FORTY-THIRD ANNUAL REPORT

of the

RESEARCH ADVISORY PANEL OF CALIFORNIA

2013

PREPARED FOR THE

LEGISLATURE AND GOVERNOR

RESEARCH ADVISORY PANEL OF CALIFORNIA
455 Golden Gate Avenue - Suite 11000
San Francisco, California 94102-7004
www.ag.ca.gov/research

TABLE OF CONTENTS

2013 PANEL MEMBERS

RESEARCH ADVISORY PANEL OF CALIFORNIA

Edward P. O'Brien, J.D.
Panel Chairman
Appointed by Attorney General

Y. Jennifer Ahn, Pharm.D.
Executive Officer

Patrick R. Finley, Pharm.D.
Appointed by the State Board of Pharmacy

Andrew S. Kayser, MD, PhD
Appointed by the University of California at San Francisco
Designated University of California

John E. Mendelson, M.D.
Appointed by the California Medical Association
Designated professional medical society

Michele T. Pato, M.D.
Appointed by the University of Southern California
Designated private university

Laurence R. Upjohn, Pharm.D.
Appointed by the Department of Public Health

RAPC Website : www.ag.ca.gov/research

E-mail contact: jennifer.ahn@doj.ca.gov

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.

SUMMARY OF 2013 PANEL ACTIVITIES

During 2013 the Panel reviewed thirty-two research study submissions. Twenty-eight were approved by the Panel. Among twenty-eighty approved studies, ten studies were Academic research studies, nine studies were Substance Abuse Treatment research protocols, and nine studies were Clinical Drug Trial research protocols.

Thirteen research studies were completed or, in a few cases, terminated in 2013, and they were closed on the Panel's records.

At the end of 2013, the Panel was monitoring eighty-nine 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, Significant Adverse Event (SAE) reports and site visits. Approval may be withdrawn if the study deviates significantly from the approved protocol.

Table 1 is a list of the studies approved by the Panel in 2013 and Table 2 is a list of the studies closed by the Panel in 2013.

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 research projects currently ongoing in California:

Alkermes has submitted Annual Progress Report titled "A Phase II Randomized, Multicenter, Safety, Tolerability, and Dose-Ranging Study of Samidorphan, A Component of ALKS3831, in Adults with Schizophrenia Treated with Olanzapine" (ALKS3831-302)

ALKS3831 is composed of two active substance: olanzapine and samidorphan and is under investigation for the treatment of schizophrenia. Olanzapine is FDA-approved for the treatment of schizophrenia and bipolar disorder and is not a controlled substance by the Drug Enforcement Agency (DEA). Samidorphan is a new chemical entity, under developement by Alkermes for the treatment of reward disorders. Samidorphan was classified as a Schedule II substance by the DEA under the Constrolled Substances Act ("CSA") (CSCN 9668).

To date, over 600 subjects have been exposed to samidorphan, either as a single agent, a co-formulation with buprenorphine or co-administered with olanzapine. Samidorphan is prepared from the uncontrolled substance naltrexone and retains the structural features of naltrexone that result in *u*-opioid receptor antagonist activity. This activity likely underlies the effect of samidorphan to block subjective and physiological effects of opioid drugs, as seen in clinical and nonclinical studies. No evidence of withdrawal has been observed after discontinuing samidorphan.

ALKS3831-302 is a Phase II, randomized, placebo-controlled multicenter study, which is being conducted in 2 parts: Part A and Part B. Part A begins with screening and includes a 1-week olanzapine lead-in period followed by a 12 week double-blind, placebo-controlled treatment period where subjects receive samidorphan or placebo (in addition to the olanzapine prescribed on Study Day 1). Part B includes an additional 12-week treatment period where all subjects receive active olanzapine + samidorphan (ie, ALKS3831). At the end of Part B, samidorphan dosing stops, but olanzapine dosing continues uninterrupted through a 4-week follow-up period, which includes 2 safety visits.

Due to the blinded nature of the study, no efficacy results are available at this time. No subjects have died during the course of the study and there were no serious adverse events during the report period.

Dr. Friedbert Weiss, PhD, and colleagues at the Scripps Research Institutes, La Jolla, CA have provided the Panel with the following summary of research titled "Ethanol Seeking and Relapse: Therapeutic Potential of Transdermal Cannabidiol"

Drug addiction is a chronically relapsing disorder. Susceptibility to relapse can be traced to multiple factors including craving elicited by drug-related clules, heightened anxiety and hypersensitivity to stress, as well as drug-induced impairments in impulse control. Thus, treatment drugs that target more than a single factor or vulnerability state for relapse are likely to offer significant clinical advantages. Our findings suggest that cannabidiol (CBD), the main non-psychoactive and non-addictive component of the cannabis sativa plant, my provide such a profile of actions. A factor limiting the therapeutic potential of CBD is the drug's low oral bioavailability in man due to a major first-pass effect. This limitation can be overcome by transdermal administration, which eliminates the first-pass effect and reduces variability in bioavailability. In collaboration with our coinvestigator, Dr. Stinchcomb, we therefore developed a transdermal CBD formulation (tCBD) suitable for behavioral testing in rats, consisting of a fast drying CBD gel applied to a shaved area of skin.

