ellis, M.D. UCSD HIV Neurobehavior Research Center 150 W. Washington St., 2nd Floor San Diego, CA 92103 Placebo-controlled, Double-blind Trial of Medicinal Cannabis in Painful HIV-Neuropathy

Howard Fields, M.D., Ph.D. Department of Neurology UCSF School of Medicine San Francisco, CA 94143 Neural Mechanisms of Analgesia

<u>Title of Study / Clinical Drug</u> <u>Trial Protocol</u>

Howard Fields, M.D, Ph.D Department of Neurology UCSF School of Medicine San Francisco, CA 94143 Mechanisms of Cannabinoid Analgesia

Grunenthal GmbH, Research and Development Aachen, Germany Randomized, multicenter, double blind, parallel-group study assessing analgesic efficacy & safety of different dosages of GRT0151Y bid compared to active Comparator bid & placebo bid in subjects with chronic knee-joint osteoarthritis (Grunenthal Protocol #KF0151Y/07)

J. David Jentsch, Ph.D. UCLA Department of Psychology 405 Hilgard Ave; B630 Franz Hall Los Angeles, CA 90095-1563 Neurocognitive and Chemical Effects of Entactogenic and Cannabinoidergic Drugs

Reese Jones, M.D. Dept. of Pysch & Langley Porter UCSF San Francisco, CA 94143-0984 Elimination of Cocaine from Patches Placed on the Skin

Reese Jones, M.D. Dept. of Pysch & Langley Porter UCSF San Francisco, CA 94143-0984 Double-Blind, Placebo-Controlled, Assessment of Intravenous Methamphetamine and Modafinil Interactions

John Lu Bionike Incorporated 100 North Hill Drive #35. Brisbane, CA 94005 Prepare Drug-Bovine Serum Albumin (BSA) Conjugate

<u>Title of Study / Clinical Drug</u> Trial Protocol

James J. McGough. M.D. UCLA Child Treatment Research Group 300 UCLA Medical Plaza # 1534A Los Angeles, CA 90095-6967 Response Variability in Stimulant Treatment of ADHD

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Clinical Pharmacology of Methamphetamine Stereoisomers

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Pharmacokinetics of Intranasal and Smoked Methamphetamine

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Pharmacokinetic Interactions between the Selegiline Transdermal Delivery System and d-Methamphetamine

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Effects of Cocaine Agonist Therapy on Cocaine Self-Administration, Tolerance, and Craving

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Clinical Pharmacology of l-Methamphetamine

<u>Title of Study / Clinical Drug</u> <u>Trial Protocol</u>

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Interaction Between the Serotonin Reuptake Blocker Paroxetine and Methamphetamine

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Interaction Between Oral Reserpine and Intravenous Methamphetamine

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Buprenorphine / Naloxone versus Methadone for Rapid Control of Opiate Withdrawal in the Hospitalized Patient

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Laboratory Observation of Acute MDMA Single Dose Withdrawal

Thomas Newton, M.D. UCLA ISAP 760 Westwood Blvd., Ste. A8-153 Los Angeles, CA 90024 The Assessment of Potential Interactions between Intravenous Methamphetamine and Oral Selegiline

Thomas Newton, M.D. UCLA ISAP 760 Westwood Blvd., Ste. A8-153 Los Angeles, CA 90024 Safety Assessment of Interaction between Cocaine and Amantadine/Baclofen

<u>Title of Study / Clinical Drug</u> Trial Protocol

Thomas Newton, M.D. UCLA ISAP 760 Westwood Blvd., Ste. A8-153 Los Angeles, CA 90024 Impact of Stressful Life Events on the Reinstatement Model of Relapse

Thomas Newton, M.D. UCLA ISAP 760 Westwood Blvd., Ste. A8-153 Los Angeles, CA 90024 The Effects of Modafinil on Tests of Inhibitory Control in Methamphetamine Addiction

Thomas Newton, M.D. UCLA ISAP 760 Westwood Blvd., Ste. A8-153 Los Angeles, CA 90024

Effects of Chronic Methamphetamine Use on Sleep Architecture and Cognition

National Institute on Drug Abuse 6001 Executive Boulevard Bethesda, Maryland 20892 Double-Blind, Placebo-Controlled Multi-Center Trial of Baclofen for the Treatment of Cocaine Dependence

Novartis Pharmaceuticals East Hanover, New Jersey A 5-week treatment, multi-center, double-blind, randomized, placebo-cntrld, parallel-group, fixed-dose study of the efficacy, tolerability and safety of Focalin XR given once daily in pediatric patients 6-12 years old. w/ ADHD (Novartis Protocol CRIT124E2305)

Progenics Pharmaceuticals Tarrytown, New York A Double-Blind Phase 3, Two-Week, Placebo Controlled Study of Methylnaltrexone (MNTX) for the Relief of Symptomatic Constipation Due to Chronic Opioid Therapy in Advanced Medical Illness; Three-Month Open Label Treatment Extension Option (Progenics Protocol MNTX 302, 302EXT)

<u>Title of Study / Clinical Drug</u> <u>Trial Protocol</u>

Purdue Pharma L.P. Stamford, Connecticut

A Multicenter, Randomized, Double-blind, Active Comparator Study to Determine the Efficacy and Safety of BTDS 20 or Oxy IR®versus BTDS 5 in Subjects with Moderate to Severe Low Back Pain (Purdue Pharma Protocol BUP3015)

Purdue Pharma L.P. Stamford, Connecticut

Randomized, Double-blind, Multicenter, Active Comparator Study to Determine the Efficacy and Safety of BTDS 20 or Oxy IR®versus BTDS 5 in Subjects with Moderate to Severe Osteoarthritis (OA) Pain (Purdue Pharma Protocol BUP3019)

