FORTY-FIFTH ANNUAL REPORT

of the

RESEARCH ADVISORY PANEL OF CALIFORNIA

2015

PREPARED FOR THE

LEGISLATURE AND GOVERNOR

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

TABLE OF CONTENTS

2015 PANEL MEMBERS

RESEARCH ADVISORY PANEL OF CALIFORNIA

The Research Advisory Panel of California (RAPC) consists of the Panel chairman, Executive officer, and the Panel members.

Edward P. O'Brien, J.D.
Deputy Attorney General IV, State of California AG's Office, San Francisco
Panel Chairman, Appointed by the State of California Attorney General

Y. Jennifer Ahn, Pharm.D.
Executive Officer
Appointed by the State of California Attorney General

David A. Baron, DO, MSEd
Asst Dean, USC Keck School of Medicine
Appointed by the University of Southern California

Chwen-Yuen Angie Chen, MD, FACP
Clinical Assistant Professor, Stanford University School of Medicine
Appointed by the California Medical Association (CMA)

Patrick R. Finley, Pharm.D.
Professor of Clinical Pharmacy, UCSF School of Pharmacy
Appointed by the California State Board of Pharmacy

Andrew S. Kayser, MD, PhD
Assistant Professor of Neurology, UCSF School of Medicine
Appointed by the University of California

Anna Lembke, M.D.
Assistant Professor of Psychiatry, Stanford University School of Medicine
Appointed by Governor Brown

Laurence R. Upjohn, Pharm.D.
Chief, Science and Education Section, CA Dept of Public Health, Food and Drug Branch
Appointed by the State of California Department of Public Health

RAPC Website : oag.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 2015 PANEL ACTIVITIES

During 2015 the Panel reviewed forty-five research study submissions. Forty-three were approved by the Panel. Among the approved studies, fourteen studies were Academic research studies, two studies were Substance Abuse Treatment research studies, and twenty-seven studies were Multi-Center Clinical Drug Trial research studies.

Thirteen research studies were completed or, in a few cases, terminated in 2014, and they were closed on the Panel's records.

At the end of 2015 the Panel was monitoring one hundred and twenty-one 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 2015 and Table 2 is a list of the studies closed by the Panel in 2015.

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:

Dr. Barth Wilsey, M.D. and colleagues at University of California Davis Medical Center, Department of Physical Medicine and Rehabilitation have provided the Panel with the following summary of research titled "A Randomized, Cross-Over Controlled Trial of Dronabinol and Vaporized Cannabis in Neuropathic Low Back Pain ".

Our primary objective is to assess whether treatment with vaporized whole plant cannabis or oral Δ9-THC reduces spontaneous and evoked pain more than placebo, and whether there are differences between the two active treatments in terms of interference with activities of daily living. The primary outcome will be measured using self-reported average numerical pain intensity during the past 24 hours. A secondary outcome measure will be level of use of breakthrough pain medication. To determine if whole plant cannabis or oral Δ9-THC have a more general analgesic effect above and

beyond medication induced changes in subjective pain intensity, pain tolerance and sensitivity will be experimentally induced using the cold pressor test (evoked pain). The secondary outcome measure of pain interference will be measured from the Repeated Measures Recommended Minimal Dataset (NIH Task Force on chronic low back pain).

Our secondary objective is to examine the effects of vaporized whole plant cannabis and oral Δ-THC (dronabinol) on mood, neuropsychological function, and psychomimetic side-effects (high, stoned, etc.) compared to placebo and to each other. The secondary outcome mood will be determined using the Profile of Mood States. The secondary outcome measures of attention, verbal learning and fine motor coordination will be determined using the Digit Symbol test, the Hopkins Verbal Learning Test, and the Grooved Pegboard Test, respectively.

Our tertiary objective is to examine the acute effects (after receiving stable treatment for 4 weeks) of vaporized whole plant cannabis and oral Δ-THC compared to placebo and each other on driving skills. Using a driving simulator, we will examine the effects of treatment on driving performance, as well as the rate at which the effects dissipate over time. We will verify the recommendation that patients who use medicinal cannabis should wait at least three to four hours before driving. This will be evaluated, for the first time, in a cohort of patients who have been treated for a month (rather than in a group of novice or recreational users). It will also be the first time that driving simulation is studied in patients taking oral Δ-THC.

The present proposal builds upon previous work funded by the University of California Center for Medicinal Cannabis Research (CMCR). In our first study, thirty-eight patients with a heterogeneous collection of neuropathic pain conditions (e.g., spinal cord injury pain, central post-stroke pain, peripheral neuropathy, post-herpetic neuralgia, and complex regional pain syndrome) resistant to standard pharmacologic treatments were recruited 32. Subjects underwent a standardized procedure for smoking high dose (7% Δ-THC), medium dose (3.5% Δ-THC), or placebo Δ-THC while continuing to use their regularly prescribed treatments. A mixed linear model demonstrated an equivalent analgesic response to smoking cannabis with both the high and medium doses. Psychoactive effects were minimal and well-tolerated, with some acute cognitive effects, particularly with memory, at the high dose (7% Δ-THC)

The present study is designed to evaluate whether or not the medium dose of cannabis (3.5%) can maintain an analgesic response over an eight week period. In addition, a direct comparison of this vaporized preparation will be made with dronabinol and placebo.

Dr. Robert C. Malenka, MD, PhD and colleagues at Stanford University, School of Medicine have submitted Annual Progress Report titled "The Role of Oxytocin in the Pathogenesis of Autism".

As described in our initial protocol application, we aim to define the pathogenesis of social dysfunction in autistic spectrum disorders (ASDs) using an array of mouse models. Genetic ASD syndromes in humans, when modeled in mice, give us some

insight into abnormal social behavior. However, acute MDMA administration is entirely unique in its ability to promote pro-social and empathic behavior in humans, potentially pointing to therapeutic avenues for human ASDs. In the course of our studies, we have identified assays of mouse social behavior reflecting these pro-social, "affiliative" human behaviors, specifically we are using a previously validated three-chamber social interaction test, wherein mice prefer to spend time with a confined mouse over spending time with a similar confining enclosure without a mouse. We have found a statistically significant enhancement of sociability with this assay at an MDMA dose of 7.5mg/kg, which has minimal effects on locomotor activation, and does not possess strong rewarding properties *per se*.