The effects of tCBD were examined in animal models of relapse (cue and stress),

anxiety, and impulsivity. Rats with a history of ethanol or cocaine self-administration were treated with tCBD (15mg/kg) at 24h intervals for 7 days.

tCBD significantly reduced cue-induced reinstatement of ethanol and cocaine seeking, as well as stress-induced reinstatement by yohimbine or electric footshock, without producing tolerance. Remarkably, both stress- and cue-induced reinstatement remained fully attenuated as late as 138 days after termination of tCBD treatment. In tests of anxiety (using the elevated plus maze), all rats showed significantly reduced anxiety-like behavior. To study tCBD's effects on impluse control, rats were subjected to a 7d ethanol intragastric intoxication procedure during which they were treated at 24h intervals with tCBD (15mg/kg). In subsequent delay discounting tests, rats with an intoxication history showed significantly reduced preference for large delated reward indicative of heightened impulsivity. This profile of high impulsivity was fully reversed in tCBD-treated rats. In tests of nonspecific behavioral effects, tCBD neither with reinstatement motivated by a palatable sweet solution, nor altered spontaneous locomotor activity.

Although presently limited to a single dose, the results are consistent with the hypothesis that tCBD has therapeutic potential for multiple vulnerability states underlying relapse risk. Particularly significant was the observation that cue- and stress-induced ethanol seeking remained effectively reduced as late as =5 months (138 days) post-treatment. This observation, paired with the finding that tCBD attenuates impulsivity in rats with a severe ethanol intoxication history, is of substantial interest both from a medication development and neurobiological perspective in that it is suggestive of diverse neuroregulatory actions that restore normal function to brain circuitries regulating reward, incentive motivation, impulsivity, stress and anxiety.

Dr. Walter Ling, M.D. and colleagues at University of California, Los Angeles have provided the Panel with the following summary of research titled "Analgesic Response to Opioid Analgesics in Buprenorphine-Maintained Individuals"

The extensive and detrimental effects of unrelieved pain are well described, with negative physiological and psychological consequences (see Brennan et al., 2007; Leykin et al., 2007). Fortunately, opiates and synthetic opioids provide powerful and effective treatment for pain. Recent national indicators show that rates of prescription opioid abuse have risen dramatically over the past decade (McCabe et al., 2008; NIDA, 2008; SAMHSA, 2009), presenting a pressing need to effectively and safely manage pain in opioid-dependent patients. To effectively treat pain and maximize health outcomes in patients at high risk for poor pain management, clinicians need a more comprehensive understanding of the effects of ongoing opioid use on pain outcomes.

Patients treated with opioids, including buprenorphine, for extended periods may develop physical dependence, and opioid-induced hyperalgesia. Managing acute pain in these patients has been hampered by misunderstanding and misinformation, and by a genuine lack of systematically gathered controlled study data. Many physicians believe that the ceiling effect of buprenorphine makes it a poor analgesic and that patients maintained on buprenorphine will not benefit from the analgesic effects of added opioids, although anecdotal reports from physician experience and observational—largely uncontrolled—data suggest otherwise. There is a dearth of data to provide guidance for clinicians for an evidence-based approach to providing meaningful analgesia using opioids in treating acute pain in buprenorphine-maintained patients.

The favorable clinical safety profile gives buprenorphine considerable latitude in practice settings and in method of medication dispensing and prescribing. Clinicians may have taken advantage of buprenorphine's off-label use to treat a variety of painful conditions. This practice in itself is within the scope of usual and customary clinical practice, but because, at least in the United States, analgesia is not the primary approved indication for buprenorphine, relevant and critical information of such use is rarely available to clinicians.

This project intends to provide information on analgesic responses to single doses of various opioid analgesics, including buprenorphine, in study participants maintained on buprenorphine. Study findings will provide needed data for an empirically based approach to using opioids in managing acute pain in buprenorphine-maintained patients. The study will also collect data related to mu receptor blockade of buprenorphine when combined w additional opioids.

The aim of this study is to examine the effects of opioid analgesics on acute pain in participants maintained on buprenorphine+naloxone (Suboxone) for opioid use disorders.

Study design is a single-blind examination of the analgesic effects of a single dose of seven test medications provided in an experimental pain paradigm using a cold pressor test (CPT). Test medication conditions include buprenorphine, morphine, hydromorphone, hydrocodone, oxycodone, and two placebo conditions to match test medication formulations (oral tablet, sublingual tablet). Each medication condition will be tested on separate days (seven total days, completing within 12 weeks), with random assignment to order of study medications.

Participants will be 12 males, age 20-50, who are currently prescribed buprenorphine maintenance treatment and are under the care of a physician not associated with the study. Presence of buprenorphine and buprenorphine metabolites will be confirmed in baseline urine toxicology tests. Participants must not require regular daily use of any other medications for pain or have any other condition that could interfere with participation, study procedures, or the interpretation of study findings.

After screening, eligible participants will be scheduled for 7 days of testing with test days at least 3 days apart to provide a sufficient medication wash-out period. Pain testing will utilize cold pressor tests (CPT), in which the participant submerges his arm and hand in a bath of ice cold water to determine pain threshold and tolerance. Participants will be given a practice trial to provide familiarity with the test and reduce test anxiety. Two CPTs will occur on each test day, and pre- and post-CPT assessments will be administered. Blood samples will be taken on each test day to measure blood levels of buprenorphine. Daily procedures include: (1) A baseline CPT (BL-CPT), (2) Administration of the test medication (active drug or placebo), (3) CPT administered at the time of maximum drug effect (Tmax-CPT) specific to medication (range 30-120 minutes), (4) Pupillometry conducted at baseline (before BL-CPT), and at time of maximum drug effect (before Tmax-CPT). Each participant will be discharged after clinical determination of the participant's safety and well-being.