Rachel D. Schrier, Ph.D. UCSD Medical Center 200 W Arbor Drive MC 8416 San Diego, CA 92103-8416 Effects of Medicinal Cannabis on CD4 Immunity in Aids

Shire Pharmaceutical Development Wayne, Pennsylvania

A Phase III, Multi-center, 24-month, Open-label Safety, Tolerability and Efficacy Study of Adderall XR® in the Treatment of Adolescents Aged 13-18 with Attention Deficit Hyperactivity Disorder (ADHD) (Shire Protocol SLI381-315)

Shire Pharmaceutical Development Wayne, Pennsylvania

A Phase III, Randomized, Double-blind, Multi-center, Placebo-controlled, Parallel-Group, Safety and Efficacy Study of SPD465 in Adults with Attention-Deficit Hyperactivity Disorder (ADHD) (Shire Protocol SPD465-301)

<u>Title of Study / Clinical Drug</u> <u>Trial Protocol</u>

Shire Pharmaceutical Development Wayne, Pennsylvania

A Phase III, Randomized, Double-blind, Multi-center, Placebo-controlled, Parallel-group, Forced Dose Titration, Safety and Efficacy Study of SPD465 in Adults with Attention-Deficit Hyperactivity Disorder (Shire Protocol SPD465-303)

Shire Pharmaceutical Development Wayne, Pennsylvania

A Phase IIIB, Rndmzd, Dbl-Blind, Multi-Ctr, Placebo-Cntrld, Dose-Optzmd, 3-way X-Over Study to Assess the Efficacy, Effect, Tolerability and Safety of 4 & 6 hour Wear Times of Methylphenidate Transderm Sys (MTS) in Pedi Sbjcts aged 6-12 w/ ADHD (Shire Protocol SPD485-304)

Shire Pharmaceutical Development Wayne, Pennsylvania

A Prospective, Open-Label, Multi-Center Study Evaluating the Safety and Tolerability of Methylphenidate Transdermal System (MTS) in Children Aged 6 - 12 Previously Treated with Extended .Release Methylphenidate Product (Shire Protocol SPD485-305)

Shire Pharmaceutical Development Wayne, Pennsylvania

A Phase II, Randomized, Double-blind, Multi-center, Placebo-controlled, Crossover Study of SPD465 in Adults with Attention-Deficit Hyperactivity Disorder (ADHD) (Shire Protocol SPD465-203)

Steven Shoptaw, Ph.D UCLA Dept. of Family Medicine 10880 Wilshire Blvd., Suite 1800 Los Angeles, CA 90095-7087 Phase 2, Double-Blind, Placebo-Controlled Trial of Two Doses of Cabergoline for the Treatment of Cocaine Dependence

<u>Title of Study / Clinical Drug</u> <u>Trial Protocol</u>

Steven Shoptaw, Ph.D UCLA Dept. of Family Medicine 10880 Wilshire Blvd., Suite 1800 Los Angeles, CA 90095-7087 An Evaluation of Two Medications (Gabapentin or Baclofen) and Placebo for the Treatment of Methamphetamine Dependence

Steven Shoptaw, Ph.D UCLA Dept. of Family Medicine 10880 Wilshire Blvd., Suite 1800 Los Angeles, CA 90095-7087 An Evaluation of Two Medications (Gabapentin or Baclofen) and Placebo for the Treatment of Methamphetamine Dependence

Solvay Pharmaceuticals, Inc. Marietta, Georgia

Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Efficacy, Safety, and Tolerability Study of Dronabinol MDI in the Acute Treatment of Migraine Headache (Solvay Protocol S175.2.103)

Donald P. Tashkin, M.D. D Geffen School of Med at UCLA 10833 Le Conte Ave 37-131 CHS Los Angeles, CA 90095-1690 Cocaine Smoking Effects on Lung Immunity and Host Defense

Mark Wallace, M.D.
UCSD Clinical Pain Research
9500 Gilman Drive #0924
La Jolla, CA 92093-0924

Analgesic Efficacy of Smoked Cannabis

Mark Wallace, M.D. UCSD Clinical Pain Research 9500 Gilman Drive #0924 La Jolla, CA 92093-0924 Evolution of Analgesic Tolerance During Long Term Treatment of Chronic Pain with Opioids

Mark Wallace, M.D. UCSD Clinical Pain Research 9500 Gilman Drive #0924 La Jolla, CA 92093-0924

Mark Wallace, M.D. UCSD Clinical Pain Research 9500 Gilman Drive #0924 La Jolla, CA 92093-0924

Barth L. Wilsey, M.D. UC Davis Medical Center 4860 Y Street Suite 2700 Sacramento, CA 95817

ZARS, Inc. Salt Lake City, Utah

<u>Title of Study / Clinical Drug</u> <u>Trial Protocol</u>

Effects of Intravenous Alfentanil on Non-Painful Thermally Induced Hyperalgesia in Healthy Volunteers

Double-Blind, Randomized, Cross-Over Study Comparing Continuous Infusion Versus Intermittent Bolus Dosing of Intrathecal Therapy for the Treatment of Chronic Pain

A Double Blind, Active Placebo Controlled Crossover Trial of the Antinociceptive Effect of Smoked Marijuana on Subjects with Neuropathic Pain; Correlation with Changes in Mood, Cognition, and Psychomotor Performance

An Open-Label Safety Study to Evaluate the Safety of the ZR-02-01 Matrix Transdermal Fentanyl Patch for Treatment of Moderate to Severe, Non-malignant Chronic Pain (ZARS Protocol ZMF-303)