In the past year, we have extended these results by examining the molecular mechanism of this MDMA effect. We have found an important role for the serotonin transporter, SERT, as well as receptor for oxytocin. We have identified the nucleus accumbens as an important brain area mediating MDMA's pro-social effect, and have done preliminary electrophysiological experiments to define MDMA's effect on synaptic function in this brain area.

In the coming year, we will assess the role of other brain areas and of specific serotonin receptors in mediating MDMA's pro-social effect. These experiments will take advantage of my lab's expertise with transgenic mice and viral-mediated gene transfer.

Dr. Steven Shoptaw, M.D. and colleagues at University of California, Los Angeles have submitted Annual Progress Report titled "Phase I Safety Interaction Trial of Ibudilast with Methamphetamine".

Summary and Findings: As detailed in the last annual report submitted 23 Feb 2015, enrollment to this trial has been completed, all subjects have completed study procedures, and research activities are limited to data analysis. This phase 1 study aimed to recruit and enroll 12 non-treatment seeking methamphetamine dependent research participants when recruitment opened in February 2011. Of the 110 subjects consented to the trial, 18 were eligible for study participation. Screen failures were primarily due to medical or psychiatric ineligibility. Of the 18 eligible, 11 participants were admitted to the hospital and completed all inpatient procedures; 4 participants were admitted to the hospital, randomized, and withdrew; 3 participants were admitted to the hospital and withdrew pre-randomization. All 4 of the non-completers voluntarily withdrew from the study stating unwillingness to remain in the unit for 27 days and none withdrew due to study related adverse events. One participant who completed the inpatient component did not complete the 14-day follow up. Nine of the completed subjects are male; two are female. Both female completers are white. Study completers are approximately 43 years old. Three of the four female subjects who terminated early are white, the other Native Hawaiian/Other Pacific Islander. Their ages are 27, 33, 35, and 27 years old. Of the three males who terminated early, two are white, one is Hispanic. Their ages are 28, 52 and 50. Demographic characteristics of the 11 completers are summarized in Table 1.
Eleven non-treatment seeking methamphetamine dependent volunteers resided in a

research facility for 27 days and nights during which they received infusions with methamphetamine (0 mg, 15mg, and 30 mg) under placebo, ibudilast 20 mg BID, and ibudilast 50 mg BID conditions using a randomized double-blind, placebo-controlled within-subjects crossover design. Participants were randomly assigned to medication dosing order (placebo, ibudilast 20 mg BID, ibudilast 50 mg BID versus ibudilast 20 mg BID, ibudilast 50 mg BID, placebo) in a counter-balanced fashion.

Aim 1: To determine whether ibudilast (20 mg BID or 50 mg BID) alters the cardiovascular response to IV methamphetamine. As described in the previous annual report submitted on 23 Feb 2015, mean changes in heart rate and blood pressure following saline or methamphetamine infusion with both doses of ibudilast and placebo were measured, shown in Figure 1. Using a linear regression model controlling for age, gender, study day, and baseline methamphetamine use, methamphetamine infusion was associated with increased heart rate, systolic blood pressure, and diastolic blood pressure, with a higher methamphetamine dose (30 mg vs. 15 mg) associated with greater increases in all 3 cardiovascular measures ($p < 0.001$.) There was no statistically significant main effect of ibudilast at either dose on mean change in heart rate ($p = 0.76$ for ibudilast 20 mg BID, $p = 0.42$ for ibudilast 50 mg BID), systolic blood pressure ($p = 0.68$ for ibudilast 20 mg BID, $p = 0.76$ for ibudilast 50 mg BID), or diastolic blood pressure ($p = 0.81$ for ibudilast 20 mg BID, $p = 0.80$ for ibudilast 50 mg BID) compared to placebo. Nor were there any significant interactions between ibudilast dose and methamphetamine dose on any of the cardiovascular measures (all $p > 0.05$).

Aim 2: To determine whether ibudilast (20 mg BID or 50 mg BID) alters the subjective effects of IV methamphetamine. The effects of ibudilast compared to placebo were assessed on self-reports of subjective effects of 15 mg, 30 mg IV methamphetamine using visual analogue and standard scales assessing responses over time. Analysis of whether ibudilast (20 mg BID or 50 mg BID) alters the subjective effects of IV methamphetamine was analyzed. Participants rated the subjective intensity of 12 drug effects (Morean et al., 2013) on a visual analog scale (VAS) ranging from 0 (Not at all) to 100 (Extremely). At 15 minutes pre-infusion and eight times post-infusion, participants rated "Effect" (Any drug effect?), "High" (How high are you?), "Good" (Any good effects?), "Like" (How much do you like the drug?), "Stimulated" (How stimulated do you feel?), "Want" (How much do you want the drug?), "Use" (How likely would you use the drug?), "Bad" (Any bad effects?), "Nervous" (How nervous do you feel?), "Sad" (How sad do you feel?), "Crave" (How much do you crave the drug?), and "Refuse" (How easily could you refuse the drug?). Subjective effect models first examined MA condition main effects and potential interactions with time and ibudilast sequence, which were retained if statistically significant ($p < .05$). Primary models then tested ibudilast X MA condition interactions, with statistically-significant interactions ($p < .05$) probed by testing the simple ibudilast effect within each MA condition. Planned contrasts compared each ibudilast condition to placebo, using an alpha (.025) and confidence interval (97.5% CI) adjusted for multiple comparisons. Ibudilast X MA condition interactions were statistically-significant for several positive subjective drug effects including "Effect" (Wald $X2(4) = 20.76, p < .001$), "High" (Wald $X2$ (4) = 12,19, $p < .05$), "Good" (Wald $X2$ (4) = 14.17, $p < .01$), "Like" (Wald $X2$ (4) = 12.68, $p < .05$).