TABLE 1

RESEARCH STUDIES
APPROVED IN 2013

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Michael Fischbach, Ph.D. Dept of Anesthesia, UCSF San Francisco, CA	Engineering a human gut bacteria to produce dimethyltryptamine
George Koob, Ph.D. The Scripps Research Institute La Jolla, CA	Prescription Opioid Addiction: Neurobiological Mechanisms
Walter Ling, M.D. Integrated Substance Abuse Programs, UCLA Los Angeles, CA	Analgesic Response to Opioid Analgesics in Buprenorphine-Maintained Individuals
Robert Malenka, M.D. School of Medicine Stanford University Palo Alto, CA	The Role of Oxytocin in the Pathogenesis of Avtism
Florian Rader, M.D. Cedars-Sinai Med Center Los Angeles, CA	Mechanisms and Modulation of Cocaine Effects on Blood Blow to the Heart
Richard Reznichek, M.D. Harbor-UCLA Los Angeles, CA	Panel approved research

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Paolo Sassone-Corsi, Ph.D. Center for Epigenetics UC Irvine Irvine, CA	The Role of Liver CB1 Receptor in Regulation of the Circadian Metabolism
Ronald Victor, M.D. Cedars-Sinai Med Center Los Angeles, CA	Effects of Cocaine on Blood Flow to the Heart
Friedbert Weiss, Ph.D. The Scripps Research Institute La Jolla, CA	Ethanol Seeking and Relapse: Therapeutic Potential of Transdermal Cannabidiol"
Roya Yumul, MD, PhD Cedars-Sinai Med Center Los Angeles, CA	Intraoperative ketamine and methadone for laminectomy: effect on recovery, postoperative pain, and opioid requirements
AcelRx Redwood City, CA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab® PCA System/15 mcg for the Treatment of Post-Operative Pain in Patients after Knee or Hip Replacement Surgery (IAP311)
Alkermes, Inc. Waltham, MA	A Phase 2, Randomized, Multicenter, Safety, Tolerability, and Dose-Ranging Study of Samidorphan, A Component of ALKS 383, in Adults with Schizophrenia Treated with Olanzapine (ALK3831-302)

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
CNS Therapeutics / CRO: Pacific-Link Consulting	A Controlled, Two-Arm Parallel Group, Randomized Withdrawal Study to Assess the Safety and Efficacy of Hydromorphone HCl Delivered by intrathecal Administration a Programmable Implantable Pump (HYD201US)
CNS Therapeutics / CRO: Pacific-Link Consulting	A Phase 3 Open-Label, Single-Arm Study To Assess The Safety of Hydromorphone HCl Delivered by Intrathecal Administration (HYD202US)
Forest Research Institute Jersey City, NJ	A Randomized, Double-Blind, Placebo- and Active-Controlled Study to Evaluate the Safety and Efficacy of GRT6005 in Patients with Moderate tot Severe Chronic Pain Due to Osteoarthritis of the Knee (GRT-MD-101)
GW Pharmaceutics Mill Valley, CA	Panel approved research
MAPS Santa Cruz, CA	A Placebo-Controlled, Randomized, Blinded, Dose Finding Phase 2 Pilot Safety Study of MDMA-Assisted Therapy for Social Anxiety in Autistic Adults (MAA-1)

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Teva Pharmaceuticals Frazer, PA	A 12-week, Randomized, Double-Blind, Placebo-Controlled, R-Withdrawal Study to Evaluate the Efficacy & Safety of Hydrocodone Bitartrate ER Tabs (CEP-33237) at 30-90mg q12 hrs for Relief of Moderate to Severe Pain in Patients with Chronic Low Back Pain Who Require Opioid Treatment for an Extended Period of Time (C33237/3103)
Teva Pharmaceuticals / CRO: RPS Upper Darby, PA	A 6 months, Open-Label, Extension Study to Evaluate the Safety of Hydrocodone Bitartrate ER tabs (CEP-33237) at 15mg-90mg q12h for Relief of Moderate to Severe Pain in Patients with Chronic Low Back Pain Who Require Opioid Treatment for an Extended Period of Time (C33237/3104)
NIDA Rockville, MD	Achieving Cannabis Cessation-Evaluating N-Acetylcysteine Treatment (ACCENT) (CTN-0053)
Courtney Kelly, M.S. UCLA Los Angeles, CA	Effects of Naltrexone on Methamphetamine Cue-Induced Brain Activity in Methamphetamine Dependence

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
US WorldMeds, LLC Louisville, KY	A Phase 3, Randomized, Multicenter, Double-Blind, Placebo-Controlled, Efficacy, Safety, and Dose-Response Study of Lofexidine in the Treatment of Opioid Withdrawal (Days 1-7) Followed by Open-Label, Variable Dose Lofexidine Treatment (Days 8-14) (USWM-LX1-300)
Keith Heinzerling, M.D. UCLA Los Angeles, CA	Randomized Trial of Ibudilast for Methamphetamine Dependence
Lara Ray, Ph.D. UCLA Los Angeles, CA	Effects of Naltrexone on Alcohol-Dependent Asian Americans
Lara Ray, Ph.D. UCLA Los Angeles, CA	Effects of Ibudilast on Non-treatment Seeking Patients Who Meet Criteria for Alcohol Abuse or Dependence
Lara Ray, Ph.D. UCLA Los Angeles, CA	Effects of Ivermectin on Non-Treatment Seeking Patients Who Meet Criteria for Alcohol Abuse or Dependence
NIDA Rockville, MD	Accelerated Development of Additive Pharmacotherapy (ADAPT) (CNS Protocol 0054)