APPENDIX A

CURRENTLY APPROVED (December 31, 2006) INDEPENDENT SCHEDULE I AND SCHEDULE II CONTROLLED SUBSTANCE RESEARCH STUDIES

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Title of Study

Donald I. Abram's, M.D. UCSF Community Consortium 3180 18th Street, Suite 201 San Francisco, CA 94110-2042 Opioid & Cannabinoid Pharmacokinetic Interactions: A Pilot Study

Mark A. Agius, M.D. Dept. of Neurology University of California, Davis 1515 Newton Court Room 510 Davis, CA 95616 Cannabis for Spasticity/Tremor in MS: Placebo Controlled Study

James T. Arnold, Ph.D. Systems and Techniques Lab. Varian Associates 3075 Hansen Way Palo Alto, CA 94304-1025 Chemical Vapor Analysis of Marijuana and Other Drugs of Abuse

Mark G. Barad, M.D., Ph.D. UCLA Dept Psych & Biobehav Sci 695 Charles E. Young Drive South Los Angeles, CA 90095-1761 Cannabinoids in Fear Extinction

Selena E. Barrett, Ph.D. Ernest Gallo Clinic & Research Ctr 5858 Horton Street, Suite 200 Emeryville, CA 94608 The role of cannabinoids and ibogaine in the treatment of alcoholism and drug addiction

Ronald W. Barrett, Ph.D. XenoPort, Inc. 3410 Central Expressway Santa Clara, CA 95051 Gamma Hydroxybutyrate as an Agonist at the GABA-B Receptor

Appendix A Cont.

Principal Investigator

Title of Study

Phillip E. Bickler, M.D., Ph.D. UCSF Dept. of Anes. & Periop. Care 513 Parnassus Ave. San Francisco, CA 94143-0542

Inhaled carbon dioxide and apnea during intravenous sedation

Nancy E. Buckley, Ph.D. California State Polytechnic Univ. 3801 W. Temple Ave. Pomona, CA 91768 The Role of the Peripheral Cannabinoid (CB2) Receptor Activation in Immune Function

Jeremy S. Caldwell, Ph.D. Genomics Inst Novartis Research Fdn 10675 John Jay Hopkins Drive San Diego, CA 92121 High-Throughput Screening of Known Drugs for Novel Biological Activity in Cell-based Assays

Karen Chang, Ph.D. ALZA Corp. 1900 Charleston Road Mountain View, CA 94039-7210 Purity Determination, Morphine and Hydromorphone

Arthur K. Cho, Ph.D.
Dept./Pharmacology, 23-272 CHS
UCLA School of Medicine
10833 Le Conte Avenue
Los Angeles, CA 90024-1721

Studies on Distribution and Metabolism of Narcotics in Animals

Kent S. Chu, Ph.D. YJ Bio-Products 11353 Pyrites Way, Suite 14 Cordova, CA 95670 Immunochromatographic Test Device for THC and LSD

Oliver Civelli, Ph.D. University of California, Irvine Rm 369, Med Surge II Dept of Pharm Irvine, CA 92697-4855 Identify the receptor(s) for gammahydroxybutynic acid (GHB)

Principal Investigator

Title of Study

Laura Colin Biostride, Inc. 1201 Douglas Avenue Redwood City, CA 94063 Research of Novel Technologies for Development of Antibodies and Immunoassay Techniques to Drugs of Abuse and Controlled Compounds of Interest

Ivan Diamond, M.D., Ph.D. CV Therapeutics, Inc. 3172 Porter Drive Palo Alto, CA 94304 Treatment of Experimental Heroin Addiction in Rats

Sean Drummond, Ph.D. UCSD/San Diego VAMC 3350 La Jolla Village Drive La Jolla, CA 92161 Sleep and Medicinal Cannabis

Robert Edwards, M.D. Dept. of Neurology & Physiology UCSF School of Medicine 600 16th St. GH-N272B San Francisco, CA 94158-2517 Role of glutamate release by monoamine neurons

Ronald Ellis, M.D., Ph.D UCSD HIV Neurobehavioral Rsch Ctr. 150 W. Washington St., 2nd Floor San Diego, CA 92103 Placebo-controlled, Double-blind Trial of Medicinal Cannabis in Painful HIV-Neuropathy

Laura J. Esserman, M.D. UCSF Breast Care Center 1600 Divisadero St. Box 1710 San Francisco, CA 94143 Postoperative Pain Control with Fentanyl Patch in Patients undergoing Mastectomy and Tram Flap Reconstruction

Aaron Ettenberg, Ph.D. Dept. Psychology, UC Santa Barbara Santa Barbara, CA 93106-9660 Dopamine Involvement in Opiate and Stimulant Drug Reinforcement

Appendix A Cont.

Principal Investigator

Title of Study

Frederick D. Frankel, Ph.D. UCLA Department of Psychiatry 300 UCLA Medical Plaza Los Angeles, CA 90095-6769

Social Skills Training for Medicated Children

Douglas Fry The NORAC Co., Inc. 405 S Motor Ave., POB 577 Azusa, CA 91702-0706 Research on the Synthesis of Schedule I Controlled Substances: delta-9-THC and LAAM

Douglas Fry
The NORAC Co., Inc.
405 S Motor Ave., POB 577
Azusa, CA 91702-0706

Preparation of Ibogaine and Its Analogs and Derivatives

Gantt P. Galloway, Pharm.D. Addict'n Pharmacology Research Lab California Pacific Medical, Center St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 A Pilot Trial of Dextroamphetamine for Treatment of Methamphetamine Dependence

Alan Gevins SAM Technology, Inc. 425 Bush Street 5th Floor San Francisco, CA 94108 Neurocognitive Index of Cannabis Effects System

Mark A. Geyer, Ph.D. Dept. of Psychiatry - 0804 University of Calif, San Diego 9500 Gilman Drive La Jolla, CA 92093-0804 Behavioral and Cytoflourimetric Studies of Psychoactive Drugs in Rats