Aim 3: To determine whether ibudilast alters the pharmacokinetics of IV methamphetamine. Based on data obtained from the 11 completers, we have been able to determine there were no clinically significant changes in methamphetamine or amphetamine pharmacokinetic parameters with ibudilast. Methamphetamine challenge sessions occurred after treatment conditions had reached steady state (ibudilast 20 mg twice daily, ibudilast 50 mg twice daily, and placebo) with sessions separated by 2 days to allow for pharmacokinetic analysis. During methamphetamine challenge sessions, participants were given either a 15 mg or 30 mg infusion of methamphetamine administered via IV push over 2 minutes using an automatic pump. Samples were collected for methamphetamine pharmacokinetic analysis following each infusion at regular intervals. Plasma levels of methamphetamine and its major metabolite, amphetamine, were assessed via liquid chromatographic-tandem mass spectrometry to determine if ibudilast alters the pharmacokinetics of intravenous methamphetamine. For pharmacokinetic analysis, methamphetamine and amphetamine were analyzed. Peak concentration (Cmax) was the observed maximum value during the collection period of 0 (pre-dose) to 18 hours. The time to peak concentration (Tmax) was the time at which Cmax was observed. The area under the curve represents the total drug exposure over time, either to the last sample time (AUC) or the estimated total drug exposure (AUC∞). Pharmacokinetic parameters (AUC, Tmax, Cmax, and elimination rates) were calculated using the times of sample collection reported by the Investigator. There were no significant differences in Cmax of methamphetamine, Tmax of methamphetamine, or methamphetamine T½ for either ibudilast dose compared to placebo following the 15 and 30 mg methamphetamine infusions. As a metabolite of methamphetamine, amphetamine pharmacokinetic analysis was also performed for Cmax, Tmax, and AUC∞. There were no significant differences in Cmax, Tmax, or AUC∞for amphetamine.

In summary, ibudilast was well tolerated in this Phase 1 safety-interaction study among methamphetamine dependent volunteers. There were no Serious Adverse Events and adverse events were mild, similar in frequency during ibudilast and placebo treatment, and typical of methamphetamine clinical trials. Ibudilast did not affect daily morning blood pressure or heart rate among methamphetamine dependent participants nor did it augment or exacerbate the cardiovascular response to methamphetamine. Ibudilast attenuated several of the prototypical subjective effects of MA, most notably "High", "Effect", and "Good", with reductions in "Stimulated" and "Like" that were less robust. There were no clinically significant changes in methamphetamine or amphetamine pharmacokinetic parameters with ibudilast. When measuring sustained attention, ibudilast showed reduced variability in response times and less perseverative responses in contrast to the placebo group. Pharmacogenetic analyses are ongoing.

Research Plans for 2016 Calendar Year: Enrollment to this trial has been completed, all subjects have completed study procedures, and research activities are limited to data analysis only for the 2016 calendar year.

Grunenthal/Janssen Pharmaceuticals has submitted Annual Progress Report titled "an Evaluation of the Efficacy & Safety of Tapentadol Oral Solution in the Treatment of Post-Operative Acute Pain Requiring Opioid Treatment in Pediatric Subjects Aged from Birth to Less than 18 Years old"

A brief summary of research performed and findings made during the year (this requirement may be augmented by including reprints of papers or copies of reports published) The trial KF5503/65 had First Subject In on 19 Feb 2015, and recruited until 31 Dec 2015 50 of the targeted 168 subjects. In parallel to this trial, the Sponsor is performing an Open label evaluation of the population pharmacokinetic profile, safety, tolerability, and efficacy of tapentadol oral solution for the treatment of post surgical pain in children aged from birth to less than 2 years (KF5503/72). The pharmacokinetic data gathered in this trial for a particular age group have been and will continue to be used to confirm the dose to be administered in the same age group in KF5503/65. Given that the age group 6 months to <2 years in KF5503/72 could already be closed and analyzed, the trial KF5503/65 has been amended to include the same age group (Amendment 05). The sponsor letter regarding DMC is included to further clarify the findings for this study by the DMC X

Research plans for the upcoming calendar year (with indication of any additional controlled substances planned for procurement in the upcoming year) It is expected that the trial KF5503/65 will continue to recruit until the end of the year 2016. No new clinical trials with oral solution are planned to start in 2016.

TABLE 1

RESEARCH STUDIES
APPROVED IN 2015

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Nicholas Butowski, M.D. UCSF Neurological Surgery San Francisco, CA	CBD Developmental Research Project
Kevin Chu, D.O. Lotus Clinical Research, LLC Pasadena, CA	A Phase 1, Open-Label, Single Ascending Dose Study to Evaluate the Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Fentanyl Sublingual Spray and Fentanyl Citrate Intravenous (IV) in Opioid Naive Subjects
Jay Keasling, Ph.D. Joint Bioenergy Institute Emeryville, CA	Engineering the Industrial Microbe Saccharomyces Cerevisiae for Biosyntheris of Cannabinoids
Christian Adam Kekoa Koch, MD Lotus Clinical Research, Inc. Pasadena, CA	A Phase I, Multiple Ascending Dose Study to Evaluate the Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Fentanyl Sublingual Spray in Opioid Naive Subjects
Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA	Panel Approved Research Study
Sara Mednick, Ph.D. UC Riverside Riverside, CA	The Effects of Zolpidem and Dextroamphetamine on Cognitive Performance

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
David E. Olson, Ph.D. UC Davis Davis, CA	Chemical Modulation of Neural Plasticity, Learning and Memory
Loren Parsons, Ph.D. The Scripps Research Institute La Jolla, CA	Cognitive and Neurochemical Effects of Δ9-tetrahydrocannabinol and related cannabinoids in rodents
Jeanne Paz, Ph.D. The J. David Gladstone Institutes San Francisco, CA	The Effects of Developmental Cannabis Exposure on Brain and Behavioral Development in Rats
Joel E. Schlosburg, Ph.D. The Scripps Research Institute La Jolla, CA	Treatment of Opiate Dependence Through Inhibition of Fatty Acid Amide Hydrolase
Jennifer Thomas, Ph.D. San Diego State University San Diego, CA	The Effects of Developmental Cannabis Exposure on Brain and Behavioral Development in Rats
Friedbert Weiss, Ph.D. The Scripps Research Institute La Jolla, CA	Implementation of Novel Methodology to Study the Anti-Relapse Potential of Cannabidiol
Bart Wilsey, M.D. UC Davis Medical Center Sacramento, CA	A Randomized, Cross-Over Controlled Trial of Dronabinol and Vaporized Cannabis in Neuropathic Low Back Pain