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Teva Pharmaceuticals Frazer, PA	A 12 week, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy & Safety of 1-week IM Injection of TV-1380 (150mg/wk or 300mg/wk) as a Treatment for Facilitation of Abstinence in Cocaine-Dependent Subjects (TV1380-COA-20)

TABLE 2

RESEARCH STUDIES CLOSED IN 2013

Sponsor / PI	Title of Study / Clinical Drug Trial Protocol
Valerie Gruber, Ph.D. UCSF / SF General Hospital San Francisco, CA	Investigation of Age Differences in Analgesic, Cognitive, and subjective effects of Oxycodone, Hydrocodone, and Acetaminophen
Reese Jones, M.D. Drug Dependence Research Ct. UCSF San Francisco, CA	Phase I Study of Interactions between Oral Naltrexone and Bupripion and Intravenous Methamphetamine in Mathamphetamine Experienced Volunteers
Edith London, Ph.D. UCLA Los Angeles, CA	A Study to Assess the Cardiovascular, Cognitive, and Subjective Effects of Atomoxetine in Combination with Intravenous Amphetamine
Richard Reznichek, M.D. Harbor-UCLA Medical Center Torrance, CA	Panel approved research
Acel Rx Redwood City, CA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab® PCA System/15 mcg for the Treatment of Post-Operative Pain in Patients after Knee or Hip Replacement Surgery (IAP311)

Table 2 Cont.

Sponsor / PI	Title of Study / Clinical Drug Trial Protocol
Alkermes, Inc. Waltham, MA	A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate ALKS 5461 in Subjects with Major Depressive Disorder and Inadequate Responses to Antidepressant Therapy (ALKS5461-202)
Noven / CRO: PRA Lenexa, KS	A Randomized, DB, PC, Cross-Over, Lab Classroom Study to Evaluate the Safety & Efficacy of d-Amphetamine Transdermal Drug Delivery System (d-ATS) Compared to Placebo in Children & Adolescents w ADHD (N25-006)
Noven Pharmaceuticals New York, NY	An Investigational Study to Evaluate the Usability of Reformulated Methylphenidate Transdermal System in Children, Adolescents and Adults with ADHD and Caregivers (N17-030)
Purdue / CRO: PRA Raleigh, NC	A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial with an Enriched Study Design to Assess the Efficacy & Safety of Oxycodone/Naloxone C-R Tabs (OXN) Compared to Placebo in Opioid-experienced Subjects with Moderate to Severe Pain due to Chronic Low Back Pain who Require A-T-C Opioid Therapy (ONU3701)

Table 2 Cont.

Sponsor / PI	Title of Study / Clinical Drug Trial Protocol
Shire / CRO: INC Research Cincinnati, OH	A Phase 3 Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, 25-week, DO Study to Eval the Efficacy, Safety, & Tolerability of SPD489 Low Dose Range 40 80 100mg & Hi Dose Range 120 140 160mg as Adj Treatment to Establish Mt Doses of Antipsychotic Medications on Neg Symptoms in Clinically Stable Adults with Persistant Predominant Neg Symptoms of Schizophrenia (SPD489-335)
Shire / CRO: INC Research Cincinnati, OH	A Phase 3 LT, Open-Label, Multicenter, 52-week Flex-D Safety Study of SPD489 as Adj Treatment of Establish Maintenant Dose of Antipsychotic Medications on Neg Symptoms in Clinically Stable Adults with Persistent Pred Neg Symptoms of Schizophrenia (SPD489-336)
Shire / CRO: INC Research Cincinnati, OH	A Phase 3 Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled 12-wk, Forc-D Tat Study to Evaluate the Efficacy, Safety, & Tolerability of SPD489 40 100 or 160mg as Adj Treatment to Establish Maintenant Dose of Antipsychotic Medications on Neg Symptoms in Clinically Stable Adults with Persistent Pred Neg Symptoms of Schizophrenia (SPD489-338)

Table 2 Cont.

Sponsor / PI	Title of Study / Clinical Drug Trial Protocol
Shire Pharmaceuticals Wayne, PA	A Phase 3b, Double-blind, Randomized, Active-controlled, Parallel-group Study to Compare the Time to Response of Lisdexamfetamine to Atomoxetine in Children & Adolescents aged 6-17 with ADHD who have had an Inadequate Response to Methylphenidate Therapy (SPD489-317)

APPENDIX A

CURRENTLY OPEN *(through December 31, 2013)*
SCHEDULE I AND SCHEDULE II
NON-HUMAN AND ACADEMIC HUMAN
RESEARCH STUDIES

Principal Investigator	Title of Study
Mark A. Agius, M.D. UC. Davis Davis, CA	Cannabis for Spasticity in MS: Placebo-Controlled Study
Philip E. Bickler, MD, PhD Dept of Anesthesia, UCSF San Francisco, CA	Detecting Apnea in Healthy Volunteers Receiving Opiate or Sedative Medications
John R. Cashman, Ph.D. Human BioMolecular Research Institute San Diego, CA	Molecular Evolution of Human Cocaine Catalysis
Kent S. Chu, Ph.D. YJ Bio-Products Cordova, CA	Immunochromatographic Test Device for THC and LSD
Laura Colin Biostride, Inc. Redwood City, CA	Panel Approved Research
Michael Fischbach UCSF San Francisco, CA	Engineering a human gut bacteria to produce dimethyltryptamine
Mark A. Geyer, Ph.D. Dept of Psychiatry, UCSD La Jolla, CA	Behavioral and Cytoflourimetric Studies of Psychoactive Drugs in Rats

Appendix A Cont.