Terry E. Grimmer, M.S. Berlex Biosciences 2600 Hilltop Drive Richmond, CA 94804-0099 Synthesis of Pharmaceutical Research Compounds

Principal Investigator

Title of Study

Charles S. Grob, M.D. Harbor UCLA Medical Center 1000 West Carson Street Torrance, CA 90509 Effects of Psilocybin in Terminal Cancer Patients with Anxiety

Kanthi F. Hettiarachchi, Ph.D. SRI International 333 Ravenswood Avenue Menlo Park, CA 94025 Analysis of Cannabinoids

Richard A. Houghten, Ph.D. Torrey Pines Inst./Molecular Study 3550 General Atomics Ct. San Diego, CA 92121 Biochemical Basis for the CNS Actions of Methaqualone

Michael Irwin, M.D. UCLA Neuropsychiatric Institute 300 UCLA Medical Plaza Ste 3109 Los Angeles, CA 90095-7076 Cocaine Dependence: Sleep and Cytokines

S.V. Penelope Jones, Ph.D. UCSD School of Medicine 9500 Gilman Drive La Jolla, CA 92093-0603

Effects of GHB on the Mesolimbic Dopaminergic System

Ari Kalechstein, Ph.D. UCLA Neuropsychiatric Inst. 740 Westwood Plaza, Rm. A8-144 NPI Los Angeles, CA 90024 Methamphetamine Dependence: Treating Neurocognitive Impairment"

Thomas B. King Alexza Molecular Delivery Corp. 1001 East Meadow Circle Palo Alto, CA 94303 Development of an FDA Approved Dronabinol Pharmaceutical Product for Inhalation Delivery

Appendix A Cont.

Principal Investigator

Title of Study

George F. Koob, Ph.D.
Dept of Neuropharmacol. CVN-7
The Scripps Research Institute
10666 N Torrey Pines Rd.
La Jolla, CA 92037

Central Mechanisms of Opiate Reinforcement and Dependence

George F. Koob, Ph.D.
Dept of Neuropharmacol. CVN-7
The Scripps Research Institute
10666 N Torrey Pines Rd.
La Jolla, CA 92037

Neuronal Substrates of Cocaine Reward

Lorrin Koran, M.D. Stanford University Schl. of Medicine 401 Quarry Road Stanford, CA 94305 Double-Blind Trial of Acute & Intermediate-Tern Dextro-Amphetamine versus Caffeine Augmentation in Treatment-Resistant Obsessive-Compulsive Disorder

Helen Lavretsky, M.D. UCLA Neuropsychiatric Institute 760 Westwood Plaza Rm 37-425 Los Angeles, CA 90024 Intervention Clinical Trial for Geriatric Depression: A Double-blind Placebo-Controlled Trial of Methylphenidate (Ritalin) Augmentation of Citalopram (Celexa) in Depressed Patients at Least 70 Years of Age

Nancy M. Lee, Ph.D. Forbes Norris ALS/MDA Rsrch Ctr. 2351 Clay Street Suite 416 San Francisco, CA 94115 Role of Cannabinoid Receptors in Central Nervous System Functions and Diseases

Jon D. Levine, M.D., Ph.D. UCSF Dept. Oral&Maxillofac Surgery San Francisco, CA 94143-0440 Mechanisms of Pain Control: V. Analgesic Combinations for Post-Operative Pain–Kappa Opioids and Morphine.

Marie Lin, Ph.D. R.Ph. Lin-Zhi International, Inc. 687 North Pastoria Ave Sunnyvale, CA 94085 Lin-Zhi Immunoassay Development Study

Principal Investigator

Title of Study

Walter Ling, M.D. UCLA ISAP 11075 Santa Monica Blvd., Suite 200 Los Angeles, CA 90025-7539 Double-Blind, Placebo-Controlled Trial of PROMETATM Pharmacotherapy for the Treatment of Methamphetamine Abuse

Walter Ling, M.D. UCLA ISAP 11075 Santa Monica Blvd., Suite 200 Los Angeles, CA 90025-7539 Optimizing Outcomes Using Suboxone for Opiate Dependence

Thomas D. Marcotte, Ph.D. UCSD HIV Neurobehav. Rsch. Ctr. 150 W. Washington St., 2nd Floor San Diego, CA 92103 Impact of Repeated Cannabis Treatments on Driving Abilities

James McCracken, M.D. UCLA Neuropsychiatric Institute 300 UCLA Medical Plaza, Suite 1534 Los Angeles, CA 90095-7057 An 8-Wk, Rndmzd, Dbl-Blind Comparison of Twice-Daily Guanfacine, Once-Daily d-Methylphenidate ER (Focalin XR) and the Combination, with a 12 Month Open-Lbl Extension for the Treatment of ADHD in Pediatric Subjects Aged 7 to 14 years

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Bioavailability and Urinary Excretion of Oral L-Methamphetamine

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Interactions of Prazosin and MDMA

Appendix A Cont.

Principal Investigator

Title of Study

John Mendelson, M.D Addiction Pharmacology Research Lab St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 Is There an Acute MDMA Single Dose Withdrawal Syndrome?