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Alkermes Waltham, MA	A Phase 3 Study to Evaluate Weight Gain of ALKS 3831 Compared to Olanzapine in Adults with Schizophrenia (ALK3831-A303)
Alkermes Waltham, MA	A Phase 3 Study to Determine the Antipsychotic Efficacy and Safety of ALKS 3831 in Adult Subjects with Acute Exacerbation of Schizophrenia (ALK3831-A305)
Alkermes Waltham, MA	A Phase 3, Multicenter Study to Assess the Long Term Safety and Tolerability of ALKS 3831 in Subjects with Schizophrenia (ALK3831-A306)
Cortbus Norwood, MA	A Phase 2, Double-Blind, randomized, Placebo-Controlled Multicenter Study to Evaluate safety, Tolerability, Efficacy, and Pharmacokinetics of JBT-101 in Cystic Fibrosis (BT101-CF-001)
Cortbus Norwood, MA	A Phase 2, Double-Blind, Randomized, Placebo-Controlled Multicenter Study to Evaluate Safety, Tolerability, Efficacy, and Pharmacokinetics of JBT-101 in Diffuse Cutaneous Systemic Sclerosis (JBT101-SSc-001)

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
GW Cambridge, UK	Panel Approved Research Study
GW Cambridge, UK	Panel Approved Research Study
GW Cambridge, UK	Panel Approved Research Study
GW Cambridge, UK	Panel Approved Research Study
INSYS Therapeutics Chandler, AZ	A multicenter, randomized, double-blind, placebo-controlled, interventional study to assess the safety and efficacy of pharmaceutical Cannabidiol Oral Solution as adjunctive therapy for treatment of subjects with inadequately controlled Lennox-Gastaut Syndrome (INS011-14-024)
INSYS Therapeutics Chandler, AZ	A multicenter, randomized, double-blind, placebo-controlled, interventional study to assess the safety and efficacy of pharmaceutical Cannabidiol Oral Solution as adjunctive therapy for treatment of subjects with inadequately controlled Dravet Syndrome (INS011-14-025)

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
INSYS Therapeutics Chandler, AZ	A Phase I/II Study to Assess the Pharmacokinetics and Safety of Multiple Doses of Pharmaceutical Cannabidiol Oral Solution in Pediatric Subjects with Treatment-Resistant Seizure Disorders (INS011-14-029)
INSYS Therapeutics Chandler, AZ	A Phase 2 Study to Assess the Efficacy and Safety of Cannabidiol Oral Solution for the Treatment of Refractory Infantile Spasms (NIS011-15-054)
Ironshore CRO: Rho Chapel Hill, NC	Panel Approved Research Study
Ironshore CRO: Rho Chapel Hill, NC	Panel Approved Research Study
Janssen Raritan, NJ	An Open-Label, Randomized, Single-Application, Two-Period Crossover, Pivotal Bioequivalence Study to Evaluate the Bioequivalence of Fentanyl Transdermal System (JNJ-35685-AAA-G021) Compared with DURAGESIC® Fentanyl Transdermal Patch in Healthy Subjects (FENPAI1023)

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Janssen Raritan, NJ	A Randomized, Partially-Blind, Two-Arm, Single-Application, 3-Way Crossover Study to Evaluate the Adherence of 2 Strengths of Newly Manufactured Samples and Aged Samples of a New Formulation (JNJ-35685-AAA-G016 and JNJ-35685-AAA-G021) of Fentanyl Transdermal System Compared with DURAGESIC® Fentanyl Transdermal Patch in Healthy Subjects (FENPAI1025)
Nektar CRO: PRA Lenexa, KS	A Phase 3, Double-Blind, Placebo-Controlled Study to Assess the Efficacy, Safety, and Tolerability of NKTR-181 in Opioid-Naive Subjects with Moderate to Severe Chronic Low Back Pain (14-181-07)
Nektar CRO: PRA Lenexa, KS	A Phase 3, Multicenter, Open-Label, 52-Week Study to Evaluate the Long-Term Safety and Tolerability of NKTR-181 in Subjects with Moderate to Severe Chronic Low Back Pain or Chronic Noncancer Pain (14-181-08)
Pfizer CRO: ICON New York, NY	An Open-Label Study to Evaluate the Pharmacokinetics and Safety of ALO-02 (Oxycodone Hydrochloride and Naltrexone Hydrochloride) Extended-Release Capsules in Children and Adolescents 7-17 Years of Age Who Require Opioid Analgesia (B4531015)

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Shire CRO: PPD San Diego, CA	A Phase 2, Open-Label, Multicenter, Exploratory Safety, Tolerability, Pharmacokinetic, and Efficacy Study of SPD489 in Preschool Children Aged 4-5 Years with Attention-deficit/Hyperactivity Disorder (SPD489-211)
Shire Wayne, PA	A Phase 3, Randomized, Double-blind, Multi-center, Placebo-controlled, Dose-Optimization, Safety and Efficacy Study of SHP465 in Children and Adolescents Aged 6-17 years with Attention Deficit Hyperactivity Disorder (ADHD) (SHP465-305)
Shire CRO: PPD San Diego, CA	A Phase 3, Open-label, Multicenter, 12-Month Safety and Tolerability Study of SPD489 in Preschool Children Aged 4-5 Years Diagnosed with Attention-Deficit /Hyperactivity Disorder (SPD489-348)
Shire CRO: Premier Research San Diego, CA	A Phase 3, Randomized, Double-Blind, Multicenter, Placebo-Controlled, Forced-Dose Titration, Safety and Efficacy Study of SHP465 in Adults Aged 18-55 Years with Attention-Deficit/Hyperactivity Disorder (ADHD) (SHP465-306)

Table 1 Cont.