Principal Investigator	Title of Study
Kanthi Hettiarachchi, Ph.D. SRI International Menlo Park, CA	Analysis of Controlled Substances
Thomas S. Kilduff, Ph.D. SRI International Menlo Park, CA	Neurobiological Studies of Gammahydroxybutyrate (GHB)
George Koob, Ph.D. The Scripps Research Institute La Jolla, CA	Prescription Opioid Addiction: Neurobiological Mechanisms
Adam Leventhal, Ph.D. USC Keck School of Medicine Alhambra, CA	Influence of Genes and Emotions on medication Effects
Daniel Levin, Ph.D. NORAC Pharma Azusa, CA	Panel Approved Research
Daniel Levin, Ph.D. NORAC Pharma Azusa, CA	Panel Approved Research
Daniel Levin, Ph.D. NORAC Pharma Azusa, CA	Panel Approved Research
Marie Lin, Ph.D. R.Ph. Lin-Zhi International, Inc. Sunnyvale, CA	Lin-Zhi Immunoassay Development Study

Principal Investigator	Title of Study
Walter Ling, M.D. Integrated Substance Abuse Programs, UCLA Los Angeles, CA	Analgesic Response to Opioid Analgesics in Buprenorphine-Maintained Individuals
Sean Mackey, MD, PhD Stanford University Palo Alto, CA	Neural and Immune Effects of Short-term Opioid Use in Chronic Pain Patients
Robert Malenka, M.D. School of Medicine Stanford University Palo Alto, CA	The Role of Oxytocin in the Pathogenesis of Avtism
Sean D. McAllister, Ph.D. CPMC Research Institute San Francisco, CA	Panel Approved Research Project
Ardis Moe, Ph.D. UCLA Center for AIDS Research Los Angeles, CA	Phase III, Placebo-Controlled, Double-Blind Crossover Study of Slow-Release Methylphenidate (Concerta ™) for Treatment of HIV Dementia
Florian Rader, M.D. Cedars-Sinai Med Center Los Angeles, CA	Mechanisms and Modulation of Cocaine Effects on Blood Blow to the Heart
Richard Reznichek, M.D. Harbor-UCLA Los Angeles, CA	Panel approved research

Appendix A Cont.

Principal Investigator	Title of Study
Rajkumar J. Sevak, Ph.D. UCLA Los Angeles, CA	Human Methamphetamine Self-Administration in a Progressive-Ratio Paradigm
Rajkumar J. Sevak, Ph.D. UCLA Los Angeles, CA	Safety and Initial Efficacy of Lisdexamfetamine for Modifying the Behavioral Effects of Intravenous Methamphetamine in Humans
Matthew L. Springer, Ph.D. UCSF San Francisco, CA	Assessment of Impairment of Vascular Function in Rats by Environmental Exposure to Marijuana Second Hand Smoke
Raymond Stevens, Ph.D. The Scripps Research Institute La Jolla, CA	Structure Determination of the Hallucinogens LSD and Psylocin Bound to the Serotonin Receptor 5-HT2B
Paolo Sassone-Corsi, Ph.D. Center for Epigenetics UC Irvine Irvine, CA	The Role of Liver CB1 Receptor in Regulation of the Circadian Metabolism
Michael Taffe, Ph.D. The Scripps Research Institute La Jolla, CA	Behavioral Toxicities of amphetamine and cathinone stimulant drugs
Michael Taffe, Ph.D. The Scripps Research Institute La Jolla, CA	Behavioral toxicities of amphetamine and cathinone stimulant drugs

Principal Investigator	Title of Study
Michael Taffe, Ph.D. The Scripps Research Institute La Jolla, CA	Behavioral and Physiological Toxicities of Cannabinoids: Effects of Cannabidiol
Stephen Van Dien, Ph.D. Genomatica, Inc. San Diego, CA	Panel Approved Research Project
Ronald Victor, M.D. Cedars-Sinai Med Center Los Angeles, CA	Effects of Cocaine on Blood Flow to the Heart
Friedbert Weiss, Ph.D. The Scripps Research Institute La Jolla, CA	Ethanol Seeking and Relapse: Therapeutic Potential of Transdermal Cannabidiol"
Jennifer L. Whistler, Ph.D. Ernest Gallo Clinic & Research Ct. Emeryville, CA	Endocytosis and Opioid Receptors
Timothy Wigal, Ph.D. UC Irvine Irvine, CA	Brain Dopamine Function in Adults with Attention Deficit/Hyperactivity Disorder (ADHD)
Barth Wilsey, M.D. UC Davis Medical Center Sacramento, CA	The Effect of Vaporized Cannabis on Neuropathic Pain in Spinal Cord Injury
Roya Yumul, MD, PhD Cedars-Sinai Med Center Los Angeles, CA	Intraoperative ketamine and methadone for laminectomy: effect on recovery, postoperative pain, and opioid requirements