Robert Messing, M.D. Ernest Gallo Clinic & Research Ctr 5858 Horton Street, Suite 200 Emeryville, CA 94608 Protein kinase C epsilon (PKCe) in Responses to Cannabinoids

Karen Miotto, M.D. UCLA Neuropsychiatric Inst. 760 Westwood Plaza Room 37-384C Los Angeles, CA 90095 GHB: Effects, Withdrawal and Treatment"

Karel Z. Newman, Ph.D. Biosite Incorporated 9975 Summers Ridge Road San Diego, CA 92121 Development of In-vitro Immunoassays for the Detection of Abused Substances

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024

Double-Blind, Placebo-Controlled Assessment of Potential Interactions between Intravenous Methamphetamine and Oral Bupropion

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024

Perindopril - Methamphetamine Interaction Study

Thomas F. Newton, M.D. UCLA ISAP
760 Westwood Plaza, Rm A8-153
Los Angeles, CA 90024

Modafinil as a Treatment for Methamphetamine Dependence: Initial Safety, Subjective Effects, and Brain Functioning - Pilot study

Principal Investigator

Title of Study

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024

Laboratory Models of Cocaine Self Administration

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024 An evaluation of the presence of psychotic symptoms in response to experimental administration of methamphetamine or placebo in the laboratory

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024

Methamphetamine Dependence: A Novel Laboratory Model

Thomas F. Newton, M.D. UCLA ISAP 760 Westwood Plaza, Rm A8-153 Los Angeles, CA 90024

The Dual Deficit Hypothesis of Stimulant Dependence: An Experiment Assessment in Human Volunteers

Karno Ng, Ph.D. California State University San Marcos San Marcos, CA 92096-0001 New Qualitative and Quantitative Methods for the Detection of Gamma-hydroxybutyrate (GHB)

Scott J. Novick, Ph.D.

Panel Approved Research Project

Stanley M. Parsons, Ph.D. Dept Chem & Biochem, UCSB Santa Barbara, CA 93106-9510 Rapid Detection of 4-hydroxybutyrate

Mark Perrone, Ph.D. 10675 John Jay Hopkins Drive San Diego, CA 92121 Application for Non-Human Research Using Schedule I Controlled Substance - Effects of Novel Agents on Food Intake, Weight Gain and Weight Loss in Rodents, Determination of Stimulation and Blockade of CB1 Receptor

Appendix A Cont.

Principal Investigator

Title of Study

John M. Polich, Ph.D.
Dept. of Neuropharmacology
The Scripps Research Institute
10550 North Torrey Pines Rd TPC10
La Jolla, CA 92037

Marijuana CNS Effects in Low- and High-Risk Adults

Robert Ramage Microgenics Corporation 46360 Fremont Boulevard Fremont, CA 94538 Use of Schedule I Controlled Substances for Cross Reactant Studies and Investigation of Customer Inquiries

Dorit Ron, Ph.D. Ernest Gallo Clinic & Research Ctr 5858 Horton Street Suite 200 Emeryville, CA 94608 Signaling Pathways Involved in the Mechanism of Action of the Anti-Addictive Drug Ibogaine

Michael C. Rowbotham, M.D. UCSF Pain Clinical Res. Cntr. 2233 Post St. Suite 104 San Francisco, CA 94115

The effect of intravenous remifentanil on the experimental heat/capsaicin sensitization model in chronic pain patients

Michael C. Rowbotham, M.D. UCSF Pain Clinical Research Center 2233 Post St. Suite 104 San Francisco, CA 94115 Evolution of Analgesic Tolerance During Long Term Treatment of Chronic Pain with Opioids

Matthew A. Schreiber, M.D., Ph.D. Ernest Gallo Clinic & Research Ctr 5858 Horton Street Ste 200 Emeryville, CA 94608 Pharmacological and genetic study of the effects of 3,4- methylenedioxymethamphetamine (MDMA) using a model organism, the nematode Caenorhabditis elegans

Gary Scott, M.D. Childrens Hospital Los Angeles 4650 Sunset Blvd. MS #3 Los Angeles, CA 90027

Comparison of On-Q PainBuster with Intrathecal Opioids for Postoperative Analgesia after Posterior Spinal Fusion

Principal Investigator

Title of Study

Steven Shoptaw, Ph.D. Semel Inst of Neurosci & Hum Behav 11075 Santa Monica Blvd. #200 Los Angeles, CA 90025 A Randomized, Double-Blind, Placebo-Controlled Evaluation of Bupropion vs Placebo for the Treatment of Methamphetamine Dependence

Lawrence Toll, Ph.D. Neuroscience Department SRI International 333 Ravenswood Avenue Menlo Park, CA 94025 Biochemical Studies into Opiate Efficacies

Lawrence Toll, Ph.D. Receptor Pharmacology SRI International 333 Ravenswood Avenue Menlo Park, CA 94025 Receptor binding assays of blind and coded schedule I controlled substances pursuant to contracts with the National Institute on Drug Abuse

Edward Tung, Ph.D. Innovacon Laboratories 4108 Sorrento Valley Blvd. San Diego, CA 92121 Development of urine and/or oral-fluid based in-vitro diagnostic tests to detect the presence of the controlled substances MDMA, GHB and THC

Edward Tung, Ph.D. Innovacon Laboratories 4108 Sorrento Valley Blvd. San Diego, CA 92121 Development of urine and/or oral-fluid based in-vitro diagnostic tests in the form of lateral flow rapid test format to detect controlled substances commonly abused and misused by individuals

David L. Valentine, Ph.D. Department of Earth Science U.C. Santa Barbara Santa Barbara, CA 93116 Isolation of bacteria capable of growth on gamma-hydroxybutyric acid (GHB) and its analogs

Jennifer L. Whistler, Ph.D. Ernest Gallo Clinic & Research Ctr 5858 Horton Street Suite 200 Emeryville, CA 94608 Endocytosis and Cannabinoid Receptors

Appendix A Cont.

Principal Investigator

Title of Study

Jennifer L. Whistler, Ph.D. Ernest Gallo Clinic & Research Ctr 5858 Horton Street Suite 200 Emeryville, CA 94608 Endocytosis and Opioid Receptors

Sharon B. Wigal, Ph.D. UCI Child Development Center 19722 MacArthur Blvd. Irvine, CA 92612 Pharmacokinetic and Pharmacodynamic Evaluation of Stimulant Drugs

Barth Wilsey, M.D. UC Davis Medical Center 4860 Y Street, Suite 3020 Sacramento, CA 95817 The Analgesic Effect of Vaporized Cannabis on Neuropathic Pain

Justin A. Zivin, M.D., Ph.D. Dept. of Neurosciences, 0624 UCSD School of Medicine 9500 Gilman Drive La Jolla, CA 92093-0624 Therapy of Central Nervous System Ischemia

APPENDIX B

CURRENTLY APPROVED (December 31, 2006) SCHEDULE II MULTICENTER CLINICAL DRUG TRIAL STUDIES

Sponsor

Description or Title

of Clinical Drug Trial Protocol

Archimedes Development, Ltd. Nottingham, UK

A Multicenter, Placebo-Controlled, Double-Blind, Two-Phase Crossover Study of Nasalfent (Fentanyl Citrate Nasal Spray) in the Treatment of Breakthrough Cancer Pain (BTCP) in Subjects Taking Regular Opioid Therapy (CPO43/06/FCNS)

Archimedes Development, Ltd. Nottingham, UK

An Open-Label Study Investigating Long-Term Safety and Tolerability of Nasalfent (Fentanyl Citrate Nasal Spray) in the Treatment of Breakthrough Cancer Pain (BTCP) in Subjects Taking Regular Opioid Therapy (CPO45/06/FCNS)

BioDelivery Sciences International Morrisville, NC

An open label, long-term treatment evaluation of the safety of BEMA fentanyl use for breakthrough pain in cancer subjects on chronic opioid therapy (BioDelivery Protocol FEN-202)

BioDelivery Sciences International Morrisville, NC

A double-blind, placebo controlled, evaluation of the efficacy, safety and tolerability of BEMA Fentanyl in the treatment of breakthrough pain in cancer subjects (BioDelivery Protocol FEN-201)

Appendix B Cont.

Sponsor

<u>Description or Title</u> of Clinical Drug Trial Protocol

Cephalon, Inc. Frazer, Pennsylvania A 4-Week, Open-Label Extension Study of ACTIQ (Oral Transmucosal Fentanyl Citrate [OTFC ®] Treatment for Opioid-Tolerant Children and Adolescents with Breakthrough Pain (C25608/3054/BP/US)

Cephalon, Inc. Frazer, Pennsylvania A 12-Week Open-Label Study With 3 Within-Patient Double-Blind Placebo-Controlled Periods to Evaluate the Efficacy and Safety of ORAVESCENT® Fentanyl Citrate Treatment for the Management of Breakthrough Pain in Opioid-Tolerant Patients With Noncancer-Related Chronic Pain (Cephalon C25608/3052/BP/US)

Endo Pharmaceuticals Chadds Ford, PA A Double-Blind, Randomized, Placebo-Controlled, multicenter Study to Evaluate the Efficacy and safety of EN3267 for the Treatment of Breakthrough Pain in Opioid Tolerant Cancer Patients Followed by a 12-Month Non-Randomized, Open-label Extension to Assess Long-Term Safety (Endo Protocol EN3267-005)

Endo Pharmaceuticals Chadds Ford, PA

A Multiple-Dose, Non Randomized, Open-Label, Multicenter Study to Evaluate the Long-Term Safety and Effectiveness of EN3267 in the Treatment of Breakthrough Pain in Cancer patients (Endo Protocol EN3267-007)

Sponsor

<u>Description or Title</u> of Clinical Drug Trial Protocol

GW Pharmaceuticals Wiltshire, UK

A double blind, randomized, placebo controlled, parallel group study of the analgesic efficacy, safety, and tolerability of Sativex compared with placebo in relieving pain in patients with advanced cancer, who experience inadequate analgesia during optimized chronic opioid therapy (GWCA0501)

Javelin Pharmaceuticals, Inc. Cambridge, MA

A Randomized, Double-Blind, Active- and Placebo-Controlled, Study of the Analgesic Efficacy & Safety of Repeated Dosing of MNS075 (Intranasal Morphine), IV Morphine and Placebo in Patients with Acute Post-Operative Pain after Elective Orthopedic Surgery (Javelin MOR-003)

Johnson & Johnson Pharmaceuticals Titusville, NJ

A Randomized, Double-Blind, Active-Control, Parallel Arm, 90 Day Safety Study of CG5503 Immediate Release or Oxycodone Immediate Release in Subjects With Chronic Pain From Low Back Pain or Osteoarthritis of the Hip or Knee (R331333-PAI-3004)

Appendix B Cont.

Sponsor

<u>Description or Title</u> <u>of Clinical Drug Trial Protocol</u>

Johnson & Johnson Pharmaceuticals Titusville, NJ

A Randomized, Double-Blind, Active- and Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy and Safety of Multiple Doses of CG5503 Immediate-Release (IR) Formulation in the Treatment of Acute Pain From Total Hip Replacement Surgery Followed by a Voluntary Open-Label Extension (R331333-PAI-3001)

Johnson & Johnson Pharmaceuticals Titusville, NJ

A Randomized, Double-blind, Active- and Placebo-Controlled, Parallel Group, Multicenter Study to Evaluate the Efficacy and Safety of Multiple Doses of CG5503 Immediate-Release (IR) Formulation In Subjects Awaiting Primary Joint Replacement Surgery for End-Stage Joint Disease (R331333-PAI-3002)

Johnson & Johnson Pharmaceuticals Titusville, NJ

A One-Year, Randomized, Open-Label; Parallel-Arm, Phase III Long-Term Safety Trial, with Controlled Adjustment of Dose, of Multiple Doses of CG5503 PR* and Oxycodone in Subjects with Chronic Pain (R331333-PAI-3007)

Johnson & Johnson Pharmaceuticals Titusville, NJ

An Open-label, Dose-Titration, Long-Term Safety to Evaluate CONCERTA at Doses of 36mg, 54mg, 72mg, 90mg and 108mg per day in Adults with Attention Deficit Hyperactivity Disorder (McNeil #12-304)

Sponsor

<u>Description or Title</u> <u>of Clinical Drug Trial Protocol</u>

Novartis Pharmaceuticals East Hanover, NJ An open-label, behavioral-treatment-controlled evaluation of the effects of extended release methylphenidate (Ritalin LA) on the frequency of cytogenetic abnormalities in children 6-12 year of age with ADHD (Novartis Protocol: CRIT 124D2201)

Pain Therapeutics, Inc. South San Francisco, California A Long-Term, Open-Label, Safety Study of PTI-821 in Patients with Moderate to Severe Chronic Low Back Pain or with Moderate to Severe Chronic Pain Due to Osteoarthritis of the Hip or Knee (Pain Therapeutics Protocol PTI-821-CM)

Pain Therapeutics, Inc. South San Francisco, California A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase III, Efficacy & Safety Study of PTI-821 in Patients with Moderate to Severe Chronic Pain Due to Osteoarthritis of the Hip or Knee (Pain Therapeutics PTI-821-CO)

Progenics Pharmaceuticals Tarrytown, New York

A Compassionate Use Study of Methylnaltrexone in Patients with Opioid-Induced Side Effects (Progenics Protocol MNTX 901)

Purdue Pharma L.P. Stamford, CT

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Pilot Study to Evaluate the Analgesic Efficacy of BTDS on Postoperative Pain During Rehabilitation Following Total Knee Arthroplasty (Purdue Pharma Protocol BUP2003)

SkyePharma, Inc. San Diego, CA A Phase 2/3, Multicenter, Randomized, Double-Blind, Dose-Finding and Dose-Confirmations Study to Evaluate the Safety and Efficacy of a Single Epidural Dose of SKY-0401 (Morphine Sulfate Extended-Release Liposome Injection) in the Management of Post-Operative Pain in Pediatric Subjects Undergoing Lower Abdominal (Below the Diaphragm), Genitourinary, or Lower Extremity Orthopedic Surgery (SkyePharma SKY0401-C2-021)

APPENDIX C

CURRENTLY APPROVED (December 31, 2006) RESEARCH STUDIES ON THE TREATMENT OF CONTROLLED SUBSTANCE ABUSE

Investigator or Sponsor

Description or Title of Research Study

Gantt P. Galloway, Pharm.D. CPMC Addiction Pharmacology Research Lab. St. Luke's Hospital, 7th Floor 3555 Cesar Chavez Street San Francisco, CA 94110 A Pilot Trial of Modafinil for Treatment of Methamphetamine Dependence

Alan Gevins, D. Sc. SAM Technology 425 Bush Street San Francisco, CA 94108 Realtime Neural Monitor for Drug Abuse Research

Ari Kalechstein, Ph.D. UCLA Neuropsychiatric Institute 740 Westwood Plaza, A7-172 NPI Los Angeles, CA 90024 Methamphetamine Dependence: Treating Neurocognitive Impairment

Walter Ling, M.D. UCLA ISAP 11075 Santa Monica Blvd. Los Angeles, CA 90025 Optimizing Outcomes Using Suboxone for Opiate Dependence

Walter Ling, M.D. UCLA ISAP 11075 Santa Monica Blvd. Los Angelès, CA 90025 Double-Blind, Placebo-Controlled Trial of Prometa Pharmacotherapy for the Treatment of Methamphetamine Abuse

Thomas F. Newton, M.D. UCLA Neuropsychiatric Institute 740 Westwood Plaza, A7-172 NPI Los Angeles, CA 90024 The Dual Deficit Hypothesis of Stimulant Dependence: An Experiment Assessment in Human Volunteers

Investigator or Sponsor

Description or Title of Research Broksct

Thomas F. Newton, M.D. UCLA Neuropsychiatric Institute 740 Westwood Plaza, A7-172 NPI Los Angeles, CA 90024 Methamphetamine Dependence: A Novel Laboratory Model

National Institute on Drug Abuse Bethesda, Maryland A Two-Phase Randomized Controlled Clinical Trial of Buprenorphine/Naloxone Treatment Plus Individual Drug Counseling for Opiod Analgesic Dependence (NIDA CTN Protocol 0030)

National Institute on Drug Abuse Bethesda, Maryland Starting Treatment with Agonist Replacement Therapies (START) (NIDA CTN Protocol 0027)

National Institute on Drug Abuse Bethesda, Maryland Phase 2, Double-Blind, Placebo-Controlled Trial of Topiramate for the Treatment of Methamphetamine Dependence (NIDA-MDS-Topiramate/meth0001)

National Institute on Drug, Abuse Bethesda, Maryland

Double-Blind, Placebo-Controlled Trial of Bupropion for the Treatment of Methamphetamine Dependence (NIDA Study CTO-0008)

National Institute on Drug Abuse Bethesda, Maryland Single-Blind, Placebo-Controlled Assessment of Potential Interactions Between Intravenous Cocaine, Ethanol and Oral Disulfiram (NIDA Study NIDA-MDS-Disulfiram-001)

Steven Shoptaw, Ph.D.
Semel Inst of Neuroscience & Human Behavior
11075 Santa Monica Blvd.
Los Angeles, CA 90025

A Randomized, Double-Blind, Placebo-Controlled Evaluation of Bupropion vs Placebo for the Treatment of Methamphetamine Dependence

APPENDIX D

SECTIONS CONCERNING THE RESEARCH ADVISORY PANEL FROM THE CALIFORNIA HEALTH AND SAFETY CODE

<u>Sec. 11213.</u> Persons who, under applicable federal laws or regulations, are lawfully entitled to use controlled substances for the purpose of research, instruction, or analysis, may lawfully obtain and use for such purposes such substances as are defined as controlled substances in this division, upon approval for use of such controlled substances in bona fide research, instruction, or analysis by the Research Advisory Panel established pursuant to Sections 11480 and 11481.

Such research, instruction, or analysis shall be carried on only under the auspices of the head of a research project which has been approved by the Research Advisory Panel pursuant to Section 11480 or Section 11481. Complete records of receipts, stocks at hand, and use of these controlled substances shall be kept.

<u>Sec. 11362.9.</u> California Marijuana Research Program; legislative intent; creation; research proposals; establishment; powers and duties; Scientific Advisory Council (In pertinent part)

- (d) If the program is administered by the Regents of the University of California any grant research proposals approved by the program shall also require review and approval by the research advisory panel.
- (f) All personnel involved in implementing approved proposals shall be authorized as required by Section 11604.
- (g) Studies conducted pursuant to this section shall include the greatest amount of new scientific research possible on the medical uses of, and medical hazards associated with, marijuana. The program shall consult with the Research Advisory Panel analogous agencies in other states, and appropriate federal agencies in an attempt to avoid duplicative research and the wasting of research dollars.
- Sec. 11374. Every person who violates or fails to comply with any provisions of this division, except one for which a penalty is otherwise in this division specifically provided, is guilty of a misdemeanor punishable by a fine in a sum not less than thirty dollars (\$30) nor more than five hundred dollars (\$500), or by imprisonment for not less than 15 nor more than 180 days, or by both.
- <u>Sec. 11392.</u> Spores or mycelium capable of producing mushrooms or other material which contains psilocyn or psyoclyin may be lawfully obtained and used for bona fide

research, instruction, or analysis, if not in violation of federal law, and if the research, instruction, or analysis is approved by the Research Advisory Panel established pursuant to Sections 11480 and 11481.

<u>Sec. 11478.</u> Marijuana may be provided by the Attorney General to the heads of research projects which have been registered by the Attorney General, and which have been approved by the Research Advisory Panel pursuant to Section 11480.

The head of the approved research project shall personally receipt for such quantities of marijuana and shall make a record of their disposition. The receipt and record shall be retained by the Attorney General. The head of the approved research project shall also, at intervals and in the manner required by the Research Advisory Panel, report the progress or conclusions of the research project.

<u>Sec. 11480.</u> The Legislature finds that there is a need to encourage further research into the nature and effects of marijuana and hallucinogenic drugs and to coordinate research efforts on such subjects.

There is a Research Advisory Panel which consists of a representative of the State Department of Health Services, a representative of the California State Board of Pharmacy, a representative of the Attorney General, a representative of the University of California who shall be a pharmacologist, a physician, or a person holding a doctorate degree in the health sciences, a representative of a private university in this State who shall be a pharmacologist, a physician, or a person holding a doctorate degree in the health sciences, a representative of a statewide professional medical society in this state who shall be engaged in the private practice of medicine and shall be experienced in treating controlled substance dependency, a representative appointed by and serving at the pleasure of the Governor who shall have experience in drug abuse, cancer, or controlled substance research and who is either a registered nurse, licensed pursuant to Chapter 6 (commencing with Section 2700) of Division 2 of the Business and Professions Code, or other health professional. The Governor shall annually designate the private university and the professional medical society represented on the Panel. Members of the Panel shall be appointed by the heads of the entities to be represented, and they shall serve at the pleasure of the appointing power.

The Panel shall annually select a chairman from among its members.

The Panel may hold hearings on, and in other ways study, research projects concerning marijuana or hallucinogenic drugs in this state. Members of the Panel shall serve without compensation, but shall be reimbursed for any actual and necessary expenses incurred in connection with the performance of their duties.

The Panel may approve research projects, which have been registered by the Attorney General, into the nature and effects of marijuana or hallucinogenic drugs, and shall inform the Attorney General of the head of the approved research projects which are entitled to receive quantities of marijuana pursuant to Section 11478.

The Panel may withdraw approval of a research project at any time, and when approval is withdrawn shall notify the head of the research project to return any quantities of marijuana to the Attorney General.

The Panel shall report annually to the Legislature and the Governor those research projects approved by the Panel, the nature of each research project, and, where available, the conclusions of the research project.

<u>Sec. 11481.</u> The Research Advisory Panel may hold hearings on, and in other ways study, research projects concerning the treatment of abuse of controlled substances.

The Panel may approve research projects, which have been registered by the Attorney General, concerning the treatment of abuse of controlled substances and shall inform the chief of such approval. The Panel may withdraw approval of a research project at any time and when approval is withdrawn shall so notify the chief.

The Panel shall, annually and in the manner determined by the Panel, report to the Legislature and the Governor those research projects approved by the Panel, the nature of each research project, and where available, the conclusions of the research project.

Sec. 11603. The Attorney General, with the approval of the Research Advisory Panel, may authorize persons engaged in research on the use and effects of controlled substances to withhold the names and other identifying characteristics of individuals who are the subjects of the research. Persons who obtain this authorization are not compelled in any civil, criminal, administrative, legislative, or other proceedings to identify the individuals who are the subjects of research for which the authorization was obtained.

<u>Sec. 11604.</u> The Attorney General, with the approval of the Research Advisory Panel, may authorize the possession and distribution of controlled substances by persons engaged in research. Persons who obtain this authorization are exempt from state prosecution for possession and distribution of controlled substances to the extent of the authorization.