PI / Sponsor	Title of Study / Clinical Drug Trial Protocol
Teva CRO: INC Raleigh, NC	A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Analgesic Efficacy and Safety of Hydrocodone Bitartrate/Acetaminophen Immediate-Release Tablets (TV-46763) at Doses of 5.0 mg/325 mg, 7.5 mg/325 mg, and 10 mg/325 mg Every 4 to 6 Hours in Patients with Moderate to Severe Pain Following Bunionectomy (TV46763-CNS-30031)
USWorldMeds Louisville, KY	A Phase 3, Open-Label, Safety Study of Lofexidine (USWM-LX1-3003-2)
Alkermes Waltham, MA	A Phase 3 Study of Evaluate the Safety, Tolerability, and Efficacy of Naltrexone for use in Conjunction with Buprenorphine in Adults with Opioid Use Disorder Prior to First Dose of Vivitrol (ALK6428-A301)

TABLE 2

RESEARCH STUDIES CLOSED IN 2015

Sponsor / PI	Title of Study / Clinical Drug Trial Protocol
Adam Leventhal, Ph.D. USC Keck School of Medicine Los Angeles, CA	Influence of Genes and Emotions on medication Effects
Jennifer Whistler, Ph.D. Ernest Gallo Clinic & Research Center Emeryville, CA 94608	Endocytosis and Opioid Receptors
Barth Wilsey, M.D. UC Davis Medical Center Sacramento, CA 95817	The Effect of Vaporized Cannabis on Neuropathic Pain in Spinal Cord Injury
AcelRx Pharmaceuticals, Inc. Redwood City, CA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sublingual Sufentanil Tablet 30 mcg for the Treatment of Post-Operative Pain in Patients after Abdominal Surgery (SAP301)
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"]

Table 2 Cont.

Sponsor / PI	Title of Study / Clinical Drug Trial Protocol
Purdue CRO: PRA Lenexa, KS	An Open-Label, Multicenter Study of the Safety of Twice Daily Oxycodone HCl Controlled-Release Tablets in Opioid Experienced Children from Ages 6 to 16 Years Old, Inclusive, with Moderate to Severe Malignant and/or Nonmalignant Pain Requiring Opioid Analgesics (Purdue OTR 3001)
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 (Purdue ONU3704)

Table 2 Cont.

Sponsor / PI	Title of Study / Clinical Drug Trial Protocol
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 Controlled Moderate to Severe Chronic Low Back Pain and a History of Opioid-induced Constipation with Require Around-the-clock Opioid Therapy (Purdue ONU3705)
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 (Purdue OTR3002)
Shire CRO: Premier Research Group Bluff City, TN	A Phase 3, Multicenter, Open-Label, 12-Month Extension Safety and Tolerability Study of SPD489 in the Treatment of Adults with Binge Eating Disorder (Shire SPD489-345)
USWorldMeds Louisville, KY	A Phase 3, Open-Label, Safety Study of Lofexidine (USWM-LX1-3003-2)

Table 2 Cont.

Sponsor / PI	Title of Study / Clinical Drug Trial Protocol
Kelly Courtney, MA UCLA Los Angeles, CA	Effects of Naltrexone on Methamphetamine Cue-Induced Brain Activity in Methamphetamine 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 Clinical Coordinating Center The EMMES Corporation Rockville, MD	Accelerated Development of Additive Pharmacotherapy Treatment (ADAPT) (NIDA CTN Protocol 0054)

APPENDIX A

CURRENTLY OPEN *(through December 31, 2015)*
SCHEDULE I AND SCHEDULE II
NON-HUMAN AND ACADEMIC HUMAN
RESEARCH STUDIES

Principal Investigator	Title of Study
Donald Abrams, M.D. UCSF / SFGH San Francisco, CA	Cannabinoid-Based Therapy and Approaches to Quantify Pain in Sickle Cell Disease
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
Nicholas Butowski, M.D. UCSF Neurological Surgery San Francisco, CA	CBD Developmental Research Project
John R. Cashman, Ph.D. Human BioMolecular Research Institute San Diego, CA	Molecular Evolution of Human Cocaine Catalysis
Kevin Chu, D.O. Lotus Clinical Research, LLC Pasadena, CA	A Phase 1, Open-Label, Single Ascending Dose Study to Evaluate the Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Fentanyl Sublingual Spray and Fentanyl Citrate Intravenous (IV) in Opioid Naive Subjects

Appendix A Cont.

Principal Investigator	Title of Study
Laura Colin Biostride, Inc. Redwood City, CA	Research of Novel Technologies for Development of Antibodies and Immunoassay Techniques to Drugs of Abuse and Controlled Compounds of Interest
Nissar A. Darmani, Ph.D. Western University Pomona, CA	Project 1: mechanisms of vomiting induced by chemotherapeutics, related emetics, & GI disorders. Project 2: Dev changes in monoamine function following prenatal & early postnatal exposure to serotonergic altering drugs in mice
Aaron Ettenberg, Ph.D. UC Santa Barbara Santa Barbara, CA	Dopamine involvement in Opiate and Stimulant Reinforcement
Michael Fischbach UCSF San Francisco, CA	Engineering a human gut bacteria to produce dimethyltryptamine
Laura Colin Biostride, Inc. Redwood City, CA	Effects of Cannabidiol on Mania-relevant Locomotor and Investigatory Behavior
Nissar A. Darmani, Ph.D. Western University Pomona, CA	Project 1: mechanisms of vomiting induced by chemotherapeutics, related emetics, & GI disorders. Project 2: Dev changes in monoamine function following prenatal & early postnatal exposure to serotonergic altering drugs in mice

Principal Investigator	Title of Study
Aaron Ettenberg, Ph.D. UC Santa Barbara Santa Barbara, CA	Dopamine involvement in Opiate and Stimulant Reinforcement
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	Effects of Cannabidiol on Mania-relevant Locomotor and Investigatory Behavior
Judith Hellman, M.D. UCSF San Francisco, CA	Cannabinoid-Dependent Modulation of the Innate Immune Response to Infection and Injury
Kanthi Hettiarachchi, Ph.D. SRI International Menlo Park, CA	Analysis of Controlled Substances
Kim D. Janda, Ph.D. The Scripps Research Institute La Jolla, CA	Vaccines for the Treatment of Opiate Addiction
Jay Keasling, Ph.D. Joint Bioenergy Institute Emeryville, CA	Engineering the Industrial Microbe Saccharomyces Cerevisiae for Biosyntheris of Cannabinoids
Thomas S. Kilduff, Ph.D. SRI International Menlo Park, CA	Neurobiological Studies of Gammahydroxybutyrate (GHB)

Appendix A Cont.

Principal Investigator	Title of Study
Christian Adam Kekoa Koch, MD Lotus Clinical Research, Inc. Pasadena, CA	A Phase I, Multiple Ascending Dose Study to Evaluate the Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Fentanyl Sublingual Spray in Opioid Naive Subjects
George Koob, Ph.D. The Scripps Research Institute La Jolla, CA	Prescription Opioid Addiction: Neurobiological Mechanisms
Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA	Panel Approved Research Project
Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA	Panel Approved Research Project
Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA	Panel Approved Research Project
Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA	Panel Approved Research Project

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
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
Sara Mednick, Ph.D. UC Riverside Riverside, CA	The Effects of Zolpidem and Dextroamphetamine on Cognitive Performance
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
Byung-Sook Moon ARK Freemont, CA	Research and Development of in-Vitro Diagnostic (IVD) Immunoassays for Drug of Abuse Testing
N.V. Myung, M.D. Nano Engineered Applications Riverside, CA	Marijuana Active Ingredient Quantification via Volatilized Sample

Appendix A Cont.

Principal Investigator	Title of Study
David E. Olson, Ph.D. UC Davis Davis, CA	Chemical Modulation of Neural Plasticity, Learning and Memory
Loren Parsons, Ph.D. The Scripps Research Institute La Jolla, CA	Cognitive and Neurochemical Effects of Δ9-tetrahydrocannabinol and related cannabinoids in rodents
Jeanne Paz, Ph.D. The J. David Gladstone Institutes San Francisco, CA	The Effects of Developmental Cannabis Exposure on Brain and Behavioral Development in Rats
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
Paolo Sassone-Corsi, Ph.D. UC Irvine Irvine, CA	The Role of Liver CB1 Receptor in Regulation of the Circadian Metabolism

Principal Investigator	Title of Study
Joel E. Schlosburg, Ph.D. The Scripps Research Institute La Jolla, CA	Treatment of Opiate Dependence Through Inhibition of Fatty Acid Amide Hydrolase
Douglas Sears, M.D. Encino, CA	A Double-Blind, Placebo-Controlled Study of Combination Therapy in Children with ADHD
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
Neil Singla, M.D. Lotus Clinical Research, LLC Pasadena, CA	A Randomized, Open Label, Prospective Study of the Analgesic Efficacy of Oral MNK795 Compared to Generic Oxycodone/APAP in the Treatment of Mod to Severe Post Operative Pain
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

Appendix A Cont.

Principal Investigator	Title of Study
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
Michael Taffe, Ph.D. The Scripps Research Institute La Jolla, CA	Behavioral and Physiological Toxicities of Cannabinoids: Effects of Cannabidiol
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
Michael Taffe, Ph.D. The Scripps Research Institute La Jolla, CA	Behavioral and Physiological Toxicities of Cannabinoids: Effects of Cannabidiol
Jennifer Thomas, Ph.D. San Diego State University San Diego, CA	The Effects of Developmental Cannabis Exposure on Brain and Behavioral Development in Rats
Stephen Van Dien, Ph.D. Genomatica, Inc. San Diego, CA	Panel Approved Research Project

Principal Investigator	Title of Study
Ronald Victor, M.D. Cedars-Sinai Med Center Los Angeles, CA	Effects of Cocaine on Blood Flow to the Heart
Tanya Wallace, Ph.D. SRI International Menlo Park, CA	Cannabinoid Regulation of Cognition
Friedbert Weiss, Ph.D. The Scripps Research Institute La Jolla, CA	Ethanol Seeking and Relapse: Therapeutic Potential of Transdermal Cannabidiol
Friedbert Weiss, Ph.D. The Scripps Research Institute La Jolla, CA	Implementation of Novel Methodology to Study the Anti-Relapse Potential of Cannabidiol
Timothy Wigal, Ph.D. UC Irvine Irvine, CA	Brain Dopamine Function in Adults with Attention Deficit/Hyperactivity Disorder (ADHD)
Bart Wilsey, M.D. UC Davis Medical Center Sacramento, CA	A Randomized, Cross-Over Controlled Trial of Dronabinol and Vaporized Cannabis in Neuropathic Low Back Pain
Roya Yumul, MD, PhD Cedars-Sinai Med Center Los Angeles, CA	Intra-operative ketamine and methadone for laminectomy: effect on recovery, post-operative pain, and opioid requirements

APPENDIX B

CURRENTLY OPEN *(through December 31, 2015)*
SCHEDULE II CLINICAL DRUG TRIAL STUDIES

Sponsor	Description or Title of Clinical Drug Trial Protocol
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)
Alkermes, Inc. Waltham, MA	A Phase 3 Efficacy & Safety Study of ALK5461 for the Adjunctive Treatment of Major Depressive Disorder (Study I) (ALKS5461-205)
Alkermes, Inc. Waltham, MA	A Phase 3 Efficacy & Safety Study of ALK5461 for the Adjunctive Treatment of Major Depressive Disorder (Study II) (ALKS5461-206)
Alkermes, Inc. Waltham, MA	A Phase 2, Randomized, Double-Blind Study to Evaluate Efficacy, Safety, and Tolerability of ALKS3831 in Subjects with Schizophrenia with Alcohol Use Disorder (ALKS3831-401)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
Alkermes, Inc. Waltham, MA	A Phase 3 Efficacy & Safety Study of ALKS5461 for the Adjunctive Treatment of Major Depressive Disorder (the FORWARD-5 Study) (ALKS5461-207)
Alkermes, Inc. Waltham, MA	A Phase 3 E & S Study of ALKS5461 for the Adjunctive Treatment of Major Depressive Disorder (the FORWARD-5 Study) (ALKS5461-208)
Alkermes, Inc. Waltham, MA	A Phase 3 Study to Evaluate Weight Gain of ALKS 3831 Compared to Olanzapine in Adults with Schizophrenia (ALK3831-A303)
Alkermes Waltham, MA	A Phase 3 Study to Determine the Antipsychotic Efficacy and Safety of ALKS 3831 in Adult Subjects with Acute Exacerbation of Schizophrenia (ALK3831-A305)
Alkermes Waltham, MA	A Phase 3, Multicenter Study to Assess the Long Term Safety and Tolerability of ALKS 3831 in Subjects with Schizophrenia (ALK3831-A306)

Sponsor	Description or Title of Clinical Drug Trial Protocol
Braeburn Pharmaceuticals Princeton, NJ	A Randomized, Double-Blind, Double-Dummy, Active-Controlled Multi-Center Study of Adult Outpatients with Opioid Dependence Transitioned from a Daily Maintenance Dose of 8mg or Less of SL Buprenorphine or Buprenolphine/Naloxone to Four Probuphine Subdermal Implants (PRO-814)
CNS Therapeutics CRO: Social & Scientific Systems	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: Social & Scientific Systems	A Phase 3 Open-Label, Single-Arm Study To Assess The Safety of Hydromorphone HCl Delivered by Intrathecal Administration (HYD202US)
Collegium CRO : INC Research	A Phase 3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Safety, Tolerability, and Efficacy Study of Oxycodone DETERx™ Versus Placebo in Opioid-Experienced and Opioid-Naïve Subjects with Moderate-to-Severe Chronic Low Back Pain (CO-OXYDET-08)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
Cortbus Norwood, MA	A Phase 2, Double-Blind, randomized, Placebo-Controlled Multicenter Study to Evaluate safety, Tolerability, Efficacy, and Pharmacokinetics of JBT-101 in Cystic Fibrosis (BT101-CF-001)
Cortbus Norwood, MA	A Phase 2, Double-Blind, Randomized, Placebo-Controlled Multicenter Study to Evaluate Safety, Tolerability, Efficacy, and Pharmacokinetics of JBT-101 in Diffuse Cutaneous Systemic Sclerosis (JBT101-SSc-001)
Grunenthal/Janssen CRO : inVentiv Cary, NC	An Evaluation of the Efficacy & Safety of Tapentadol Oral Solution in the Treatment of Post-Operative Acute Pain Requiring Opioid Treatment in Pediatric Subjects Aged from Birth to Less than 18 Years old (KF5503/65)
GW Cambridge, UK	Panel Approved Research Project
GW Cambridge, UK	Panel Approved Research Project

Sponsor	Description or Title of Clinical Drug Trial Protocol
GW Cambridge, UK	Panel Approved Research Project
GW Cambridge, UK	Panel Approved Research Project
GW Cambridge, UK	Panel Approved Research Project
GW Cambridge, UK	Panel Approved Research Project
GW Cambridge, UK	Panel Approved Research Project
GW Cambridge, UK	Panel Approved Research Project
GW Cambridge, UK	Panel Approved Research Project
GW Cambridge, UK	Panel Approved Research Project

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
INSYS Therapeutics Chandler, AZ	A multicenter, randomized, double-blind, placebo-controlled, interventional study to assess the safety and efficacy of pharmaceutical Cannabidiol Oral Solution as adjunctive therapy for treatment of subjects with inadequately controlled Lennox-Gastaut Syndrome (INS011-14-024)
INSYS Therapeutics Chandler, AZ	A multicenter, randomized, double-blind, placebo-controlled, interventional study to assess the safety and efficacy of pharmaceutical Cannabidiol Oral Solution as adjunctive therapy for treatment of subjects with inadequately controlled Dravet Syndrome (INS011-14-025)
INSYS Therapeutics Chandler, AZ	A multicenter, open-label, flexible dose study to assess the long-term safety of pharmaceutical Cannabidiol Oral Solution as an adjunctive treatment for pediatric and adult subjects with a treatment-resistant seizure disorder who complete INS011-14-024, INS011-14-025, or INS011-14-029 (INS011-14-030)

Sponsor	Description or Title of Clinical Drug Trial Protocol
INSYS Therapeutics Chandler, AZ	A Phase 2 Study to Assess the Efficacy and Safety of Cannabidiol Oral Solution for the Treatment of Refractory Infantile Spasms (NIS011-15-054)
INSYS Therapeutics Chandler, AZ	A Phase I/II Study to Assess the Pharmacokinetics and Safety of Multiple Doses of Pharmaceutical Cannabidiol Oral Solution in Pediatric Subjects with Treatment-Resistant Seizure Disorders (INS011-14-029)
Ironshore CRO: Rho Chapel Hill, NC	Panel Approved Research Study
Ironshore CRO: Rho Chapel Hill, NC	Panel Approved Research Study
Janssen Raritan, NJ	An Open-Label, Randomized, Single-Application, Two-Period Crossover, Pivotal Bioequivalence Study to Evaluate the Bioequivalence of Fentanyl Transdermal System (JNJ-35685-AAA-G021) Compared with DURAGESIC® Fentanyl Transdermal Patch in Healthy Subjects (FENPAI1023)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
Janssen Raritan, NJ	A Randomized, Partially-Blind, Two-Arm, Single-Application, 3-Way Crossover Study to Evaluate the Adherence of 2 Strengths of Newly Manufactured Samples and Aged Samples of a New Formulation (JNJ-35685-AAA-G016 and JNJ-35685-AAA-G021) of Fentanyl Transdermal System Compared with DURAGESIC® Fentanyl Transdermal Patch in Healthy Subjects (FENPAI1025)
Lannett CRO : Parexel Waltham, MA	A Phase 3 Investigation of Topical Application of Cocaine 4% and 10% on Safety & Efficacy in Local Anesthesia for Dx Procedures & Surgeries on or through Accessible Mucous Membranes of the Nasal Cavities (COCA4vs10-001)
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
MAPS Santa Cruz, CA	A Randomized, Double-Blind, Placebo-Controlled Study of MDMA-Assisted Psychotherapy for Anxiety Associated with a Life-Threatening Illness (MDA-1)
Nektar CRO: PRA Lenexa, KS	A Phase 3, Double-Blind, Placebo-Controlled Study to Assess the Efficacy, Safety, and Tolerability of NKTR-181 in Opioid-Naive Subjects with Moderate to Severe Chronic Low Back Pain (14-181-07)
Nektar CRO: PRA Lenexa, KS	A Phase 3, Multicenter, Open-Label, 52-Week Study to Evaluate the Long-Term Safety and Tolerability of NKTR-181 in Subjects with Moderate to Severe Chronic Low Back Pain or Chronic Noncancer Pain (14-181-08)
Pfizer CRO: ICON New York, NY	An Open-Label Study to Evaluate the Pharmacokinetics and Safety of ALO-02 (Oxycodone Hydrochloride and Naltrexone Hydrochloride) Extended-Release Capsules in Children and Adolescents 7-17 Years of Age Who Require Opioid Analgesia (B4531015)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
Shire CRO : Premier Research Group Alexander, NC Alkermes Waltham, MA	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)
Shire CRO : Premier Research Group Little Egg Harbor, NJ	A Phase 4, Randomized, Double-blind, Multicenter, Parallel-group, Active-controlled, Dose-optimization Safety and Efficacy Study of SPD489 (Vyvanse®) Compared with OROS-MPH (Concerta®) with a Placebo Reference Arm, in Adolescents Aged 13-17 Years with Attention-deficit/Hyperactivity Disorder (ADHD) (SPD489-405)
Shire CRO : Premier Research Group Little Egg Harbor, NJ	A Phase 4, Randomized, Double-blind, Multicenter, Parallel-group, Active-controlled, Forced-dose Titration, Safety and Efficacy Study of SPD489 (Vyvanse®) Compared with OROS-MPH (Concerta®) with a Placebo Reference Arm, in Adolescents Aged 13-17 Years with Attention-deficit/Hyperactivity Disorder (ADHD) (SPD489-406)

Sponsor	Description or Title of Clinical Drug Trial Protocol
Shire CRO: PPD San Diego, CA	A Phase 2, Open-Label, Multicenter, Exploratory Safety, Tolerability, Pharmacokinetic, and Efficacy Study of SPD489 in Preschool Children Aged 4-5 Years with Attention-deficit/Hyperactivity Disorder (SPD489-211)
Shire Wayne, PA	A Phase 3, Randomized, Double-blind, Multi-center, Placebo-controlled, Dose-Optimization, Safety and Efficacy Study of SHP465 in Children and Adolescents Aged 6-17 years with Attention Deficit Hyperactivity Disorder (ADHD) (SHP465-305)
Shire CRO: PPD San Diego, CA	A Phase 3, Open-label, Multicenter, 12-Month Safety and Tolerability Study of SPD489 in Preschool Children Aged 4-5 Years Diagnosed with Attention-Deficit /Hyperactivity Disorder (SPD489-348)
Shire CRO: Premier Research San Diego, CA	A Phase 3, Randomized, Double-Blind, Multicenter, Placebo-Controlled, Forced-Dose Titration, Safety and Efficacy Study of SHP465 in Adults Aged 18-55 Years with Attention-Deficit/Hyperactivity Disorder (ADHD) (SHP465-306)

Appendix B Cont.

Sponsor	Description or Title of Clinical Drug Trial Protocol
Teva Raleigh, NC	A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Analgesic Efficacy and Safety of Hydrocodone Bitartrate/Acetaminophen Immediate-Release Tablets (TV-46763) at Doses of 5.0 mg/325 mg, 7.5 mg/325 mg, and 10 mg/325 mg Every 4 to 6 Hours in Patients with Moderate to Severe Pain Following Bunionectomy (TV46763-CNS-30031)
Tris Chapel Hill, NC	Amphetamine Extended-Release Oral Suspension in the Treatment of Children with ADHD: A Laboratory School Study (TRI102-ADD-001)
USWorldMeds Louisville, KA	A Phase 3, Open-Label, Safety Study of Lofexidine (USWM-LX1-3003-2)

APPENDIX C

CURRENTLY OPEN *(December 31, 2015)*
RESEARCH STUDIES
ON THE TREATMENT OF CONTROLLED SUBSTANCE ABUSE

Investigator or Sponsor	Description or Title of Research Study
Keith Heinzerling, M.D. UCLA Los Angeles, CA	Randomized Trial of Ibudilast for Methamphetamine Dependence
Lara Ray, Ph.D. UCLA Los Angeles, CA	The Effects of Naltrexone on Neural Responses to Methamphetamine Cues
Lara Ray, Ph.D. UCLA Los Angeles, CA	Effects of Ibudilast on Non-treatment Seeking Patients Who Meet Criteria for Alcohol Abuse or Dependence
Steven Shoptaw, Ph.D. UCLA. Los Angeles, CA	Phase I Safety Interaction Trial of Ibudilast with Methamphetamine
Steven Shoptaw, Ph.D. UCLA. Los Angeles, CA	Varenicline for Methamphetamine Dependence

Appendix C Cont.

Investigator or Sponsor	Description or Title of Research Project
Alkermes Waltham, MA	A Phase 3 Study of Evaluate the Safety, Tolerability, and Efficacy of Naltrexone for use in Conjunction with Buprenorphine in Adults with Opioid Use Disorder Prior to First Dose of Vivitrol (ALK6428-A301)
NIDA Bethesda, MD	Phase 2, Double-Blind, Placebo-Controlled, Parallel-Group, Multi-Center Trial of Nepicastat for Cocaine Dependence (NIDA/VA CS# 1031)
NIDA The EMMES Corp. Rockville, MD	Achieving Cannabis Cessation-Evaluating N-Acetylcysteine Treatment (ACCENT) (NIDA CTN Protocol 0053)
NIDA The EMMES Corp. Rockville, MD	Extended-Release Naltrexone vs. Buprenorphine for Opioid Treatment (X:BOT)

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.