APPENDIX B

CURRENTLY OPEN *(through December 31, 2013)*
SCHEDULE II CLINICAL DRUG TRIAL STUDIES

Sponsor	Description or Title of Clinical Drug Trial Protocol
AcelRx Redwood City, CA	A Multicenter, Randomazied, Open-Label, Parrell-Group Trial to Compare the Efficacy & Safety of the Sufentanil Nano Tab PCA System 15 mcg to Intravenous Patient-Controlled Analgesia with Morphine for the Treatment of Post-Operative Pain (IAP309)
AcelRx Redwood City, CA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab for the Management of Acute Pain Following Bunionectomy Alone or with Hammertoe Repair (SAP202)
AcelRx Redwood City, CA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab PCA System/15 mcg for the Treatment of Post-Operative in Patients after Open Abdominal Surgery (IAP310)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
AcelRx Redwood City, CA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab® PCA System/15 mcg for the Treatment of Post-Operative Pain in Patients after Knee or Hip Replacement Surgery (IAP311)
Alkermes, Inc. Waltham, MA	A Phase 2, Randomized, Multicenter, Safety, Tolerability, and Dose-Ranging Study of Samidorphan, A Component of ALKS 383, in Adults with Schizophrenia Treated with Olanzapine (ALK3831-302)
Astra Zenica / CRO - Quintiles Overland Park, KS	A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of NKTR-118 in Relieving Opioid-Induced Constipation (OIC) in Patients with Cancer-Related Pain (D3820C00006)
Astra Zenica / CRO - Quintiles Overland Park, KS	A Randomized, Double-Blind, Placebo-Controlled 12-Week Extension Study to Assess the Safety and Tolerability of NKTR-118 in Patients with Non-Cancer-Related Pain and Opioid-Induced Constipation (OIC) (D3820C00007)

Sponsor	Description or Title of Clinical Drug Trial Protocol
Astra Zenica / CRO - Quintiles Overland Park, KS	An Open-Label 52 week Study to Assess the Long-Term Safety of NKTR-118 in Opioid-Induced Constipation (OIC) in Patients with Non-Cancer-Related Pain (D3820C00008)
Astra Zenica / CRO - Quintiles Overland Park, KS	An Open-label, Parallel-group, Phase I Study to Compare the Pharmacokinetics of NKTR-118 Following a Single-Oral Dose in Subjects with Renal Impairment and Subjects with Normal Renal Function (D3820C00009)
CNS Therapeutics / CRO: Pacific-Link Consulting	A Controlled, Two-Arm Parallel Group, Randomized Withdrawal Study to Assess the Safety and Efficacy of Hydromorphone HCl Delivered by intrathecal Administration a Programmable Implantable Pump (HYD201US)
CNS Therapeutics / CRO: Pacific-Link Consulting	A Phase 3 Open-Label, Single-Arm Study To Assess The Safety of Hydromorphone HCl Delivered by Intrathecal Administration (HYD202US)
Forest Research Institute Jersey City, NJ	A Randomized, Double-Blind, Placebo- and Active-Controlled Study to Evaluate the Safety and Efficacy of GRT6005 in Patients with Moderate tot Severe Chronic Pain Due to Osteoarthritis of the Knee (GRT-MD-101)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
GW Pharmaceutics Mill Valley, CA	Panel approved research
GW Pharmaceutics Mill Valley, CA	Panel approved research
GW Pharmaceuticals Milly Valley, CA	Panel Approved Research Project
GW Pharmaceuticals Mill Valley, CA	Panel Approved Research Project
INTRuST Clinical Consortium La Jolla, CA	Randomized Controlled Trial of Galantamine, Methylphenidate, and Placebo for the Treatment of Cognitive Symptoms in Patients with Mild Traumatic Brain Injury (mTBI) and/or Posttraumatic Stress Disorder (PISD) ["Cognitive REmediation After Trauma Exposure" Trial = CREATE Trial"]
MAPS Santa Cruz, CA	A Placebo-Controlled, Randomized, Blinded, Dose Finding Phase 2 Pilot Safety Study of MDMA-Assisted Therapy for Social Anxiety in Autistic Adults (MAA-1)

Sponsor	Description or Title of Clinical Drug Trial Protocol
Mitsubishi / CRO-Quintiles Overland Park, KS	A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Fixed-Dose, Parallel-Group, Multicenter, Efficacy, and Safety Study of MT-9938 for Treatment of Uremic Pruritus in Subjects with End-Stage Renal Disease Receiving Hemodialysis (MT-9938-01)
Nektar San Francisco, CA	A Phase 2, Enriched-Enrollment, Randomized-Withdrawal, DB, PC, MC Study to Assess the Efficacy, Tolerability, & Safety of NKTR-181 in Opioid-Naïve Subjects w Mod to Sev Chr Pain Due to Osteoarthritis of the Knee (12-181-04)
Pfizer Inc. New York, NY	An Investigational Study to Evaluate the Usability of Reformulated Methylphenidate Transdermal System in Children, Adolescents and Adults with ADHD and Caregivers (B4531002)
Purdue / CRO-INC Research Raleigh, NC	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study with an Open-Label Run-in to Assess the Efficacy & Safety of Hydrocodone Bitartrate (HYD) Tabletss 20 to 120 mg Once-day in Subjects with Moderate to Severe Chronic Low Back Pain (HYD3002)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
Purdue / CRO-INC Research Raleigh, NC	A Randomized, Double-blind, Placebo-controlled, Multicenter Trial with an Enriched Study Design to Assess the Efficacy and Safety of Oxycodone/Naloxone Controlled-release Tablets (OXN) Compared to Placebo in Opioid-experienced Subjects with Moderate to Severe Pain due to Chronic Low Back Pain who Require Around-the-clock Opioid Therapy (ONU3701)
Purdue / CRO-Quintiles Overland Park, KS	A Randomized, Double-blind, Double-dummy, Placebo-controlled, Active-controlled, Parallel-group, Multicenter Trial of Oxycodone Naloxone Controlled-release Tablets (OXN) to Assess the Analgesic Efficacy (Compared to Placebo) and the Management of Opioid-induced Constipation (Compared to Oxycodone Controlled-release Tablets (OXY) in Opioid-experienced Subjects with Uncontrolled Moderate to Severe Chronic Low Back Pain and a History of Opioid-induced Constipation who Require Around-the-clock Opioid Therapy (ONU3704)

Sponsor	Description or Title of Clinical Drug Trial Protocol
Purdue / CRO-Quintiles Overland Park, KS	A Randomized, Double-Blind, DD, Placebo-controlled, AC, Parallel-Group, Multicenter Trial of OXN to Assess the Analgesic Efficacy (Compare to Placebo) and the management of Opioid-induced Const (Compare to OXY) in Opioid-exp Sub with Cont Moderate to Severe Chronic Low Back Pain and a History of Opioid-induced Const with Req ATC Opioid Therapy (ONU3705)
Purdue / CRO-INC Research Raleigh, NC	An Open-label, Multicenter Study to Assess the Long-Term Safety of Hydrocodone Bitartrate (HYD) Tablets 20 to 120 mg Once-daily in Subjects with Moderate to Severe Chronic Non-malignant and Non-neuropathic Pain (HYD3003)
Purdue / CRO-PRA Charlottesville, VA	An Open-label, Extension Study to Assess the Long-Term Safety of Twice Daily Oxycodone Hydrochloride Controlled-release Tablets in Opioid Experienced Children Who Completed the OTR3001 Study (OTR3002)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
QrxPharma / CRO-INC Austin, TX	A Double-Blind, Randomized, Placebo, & Active-Controlled, Parallel-Group Study to Evaluate the Safety, Tolerability & Efficacy of Q8011 Compared to OxyContin & Placebo in Patients with Moderate to Severe Chronic Hip or Knew with Pain Due to Osteoarthritis (Q8011-201)
Shire / CRO - ICON Brentwood, TN	Phase 3, Multicenter, Randomized, Double-blind, Parallel-group, Placebo-controlled, Flexible Dose Titration, Efficacy and Safety Study of SPD489 in Combination with an Antidepressant in the Treatment of Adults with Major Depressive Disorder with Inadequate Response to Prospective Treatment with an Antidepressant (SPD489-323)
Shire Pharmaceuticals Wayne, PA	A Phase 2, Multicenter, Double-blind, Parallel-group, Randomized, Placebo-controlled, Forced-dose Titration, Dose-ranging Efficacy and Safety Study of SPD489 in Combination with an Antidepressant in the Treatment of Adults with Major Depressive Disorder with Inadequate Response to Prospective Treatment with an Antidepressant (SPD 489-209)

Sponsor	Description or Title of Clinical Drug Trial Protocol
Shire / CRO-Premier Research Group Alexander, NC	A Phase 3, Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose-Optimization Study to Evaluate the Efficacy, Safety, and Tolerability of SPD489 in Adults Aged 18-55 Years with Moderate to Severe Binge Eating Disorder (SPD489-344)
Shire / CRO-ICON Brentwood, TN	Phase 3, Open-label, Multicenter, 12-month Extension Safety and Tolerability Study of SPD489 in Combination with an Antidepressant in the Treatment of Adults with Major Depressive Disorder with Residual Symptoms or Inadequate Response Following Treatment with an Antidepressant (SPD489-329)
Shire / CRO-Premier Research Group Alexander, NC	A Phase 3, Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose-Optimization Study to Evaluate the Efficacy, Safety, and Tolerability of SPD489 in Adults Aged 18-55 Years with Moderate to Severe Binge Eating Disorder (SPD489-343)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
Shire Pharmaceuticals Wayne, PA	A Phase 3b, Double-Blind, Randomized, Active-Controlled, Parallel-Group Study to Compare the Time to Response of Lisdexamfetamine to Atomoxetine in Children and Adolescents Aged 6-17 with ADHD who have had an Inadequate Response to Methylphenidate Therapy (SPD489-317)
Sunovion / CRO: INC Research Seattle, WA	A Randomized, Double-Blind, Parallel-Group, Multicenter Efficacy and Safety Study of SEP-225289 Versus Placebo in Adults with ADHD (SEP360-20)
Teva Pharmaceuticals Frazer, PA	A 12-week, Randomized, Double-Blind, Placebo-Controlled, R-Withdrawal Study to Evaluate the Efficacy & Safety of Hydrocodone Bitartrate ER Tabs (CEP-33237) at 30-90mg q12 hrs for Relief of Moderate to Severe Pain in Patients with Chronic Low Back Pain Who Require Opioid Treatment for an Extended Period of Time (C33237/3103)
Teva Pharmaceuticals / CRO: RPS Upper Darby, PA	A 6 months, Open-Label, Extension Study to Evaluate the Safety of Hydrocodone Bitartrate ER tabs (CEP-33237) at 15mg-90mg q12h for Relief of Moderate to Severe Pain in Patients with Chronic Low Back Pain Who Require Opioid Treatment for an Extended Period of Time (C33237/3104)

APPENDIX C

CURRENTLY OPEN *(December 31, 2013)*
RESEARCH STUDIES
ON THE TREATMENT OF CONTROLLED SUBSTANCE ABUSE

Investigator or Sponsor	Description or Title of Research Study
Gantt P. Galloway, Pharm.D. APRL/CPMC Research Institute San Francisco, CA	A Dose Ranging Study of Modafinil for Methamphetamine Dependence
Liza Gorgon NIDA Bethesda, MD	Phase 2, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Trial of Nepicastat for Cocaine Dependence (CS#1031)
Walter Ling, M.D. UCLA ISAP Los Angeles, CA	Sustained-Release Methylphenidate for management of Methamphetamine Dependence
Edythe London, Ph.D. Semel Institute, UCLA Los Angeles, CA	Safety and Initial Efficacy of Buspirone for Methamphetamine Dependence
Steven Shoptaw, Ph.D. UCLA. Los Angeles, CA	Phase I Safety Interaction Trial of Ibudilast with Methamphetamine

Appendix C Cont.

Investigator or Sponsor	Description or Title of Research Study
Steven Shoptaw, Ph.D. UCLA. Los Angeles, CA	Varenicline for Methamphetamine Dependence
Douglas Winship Catalyst Coral Gables, FI	Vigabatrin for Treatment of Cocaine Dependence: A Phase II Study Multi-Center Drug Trial

APPENDIX D

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

§ 11213. 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 § 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 § 11480 or § 11481. Complete records of receipts, stocks at hand, and use of these controlled substances shall be kept.

§ 11480. 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 § 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.

§ 11480. Cont.

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 § 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.

§ 11481. 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.

§ 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.

§ 11604. 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.

§ 24172. Experimental subject's bill of rights; contents

As used in the chapter, "experimental subject's bill of rights," means a list of the rights of a subject in a medical experiment, written in a language in which the subject is fluent. Except as otherwise provided in § 24175, this list shall include, but not be limited to the subject's right to:

(a) Be informed of the nature and purpose of the experiment.

(b) Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

(c) Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

(d) Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

(e) Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

(f) Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

(g) Be given an opportunity to ask any questions concerning the experiment or the procedures involved.

(h) Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

§ 24172. Cont.

(i) Be given a copy of the signed and dated written consent form as provided for by § 24173 or § 24178.

(j) Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

§ 24173. Informed consent

As used in this chapter, "informed consent" means the authorization given pursuant to § 24175 to have a medical experiment performed after each of the following conditions have been satisfied:

(a) The subject or subject's conservator or guardian, or other representative, as specified in § 24175, is provided with a copy of the experimental subject's bill of rights, prior to consenting to participate in any medical experiment, containing all the information required by § 24172, and the copy is signed and dated by the subject or the subject's conservator or guardian, or other representative, as specified in § 24175.

(b) A written consent form is signed and dated by the subject or the subject's conservator or guardian, or other representative, as specified in § 24175.

(c) The subject or subject's conservator or guardian, or other representative, as specified in § 24175, is informed both verbally and within the written consent form, in nontechnical terms and in a language in which the subject or the subject's conservator or guardian, or other representative, as specified in § 24175, is fluent, of the following facts of the proposed medical experiment, which might influence the decision to undergo the experiment, including, but not limited to:

(1) An explanation of the procedures to be followed in the medical experiment and any drug or device to be utilized, including the purposes of the procedures, drugs, or devices. If a placebo is to be administered or dispensed to a portion of the subjects involved in a medical experiment, all subjects of the experiment shall be informed of that fact; however, they need not be informed as to whether they will actually be administered or dispensed a placebo.

§ 24173. Cont.

(2) A description of any attendant discomfort and risks to the subject reasonably to be expected.

(3) An explanation of any benefits to the subject reasonably to be expected, if applicable.

(4) A disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.

(5) An estimate of the expected recovery time of the subject after the experiment.

(6) An offer to answer any inquiries concerning the experiment or the procedures involved.

(7) An instruction to the subject that he or she is free to withdraw his or her prior consent to the medical experiment and discontinue participation in the medical experiment at any time, without prejudice to the subject.

(8) The name, institutional affiliation, if any, and address of the person or persons actually performing and primarily responsible for the conduct of the experiment.

(9) The name of the sponsor or funding source, if any, or manufacturer if the experiment involves a drug or device, and the organization, if any, under whose general aegis the experiment is being conducted.

(10) The name, address, and phone number of an impartial third party, not associated with the experiment, to whom the subject may address complaints about the experiment.

(11) The material financial stake or interest, if any, that the investigator or research institution has in the outcome of the medical experiment. For purposes of this section, "material" means ten thousand dollars ($10,000) or more in securities or other assets valued at the date of disclosure, or in relevant cumulative salary or other income, regardless of when it is earned or expected to be earned.

§ 24173. Cont.

(d) The written consent form is signed and dated by any person other than the subject or the conservator or guardian, or other representative of the subject, as specified in § 24175, who can attest that the requirements for informed consent to the medical experiment have been satisfied.

(e) Consent is voluntary and freely given by the human subject or the conservator or guardian, or other representative, as specified by § 24175, without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence.