# FORTY-SEVENTH ANNUAL REPORT

of the

# RESEARCH ADVISORY PANEL OF CALIFORNIA

2017



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

	Page
LIST OF 2017 PANEL MEMBERS	2
SUMMARY OF 2017 PANEL ACTIVITIES and SELECTED RESEARCH FINDINGS	3
TABLE 1 - Research Studies approved in 2017	9
TABLE 2 - Research Studies closed in 2017	17
APPENDICES	
Appendix A - Currently Open Schedule I and II Non-Human & Academic Human Studies	29
Appendix B - Currently Open Schedule II Clinical Drug Trial Studies	39
Appendix C - Currently Open Research Studies on the Treatment of Controlled Substance Abuse	47
Appendix D - Pertinent Sections - California Health and Safety Code	·
§ 11213 - Persons and researches using controlled substances	49
§ 11480 & 11481 - Research Advisory Panel	49
§ 11603 & 11604 - Attorney General	50
§ 24172 - Experimental subject's bill of rights	51
§ 24173 - Informed consent	52

#### 2017 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 Director

Appointed by the State of California Attorney General

David A. Baron, DO, MSEd

Assistant Dean, ÚSC 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

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: https://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 2017 PANEL ACTIVITIES**

During 2017 the Panel reviewed forty-two research study submissions. Forty were approved by the Panel. Among the approved studies, eighteen studies were Academic research studies, eighteen studies were Multi-Center Clinical Drug Trial research studies, and four studies were Substance Abuse Treatment research studies.

Forty-eight research studies were completed or, in a few cases, terminated in 2017, and they were closed on the Panel's records.

At the end of 2017 the Panel was monitoring one hundred and fifteen 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 2017 and Table 2 is a list of the studies closed by the Panel in 2017.

#### 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:

<u>Dr. Thomas Marcotte, Ph.D.</u> and colleagues at University of California, San Diego Health Care System have provided the Panel with the following summary of human research titled "A Randomized, Controlled Trial of Cannabis in Healthy Volunteers Evaluating Simulated Driving, Field Performance Tests and Cannabinoid Levels"

We have not begun to recruit participants. We expect to do so in the near future. The reason for this delay was a decision by the FDA to put a partial clinical hold on the protocol in September 2017 because of the vaporization of 16.93% cannabidiol (CBD). We selected this concentration as our highest proposed CBD dose based on the cannabis batches that were currently available from NIDA Drug Supply. We noted that there are many protocols on ClinicalTrials.gov using various concentrations of oral CBD without there being reports of adverse effects. Of particular relevance, a review of 25 studies on the safety and efficacy of CBD exemplifies the safety of this cannabinoid. 1 The authors of this review did not identify significant side effects across a wide range of dosages, including acute and chronic dose regimens. However, we were unable to convince the

FDA that we could reliably convert 16.93% vaporized cannabis to an oral dose that had been previously shown to be safe by other investigators. Therefore, we proposed an alternative option to administer a lower drug concentration. This new plan has been reviewed and approved by the FDA.

We originally planned on using 3 strengths of CBD (characterized as low, medium and high in Table 1 below) to better understand the effect of this cannabinoid on THC in the treatment of HIV peripheral neuropathy.

Our revised plan involves using more puffs rather than a higher concentration of CBD. To provide this higher amount (in milligrams) of CBD, participants will vaporize 8 instead of 4 puffs of the 5.7% CBD study medication. To prevent unblinding, all three sessions will involve the use of 8 puffs rather than 4 puffs. This will necessitate vaporizing 2 vials of 400 mg of NIDA cannabis similar to what we did in a previous human laboratory experiment.2

After the participant consumes 4 puffs from vial #1, the research nurse will empty the vaporizer canister into the prescription vial. The research nurse will then refill the vaporizer canister with vial #2. To avoid administering more THC and thus unblinding participants through introduction in increased psycho-activity, the amount of THC will be halved in both vial #1 and vial #2.

Utilizing the current NIDA Drug Supply Program (DSP) list of available bulk cannabis, the following are blends that we will request from Robert Walsh of the DSP:

<u>Jazz Pharmaceuticals CRO: Quintiles</u> has provided the Panel with the following Annual Progress Report of multicenter clinical drug trial research titled "A Double-Blind, Placebo-Controlled, Randomized-Withdrawal, Multicenter Study of the Efficacy and Safety of JZP-258 in Subjects with Narcolepsy with Cataplexy (Protocol 15-006)"

A brief summary of research performed and findings made during the calendar year (this requirement may be augmented by including reprints of papers or copies of reports published).

California Sites: The California sites have contributed I screened subject which was a screen failure. There are currently three sites in California.

Research plans for the upcoming calendar year (with indication of any additional controlled substances

planned for procurement in the upcoming year)

The study will continue per Amendment 3, with a current LPL V in October 2018. The controlled substance

distribution will continue as detailed in the protocols, with no additional procurement. During the course of 2018, pending approvals, sites will become active under protocol amendment 4 -see section c.

Notation of any changes in the research project, (substantive changes should be explained in detail so that the Panel can review them as protocol amendments)

Rationale for amendment:

15-006 -Protocol Amendment 4

Protocol 15-006 Amendment 4, dated 15 December 2017 is an update to Protocol 15-006 Amendment 3, previously dated 10 April 2017. The more significant changes that are included in Amendment 4 are summarized below in the order they appear in the protocol: Throughout the document, the addition of text applicable to the Open-Label Extension, including:

- o The use of "Main Study" and "Open-Label Extension" to differentiate
- o New inclusion/exclusion criteria, figure, estimated blood volume table, and Summary of Events
- o Consistent use and defining of "Rollover" and "Re-entry" Subjects
- o Set timing for tapering of other anticataplectic therapies
- o Definition and clarification of Treatment Emergent Adverse Events (TEAE) for the Open-Label Extension
- o Addition of language for a final efficacy analysis and safety analysis after all subjects have completed or early terminated from the Main Study under the Interim Analysis section

<u>Jay Keasling, Ph.D.</u> and colleagues at Joint Bioenergy Institute, Lawrence Berkeley National Laboratory have provided the Panel with the following summary of academic non-human research titled "Engineering the Industrial Microbe Saccharomyces Cerevisiae for Biosynthesis of Cannabinoids"

This summary covers the period from January 1, 2017, through December 31, 2017. Our project received DEA registration approval on 4/19/2016. In the previous year, we discovered a new geranyl:olivetolic transferase (CsPT4) which can catalyze the formation of the key cannabinoid, cannabigerolic acid (CBGA). We then introduced CsPT4 into the strain with both biosynthetic pathways for the olivetolic acid (OA) and geranyl pyrophosphate (GPP) we constructed in 2016. The resulting strain was able to produce CBGA from galactose. We then introduced the synthesis for THCA (THCAS) and CBDA (CBDAS) found in Cannabis sativa into the CBGA-producing strain, the resulting strains produced THCA and CBDA, respectively. The production of THCA/CBDA has been confirmed by Quadruple Time-of-Flight Mass Spectrometry (QTOF-MS) without isolation and the samples were destroyed after analysis with bleach. We also observed the production of three other cannabinoid precursors (CBGVA, THCVA, CBDVA). We purchased THCA, CBDA, THC, and CBD standards (1 mg/ml each) which are DEA-exempt preparations. Controlled substances have not yet been purchased for this project.

Research Plans for 2018

In the coming year, we plan to feed short- to medium-chain fatty acids with various functional groups to the engineered yeast. If this idea works as planned, the engineered yeast should produce different cannabinoid analogues with the various functional groups

that were contained in the fatty acids. We also want to improve THCA or CBDA production through protein and metabolic engineering. Using the 30+ cannabinoid syntheses candidates we identified in our genome mining work, we will try to identify their corresponding products through QTOF-MS. In 2018, we plan to purchase 1 mg of THC and CBD standards, which is covered by the approved Research Advisory Panel of California letter. In the near future, we anticipate submitting an amendment to our protocol to expand into looking for different cannabinoid compounds.

<u>Dr. Steven Shoptaw, Ph.D.</u> and colleagues at University of California, Los Angeles have provided the Panel with the following summary of the substance abuse treatment research titled "Varenicline for Methamphetamine Dependence"

his phase 2 randomized double-blind, placebo-controlled trial aimed to recruit and enroll 90 treatment-seeking methamphetamine dependent participants. As described in the last annual progress report, the trial opened recruitment in February 2012 and closed enrollment in May 2014 due to the recommendation from the DSMB to halt enrollment after review of the results of an interim analysis. In total, 277 participants opened informed consent, of which 225 screen failed and 52 participants were randomized onto the trial. Screen fails were due to: psychological ineligibility (n=82); failure to complete baseline assessments (n=60); medical ineligibility (n=30); voluntarily withdrew (n=22); failing to provide an MA positive urine drug screen (n=16); PI discretion (n=8); not seeking treatment (n=6); and probation/parole (n=1). Of the 52 randomized participants, 26 completed the study and 26 dropped. Reasons for dropping include: withdrawn by the investigator (n=1), transferred to a higher level of care (n=2), incarcerated (n=1) and missed 6 consecutive visits (n=22). Demographic characteristics of randomized participants are summarized in Table 1.

During the reporting period, we have continued with data analysis, the current results for each aim are described below.

Aim 1: To determine whether varenicline reduces MA use and delays time to MA relapse more than placebo among MA dependent participants during weeks 2 through 9 of the medication phase.

The effects of varenicline on reductions in MA use were assessed using results from thrice weekly urine drug screens for MA-metabolites and self-reported MA use (time line follow-back) as an intent-to-treat analysis that included the period from day 0 to the end of the 9 week active medication period. Treatment-seeking MA-dependent adults (n=52) received varenicline or placebo and adjunct cognitive behavioral therapy, with some (n=18) also completing an inpatient detoxification during week 2. Univariate composites of urine drug screen results included continuous MA abstinence for two weeks at end of treatment (EOTA), the treatment effectiveness score (TES), joint probability index, and mean time to MA relapse. The primary outcome, EOTA, was confirmed by urine drug screens during weeks 8 and 9. Secondary outcome, TES, was defined as the number of MA-free urine specimens provided during the medication phase (weeks 1-9).

Primary analyses examined EOTA and TES, controlling for sex, age, baseline MA use, and smoking status. End-of-treatment abstinence was achieved by 17% of the sample (n = 9), and rates of abstinence were comparable between treatment conditions; 15% of varenicline participants (4/27) vs. 20% of placebo participants (5/25), OR = 0.9, p = .9, 95% CI (0.17, 4.70). The Bayes factor for the hypothesis that the likelihood of EOTA differed between varenicline and placebo participants was 0.77, suggesting no difference between groups. Mean TES across the sample was 8.4 (SD = 9.1) and mean TES was similar for varenicline (8.6, SD = 10.1) and placebo (8.1, SD = 8.2). In adjusted analysis, treatment condition was not a statistically significant predictor of TES, IRR = 1.01, p = .9, 95% CI (0.39, 2.70). The Bayes factor for the hypothesis that varenicline impacted TES was 0.50, also suggesting no difference. Baseline MA use significantly predicted TES, as participants with greater pre-treatment MA use were less likely to provide negative urine samples, IRR = 0.94 for one additional day of MA use in the month preceding enrollment, p = .01, 95% CI (0.88, 0.99). Varenicline treatment did not interact with baseline MA use to predict EOTA or TES, and age, sex, and smoking status did not have significant effects on abstinence or TES.

Some participants (n=18) completed an inpatient detoxification during week 2 and a post-hoc analysis examined whether inpatient detoxification and the inpatient by medication interaction predicted primary clinical outcomes. Eleven of 27 varenicline participants underwent inpatient detoxification (41%) vs. 7/25 placebo participants (28%). There was no main effect of inpatient detoxification on EOTA [OR = 0.93, p = .9, 95% CI (0.18, 4.09)], and the effect of detoxification on TES was positive, but did not reach statistical significance [IRR = 1.98, p = .1, 95% CI (0.91, 4.54)]. No inpatient placebo participants achieved EOTA, resulting in an undefined odds ratio in the strata of inpatient participants. Consequently, the interaction effect between treatment and inpatient detoxification on EOTA was not estimated. Additionally, inpatient detoxification did not modify the treatment—TES relationship (p value for interaction=5). The joint probability index, which is the probability of whether a participant is retained and abstinent at a given point in the trial, was not completed.

he mean time to MA relapse was calculated from the Friday visit of study week 2, or if not abstinent in the second week, from the first point of two consecutive meth-negative urine samples after the end of week 2. The number of days from Friday visit of study week 2 to the first MA-positive urine drug screen was defined as the time to MA relapse. Forty-eight percent of varenicline participants (13/27) achieved abstinence during treatment compared to 56% of placebo (14/25). Of those achieving abstinence, 62% of varenicline participants relapsed (8/13) vs. 43% of placebo

(6/14). Kaplan-Meier median time-to-relapse was 38 days in the varenicline group and not estimable in the placebo group, as overall "survival" did not drop below 50% during the treatment phase. In a Cox proportional hazards model, treatment condition did not predict relapse; Hazard Ratio (HR) = 1.42, p = .52, 95% CI (0.49, 4.10).

Aim 2: To determine whether varenicline reduces MA withdrawal symptoms more than placebo among MA dependent participants.

The effects of varenicline compared to placebo on reducing MA withdrawal symptoms

was measured via the Amphetamine Cessation Symptoms Assessment (ACSA) scale administered at baseline and weekly during the weeks 1 through 9. Analysis of whether varenicline (1 mg BID) reduced mean ACSA scores at the end of the 9-week treatment period compared to placebo was not completed.

Aim 3: To determine whether varenicline reduces cigarette smoking more than placebo among cigarette smoking MA dependent participants.

The effects of varenicline compared to placebo on reducing cigarette smoking was assessed using a mixed negative binomial regression model to examine the weekly number of cigarettes smoked among participants who smoked any cigarettes during the active treatment phase (N = 35, n = 15 varenicline, n = 20 placebo). Greater reductions in cigarette smoking were observed in the varenicline group, as evidenced by a significant, negative time by varenicline treatment interaction (b = -.56, se = .21, p = .007). Pre-specified comparisons of fitted values showed no difference between treatment groups at baseline (p = .83), a non- significant difference of about 14 cigarettes at 5 weeks (p = .056) and a statistically significant difference of about 18 cigarettes at 9 weeks (p = .01).

#### TABLE 1

#### RESEARCH STUDIES APPROVED IN 2017

PI / Sponsor

Title of Study / Clinical Drug

Trial Protocol

Richard Baldwin, Ph.D.

nanoComposix San Diego, CA Biosensor for the Detection of Synthetic

Cannabinoids

Nelson Barton, Ph.D.

Genomatica San Diego, CA Microbial Processes for the Manufacture of

**Specialty Chemicals** 

Neal Benowitz, M.D.

**UCSF** 

San Francisco, CA

Intake and Pharmacokinetics of THC Vaped

from Electronic Cigarettes

Karl Deisseroth, MD, PhD

Stanford University

Palo Alto, CA

Neural Circuit Dynamics of LSD-Induced

Psychosis

Christie Fowler, Ph.D.

UC Irvine Irvine, CA Mechanisms of Drug Reinforcement

Alidad Ghiassi, M.D. Keck School of Medicine USC

Los Angeles, CA

A Randomized Trial Comparing Ibuprofen
Plus Acetaminophen Versus Oxycodone After

Outpatient Soft Tissue Hand Surgery

#### Table 1 Cont.

#### PI / Sponsor

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

William Haseltine, Ph.D. Demetrix, Inc. Emeryville, CA Production of Natural and Modified Cannabinoids using Engineered, Industrial Microorganisms

Brook Henry, Ph.D. UC San Diego San Diego, CA Effect of Cannabis Administration and Endocannabinoids on HIV Neuropathic Pain Study - Phase 2

Stephen Mahler, Ph.D. UC Irvine Irvine, CA Neural Circuits Underlying Motivation and Addiction

Alysson Muotri, Ph.D. UC San Diego La Jolla, CA The Impact of CBD/THC on Human Neurodevelopment

Lori Olson, M.S. SRI International Menlo Park, CA

Identification and isolation of specific pesticides from cannabinoid oils

David Schubert, Ph.D. Salk Institute La Jolla, CA The Identification of Neuroprotective Compounds in Cannabis

Philip Schwartz, Ph.D. Children's Hospital of Orange County Orange, CA Effect of Cannabinoid Receptor Activation on Human Neural Stem Cell Function

#### PI / Sponsor

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

Joshua Woolley, MD, PhD UC San Francisco SF VA Medical Center San Francisco, CA Psilocybin-Assisted Group Therapy for Demoralization in Long-Term Aids Survivors

Alkermes Waltham, MA A Study to Evaluate the Effect of ALKS 3831 Compared to Olanzapine on Body Weight in Young Adults with Schizophrenia, Schizophreniform or Bipolar I Disorder Who are Early in Their Illness (ALK3831-A307)

Alkermes Waltham, MA A Phase 3 Study to Assess the Long Term Safety, Tolerability, and Durability of Treatment Effect of ALKS 3831 in Subjects with Schizophrenia, Schizophreniform Disorder, or Bipolar I Disorder (ALK3831-A308)

Alkermes Waltham, MA

A Phase 3b Efficacy and Safety Study of Adjunctive ALKS5461 in Treatment Refractory Major Depressive Disorder (ALK5461-217)

Corbus Norwood, MA A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial to Evaluate Efficacy and Safety of Lenabasum in Diffuse Cutaneous Systemic Sclerosis (JBT101-SSc-002) Table 1 Cont.

PI / Sponsor

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

Alkermes Waltham, MA

A Phase 1 Study to Evaluate the Effect of Multiple Doses of ALKS 3831 on QTc interval in Subjects with Schizophrenia (ALK3831-A109)

Insys Chandler, AZ

A Phase 2, Randomized, Open Label, Multiple-Dose, Comparator, Parallel-Group, Safety and Tolerance Study of Buprenorphine Sublingual Spray (0.5mg TID) versus Standard of Care Post-Operative Narcotic Therapy for the Treatment of Post-Operative Pain (INS005-17-111)

Insys Chandler, AZ A Phase 2, Open-Label, Dose-Finding Study to Assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of Pharmaceutical Grade Synthetic Cannabidiol Oral Solution in Pediatric Patients with Treatment-Resistant Childhood Absence Seizures (INS011-17-103)

Insys Chandler, AZ A Multicenter, Open-Label, Flexible Dose Study to Assess the Long-Term Safety of Pharmaceutical Grade Synthetic Cannabidiol Oral Solution as in Pediatric Patients with Treatment-Resistant Childhood Absence Seizures (INS011-17-113)

Jazz Pharmaceuticals CRO: Quintiles Overland Parks, KS

A Double-Blind, Placebo-Controlled, Randomized-Withdrawal, Multicenter Study of the Efficacy and Safety of JZP-258 in Subjects with Narcolepsy with Cataplexy

#### PI / Sponsor

# Title of Study / Clinical Drug

**Trial Protocol** 

MAPS Santa Cruz, CA

Panel Approved Research Study

NIH/NIAID Rockville, MD

A Phase 2, Double-blind, Randomized, Placebo-controlled Multicenter Study to Evaluate Efficacy, Safety, and Tolerability of JBT-101 in Systemic Lupus Erythematosus (ALE09)

Noven New York City, NY A Randomized, Multiple-Dose, Open-Label, 4-Week Study to Characterize the Pharmacokinetics, Cumulative Irritation, Safety, and Tolerability of d-Amphetamine Transdermal System (d-ATS) in Adults Diagnosed with ADHD (N25-015)

Purdue CRO: PRA Raleigh, NC A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel Group, Laboratory Classroom Study to Evaluate the Safety and Efficacy of PRC-063 Compared to Placebo in Children (6-12 years of age) with ADHD (063-015) Table 1 Cont.

PI/Sponsor

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

Recro Pharma Malvern, PA

A Phase 2, Multicenter, Randomized, Double-Blind, Placebo- and Active-Controlled, Evaluation of the Efficacy and Safety of DEX-IN following Painful Outpatient Procedures (REC-17-023)

Vertex Boston, MA

A Phase 2 randomized, Double-Bind, Placebo-Controlled, 3-Arm, Parallel-Design Study of the Efficacy and Safety of VX-150 for Acute Pain Following Bunionectomy (VX16-150-103)

NIDA/NSC/NIH Bethesda, MD Phase 2, Multi-Center Trial of Lorcaserin for the Treatment of Cocaine Use Disorder (NIDA/VA CS #1033)

NIDA/NSC/NIH Bethesda, MD Comparing Treatments for HIV-Infected Opioid Users in an Integrated Care Effectiveness Study (CHOICES) Scale-Up (NIDA CTN 0067)

# PI / Sponsor

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

NIDA/CTN Rockville, MD

Accelerated Development of Additive Pharmacotherapy Treatment (ADAPT-2) for Methamphetamine Use Disorder (NIDA CTN 0068)

Keith Heinzerling, M.D. UC Los Angeles Los Angeles, CA

Phase 1 Safety-Interaction Study of Pomaglumetad Methionil for Methamphetamine Use Disorder

#### TABLE 2

#### **RESEARCH STUDIES CLOSED IN 2017**

Sponsor / PI

Title of Study / Clinical Drug

Trial Protocol

Thomas Kilduff, Ph.D.

SRI International Menlo Park, CA Neurobiological Studies of Gammahydroxybutyrate (GHB)

Christian Koch, M.D.

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

Walter Ling, M.D.

**UCLA** 

Integrated Substance Abuse Programs

Los Angeles, CA

Analgesic Response to Opioid Analgesics in Buprenorphine-Maintained Individuals

Lalitha Lyer, Ph.D.

SRI International Menlo Park, CA

Pharmacokinetics of Cannabidiol in Dogs

Following Oral Administration

John E. Mendelson, M.D.

CPMC Research Institute/APRL

San Francisco, CA

The Effects of MDMA on Sleep Architecture, Water Homeostasis, and

Cognitive Function

Table 2 Cont.

#### Sponsor / PI

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

Florian Rader, M.D. Cedars-Sinai Medical Center Los Angeles, CA Mechanisms and Modulation of Cocaine Effects on Blood Blow to the Heart

Douglas Sears, MD Encino, CA A Double-Blind, Placebo-Controlled Study of Combination Therapy in Children with ADHD

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 Moderate to Severe Post Operative Pain.

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

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

Ronald G. Victor, M.D. Cedars-Sinai Medical Center Los Angeles, CA

Effects of Cocaine on Blood Flow to the Heart

Cathy Zhang, M.S. Pfizer La Jolla La Jolla, CA

Induction of Myeloid-Derived Suppressor Cells (MDSC) by Tetrahydrocannabinol (THC)

AcelRx Redwood City, CA

A Multicenter, Randomized, Open-Label, Parallel-Group Trial to Compare the Efficacy and Safety of the Sufentanil NanoTab PCA System/15 mcg to Intravenous Patient-Controlled Analgesia with Morphine for the Treatment of Acute Post-Operative Pain (AcelRx 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 (AcelRx SAP202)

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

Alkermes Waltham, MA A Phase 3 Efficacy and Safety Study of ALKS5461 for the Adjunctive Treatment of Major Depressive Disorder (Study I) (ALK5461-205)

Alkermes Waltham, MA A Phase 3 Efficacy and Safety Study of ALKS5461 for the Adjunctive Treatment of Major Depressive Disorder (Study II) (ALK5461-206)

Astra Zeneca, CRO-Quintiles Overland Park, KS A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of NKTR-118 in Patients with Non-Cancer-Related Pain and Opioid-Induced Constipation (OIC) (AstraZeneca D3820C00004)

Astra Zeneca, CRO-Quintiles Overland Park, KS A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of NKTR-118 in Patients with Non-Cancer-Related Pain and Opioid-Induced Constipation (OIC) (AstraZeneca D3820C00005)

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

Astra Zeneca, 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 (AstraZeneca D3820C00006)

Astra Zeneca, 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) (AstraZeneca D3820C00007)

Astra Zeneca, 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 (AstraZeneca D3820C00008)

By Braeburn Pharmaceuticals Princeton, NJ A Randomized, Double-Blind, Double-Dummy, Active-Controlled Multicenter Study of Adult Outpatients with Opioid Dependence Transitioned from a Daily maintenance Dose of 8 mg or Less of sublingual Buprenorphine or Buprenolphine/Naloxone to Four Probuphine Subdermal Implants (PRO-814)

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

Collegium, CRO - INC Research Raleigh, NC

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-Naive Subjects with Moderate-to-Severe Chronic Low Back Pain (Collegium CO-OXYDET-08)

Corbus Pharmaceuticals 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 (JBT101-CF-001)

Egalet, CRO: PPD Wilmington, NC

A Randomized Withdrawal, Double-Blind, Placebo-Controlled Phase 3 Trial to Evaluate the Efficacy and Safety of Egalet® ADER Oxycodone Tablet, Egalet-002 in Patients with Moderate-to-Severe Chronic Low Back Pain (OC-EG-302)

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

Insys Development Company, Inc. Chandler, AZ

A Phase 2 Multicenter, Randomized, Double-Blind, Multiple-Dose, Parallel-Group, Placebo-Controlled Study of Fentanyl Sublingual Spray for the Treatment of Moderate to Severe Post-Operative Pain (INS002-16-092)

By INSYS Therapeutics, Inc. 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)

By INSYS Therapeutics, Inc. 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)

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

Ironshore Pharmaceuticals Camana Bay, Grand Cayman, Cayman Islands A Phase III Clinical Endpoint Evaluation Study Examining the Safety and Efficacy of HLD200 in Pediatric Subjects with Attention-Deficit Hyperactivity Disorder (CEES ADHD) (HLD200-106)

MAPS Santa Cruz, CA Panel Approved Research Study

Pfizer, Inc. New York, NY A Multicenter, 12-Week, Double-Blind, Placebo-Controlled, Randomized Withdrawal Study to Determine the Efficacy and Safety of ALO-02 (Oxycodone Hydrochloride and Naltrexone Hydrochloride) Extended-Release Capsules in Subjects with Moderate to Severe Chronic Low Back Pain (Pfizer B4531002)

Purdue Pharma, 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 (Purdue HYD3003)

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

Purdue Pharma, CRO - INC Research Raleigh, NC

A Multicenter, Randomized, Double-blind, Placebo-controlled Study with an Openlabel Run-in to Assess the Efficacy and Safety of Hydrocodone Bitartrate (HYD) Tablets 20 to 120 mg Once-daily in Subjects with Moderate to Severe Chronic Low Back Pain (Purdue HYD3002)

QRxPharma, CRO: INC Research Austin, TX

A Double-Blind, Randomized, Placebo and Active-Control, Parallel-Group Study to Evaluate the Safety, Tolerability, and Efficacy of Q8011 Compared to OxyContin® and Placebo in Patients with Moderate to Severe Chronic Hip or Knee Pain Due to Osteoarthritis (QRxPharma Q8011)

Shire, CRO: Premier Research 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) (Shire SPD489-405)

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

Shire, CRO: Premier Research 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) (Shire SPD489-406)

Trevena King of Prussia, PA A Phase 3, Multicenter, Randomized, Double-Blind, Placebo- and Active-Controlled Study of Oliceridine (TRV130) for the Treatment of Moderate to Severe Acute Pain After Bunionectomy (CP130-3001)

Trevena King of Prussia, PA A Phase 3, Multicenter, Randomized, Double-Blind, Placebo- and Active-Controlled Study of Oliceridine (TRV130) for the Treatment of Moderate to Severe Acute Pain After Abdominoplasty (CP130-3002)

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

Trevena Chesterbrook, PA

A Phase 3, Open-Label Study to Evaluate the safety of Oliceridine (TRV130) in Patients with Acute Pain for Which Parenteral Opioid Therapy is Warranted (CP130-3003)

US World Meds 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-LX1-3003-1)

Gantt Galloway, Pharm.D. CPMC Research Institute San Francisco, CA A Dose Ranging Study of Modafinil for Methamphetamine Dependence

Keith Heinzerling, MD, MPH UCLA Los Angeles, CA Pharmacogenomics and Medication Development for Methamphetamine Dependence

Lara Ray, Ph.D. UCLA Los Angeles, CA Effects of Naltrexone on Alcohol-Dependent Asian Americans Table 2 Cont.

#### Sponsor / PI

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

Lara Ray, Ph.D. UCLA Los Angeles, CA

Effects of Ibudilast on Non-treatment Seeking Patients Who Meet Criteria for Alcohol Abuse or Dependence

Alkermes Waltham, MA A Phase 3 Study to 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)

Catalyst Pharmaceutical Partners Coral Gables, FL

Vigabatrin for Treatment of Cocaine Dependence: A Phase II Study" (Catalyst CPP-01005)

Teva Pharmaceuticals Frazer, PA

A 12-Week, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of One-Weekly Intra-Muscular Injections of TV-1380 (150mg/week or 300mg/week) as a Treatment for Facilitation of Abstinence in Cocaine-Dependent Subjects (TV1380-COA-201)

#### APPENDIX A

# CURRENTLY OPEN (through December 31, 2017) SCHEDULE I AND SCHEDULE II NON-HUMAN AND ACADEMIC HUMAN RESEARCH STUDIES

Princi	pal Inv	restig	ator

Title of Study

Richard Baldwin, Ph.D.

nanoComposix San Diego, CA Biosensor for the Detection of Synthetic

Cannabinoids

Nelson Barton, Ph.D.

Genomatica, Inc. San Diego, CA Microbial Processes for the Manufacture of

Specialty Chemicals

Nancy E. Buckley, Ph.D. CA State Polytech University

Pomona, CA

Investigating the effect of THC on the susceptibility to systemic C. Albicans infection in mice treated with an anti-cancer

drug

Nicholas Butowski, M.D. UCSF Neurological Surgery San Francisco, CA

CBD Developmental Research Project

Jeremy Caldwell, Ph.D. Genomics Institute Novartis Foundation San Diego, CA High-Throughput Screening of Known Drugs for Novel Biological Activity in Cell-based

Assays

#### Appendix A Cont.

#### **Principal Investigator**

#### Title of Study

John R. Cashman, Ph.D. Human BioMolecular Research Institute San Diego, CA Molecular Evolution of Human Cocaine Catalysis

Kent Chu YJ Bio-Products Cordova, CA Immunochromatographic Test Device for THC and LSD

Laura Colin Biostride, Inc. Redwood City, CA Panel Approved Research Study

Karl Deisseroth, MD, PhD Stanford University Palo Alto, 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

Davide Dulcis, Ph.D. UCSD La Jolla, CA Effects of Neonatal Nicotine Exposure on Dopamine Neurons Affecting Consumption of Substances of Abuse in the Adult

# Principal Investigator

#### Title of Study

Aaron Ettenberg, Ph.D. UC Santa Barbara Santa Barbara, CA Dopamine involvement in Opiate and Stimulant Reinforcement

Christie Fowler, Ph.D. UC Irvine Irvine, CA

Mechanisms of Drug Reinforcement

Olivier George, Ph.D. The Scripps Research Institute La Jolla, CA Animal Models of Addiction: Preliminary Studies of Vaporized THC Self-Administration in a Rat Model

Olivier George, Ph.D. The Scripps Research Institute La Jolla, CA Animal Models of Addiction: Preliminary Studies for Heroin Dependence and Treatments

Mark A. Geyer, Ph.D. Dept of Psychiatry, UCSD La Jolla, CA Effects of Cannabidiol on Mania-relevant Locomotor and Investigatory Behavior

Alidad Ghiassi, M.D. Keck School of Medicine USC Los Angeles, CA A Randomized Trial Comparing Ibuprofen Plus Acetaminophen Versus Oxycodone After Outpatient Soft Tissue Hand Surgery Appendix A Cont.

**Principal Investigator** 

Title of Study

William Haseltine, Ph.D. Demetrix, Inc.

Emeryville, CA

Production of Natural and Modified Cannabinoids using Engineered, Industrial

Microorganisms

Brook Henry, Ph.D. UC San Diego

San Diego, CA

Effect of Cannabis Administration and Endocannabinoids on HIV Neuropathic Pain

Study - Phase 2

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

Kim D. Janda, Ph.D. The Scripps Research Institute

San Diego, CA

Immunopharmaco Therapy for Methamphetamine Addiction

Gunjan Junnarkar, Ph.D. Jazz Pharmaceuticals

Menlo Park, CA

Oxybate Research

# **Principal Investigator**

# Title of Study

Jay Keasling, Ph.D. Joint Bioenergy Institute Emeryville, CA Engineering the Industrial Microbe Saccharomyces Cerevisiae for Biosyntheris of Cannabinoids

Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA

Panel Approved Research Study

Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA

Panel Approved Research Study

Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA Panel Approved Research Study

Daniel Levin, Ph.D. S&B Pharma, Inc. Azusa, CA Panel Approved Research Study

Marie Lin, Ph.D. Lin-Zhi International Sunnyvale, CA Lin-Zhi Immunoassay Development Study

#### Appendix A Cont.

#### Principal Investigator

#### Title of Study

Stephen Mahler, Ph.D. UC Irvine Irvine, CA Neural Circuits Underlying Motivation and Addiction

Robert Malenka, M.D. School of Medicine Stanford University Palo Alto, CA The Role of Oxytocin in the Pathogenesis of Avtism

Thomas Marcotte, Ph.D. UCSD Health Care System San Diego, CA A Randomized, Controlled Trial of Cannabis in Healthy Volunteers Evaluating Simulated Driving, Field Performance Tests and Cannabinoid Levels

Sean D. McAllister, Ph.D. CPMC Research Institute San Francisco, CA

Panel Approved Research Study

Sara Mednick, Ph.D. UC Riverside Riverside, CA The Effects of Zolpidem and Dextroamphetamine on Cognitive Performance

Byung-Sook Moon ARK Freemont, CA Research and Development of in-Vitro Diagnostic (IVD) Immunoassays for Drug of Abuse Testing

# Principal Investigator

# Title of Study

Stephen Morairty, Ph.D.

SRI International Menlo Park, CA Panel Approved Research Study

Heinz Moser, Ph.D. Novartis Institute Emeryville, CA Synthesis and Optimization of Novel Therapeutics

Alysson Muotri, Ph.D. UC San Diego La Jolla, CA The Impact of CBD/THC on Human Neurodevelopment

Lori Olson, M.S. SRI International Menlo Park, CA

Identification and isolation of specific pesticides from cannabinoid oils

David E. Olson, Ph.D. UC Davis Davis, CA Chemical Modulation of Neural Plasticity, Learning and Memory

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

Mark Peterman, Ph.D. OndaVia Hayward, CA Development of a Rapid and Field-Ready Heroin analysis Tool

# Principal Investigator

# Title of Study

Daniele Piomelli, Ph.D. UC Irvine Irvine, CA 1. Effect of Adolescent Cannabis Exposure in Adults Mice and Rats

Richard Reznichek, M.D. Harbor-UCLA Los Angeles, CA Panel Approved Research Study

David Schubert, Ph.D. Salk Institute La Jolla, CA The Identification of Neuroprotective Compounds in Cannabis

Philip Schwartz, Ph.D. Children's Hospital of Orange County Orange, CA Effect of Receptor Activation on Human Neuron Stem Cell Function

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

Ivan Soltesz, Ph.D. Stanford University Stanford, CA Investigating the Effect of Naturally-Occurring Cannabinoids on Synaptic Physiology, Cognition and Epilepsy

# Principal Investigator

# Title of Study

Matthew L. Springer, Ph.D. UCSF San Francisco, CA Assessment of Harmful Cardiovascular Effects of Marijuana Secondhand Smoke and Vaporizers

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

Francesca Telese, Ph.D. UCSD La Jolla, CA Epigenetic Regulation of Gene Expression in the Brain

Friedbert Weiss, Ph.D. The Scripps Research Institute La Jolla, CA Ethanol Seeking and Relapse: Therapeutic Potential of Transdermal Cannabidiol

# Principal Investigator

# Title of Study

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

Joshua Woolley, MD, PhD UCSF VA Medical Ct. San Francisco, CA Psilocybin-Assisted Group Therapy for Demoralization in Long-Term Aids Survivors

Matthew Worley, Ph.D. UCSD La Jolla, CA Behavioral Economic Mechanisms of Prescription Opioid Addiction in Chronic Pain

Roya Yumul Cedars-Sinai Medical Ct. Los Angeles, CA Intra-operative ketamine and methadone for laminectomy: effect on recovery, post-operative pain, and opioid requirements

Brandon Zipp, Ph.D. Vitality Biopharma, Inc. Los Angeles, CA Cannabinoid-Glycoside Pharmaceutical Prodrug Development and Evaluation

#### APPENDIX B

# CURRENTLY OPEN (through December 31, 2017) SCHEDULE II CLINICAL DRUG TRIAL STUDIES

**Sponsor** 

Description or Title

of Clinical Drug Trial Protocol

Alkermes, Inc. Waltham, MA

A Study to Evaluate the Effect of ALKS 3831 Compared to Olanzapine on Body Weight in

Young Adults with Schizophrenia,

Schizophreniform or Bipolar I Disorder Who

are Early in Their Illness

(ALK3831-A307)

Alkermes, Inc. Waltham, MA

A Phase 3 Study to Assess the Long Term Safety, Tolerability, and Durability of

Treatment Effect of ALKS 3831 in Subjects with Schizophrenia, Schizophreniform

Disorder, or Bipolar I Disorder

(ALK3831-A308)

Alkermes, Inc. Waltham, MA

A Phase 3b Efficacy and Safety Study of Adjunctive ALKS5461 in Treatment Refractory Major Depressive Disorder

(ALK5461-217)

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)

**Sponsor** 

Description or Title

of Clinical Drug Trial Protocol

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, Inc. 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, Inc. Waltham, MA

A Phase 3, Multicenter Study to Assess the Long Term Safety and Tolerability of ALKS

3831 in Subjects with Schizophrenia

(ALK3831-A306)

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)

### **Sponsor**

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

Alkermes, Inc. Waltham, MA A Randomized, Double-Blind, Parallel-Group Study in Healthy Subjects to Characterize Insulin Sensitivity and Lipid Metabolism in Response to Treatment with ALKS 3831 and Olanzapine (ALK3831-A108)

Alkermes, Inc. Waltham, MA

A Phase 3, Multicenter Study to Assess the Long Term Safety and Tolerability of ALKS 3831 in Subjects with Schizophrenia (ALK3831-A304)

CNS Therapeutics

CRO: Social & Scientific Systems

Panel Approved Research Study

**CNS Therapeutics** 

CRO: Social & Scientific Systems

Panel Approved Research Study

Corbus Pharmaceuticals Norwood, MA A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial to Evaluate Efficacy and Safety of Lenabasum in Diffuse Cutaneous Systemic Sclerosis (JBT101-SSc-002)

Sponsor

Description or Title

of Clinical Drug Trial Protocol

Flamel Ireland CRO: INC Research Austin, TX

A Double-Blind, Randomized, Placebo-Controlled, Two Arm Multi-Center Study to Assess the Efficacy and Safety of a Once Nightly Formulation of Sodium Oxybate for Extended-Release Oral Suspension (FT218) for the Treatment of Excessive Daytime Sleepiness and Cataplexy in Subjects with Narcolepsy

(CLFT218-1501)

Grunenthal/Janssen CRO: inVentiv Cary, NC

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

# **Sponsor**

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

Insys Chandler, AZ A Phase 2, Randomized, Open Label, Multiple-Dose, Comparator, Parallel-Group, Safety and Tolerance Study of Buprenorphine Sublingual Spray (0.5mg TID) versus Standard of Care Post-Operative Narcotic Therapy for the Treatment of Post-Operative Pain (INS005-17-111)

Insys Chandler, AZ A Phase 2, Open-Label, Dose-Finding Study to Assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of Pharmaceutical Grade Synthetic Cannabidiol Oral Solution in Pediatric Patients with Treatment-Resistant Childhood Absence Seizures (INS011-17-103)

Insys Chandler, AZ

A Multicenter, Open-Label, Flexible Dose Study to Assess the Long-Term Safety of Pharmaceutical Grade Synthetic Cannabidiol Oral Solution as in Pediatric Patients with Treatment-Resistant Childhood Absence Seizures (INS011-17-113)

Sponsor

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

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)

Jazz Pharmaceuticals CRO: Quintiles Overland Parks, KS A Double-Blind, Placebo-Controlled, Randomized-Withdrawal, Multicenter Study of the Efficacy and Safety of JZP-258 in Subjects with Narcolepsy with Cataplexy (15-006)

MAPS Santa Cruz, CA Panel Approved Research Study

MAPS Santa Cruz, CA Panel Approved Research Study

NIH/NIAID Rockville, MD A Phase 2, Double-blind, Randomized, Placebo-controlled Multicenter Study to Evaluate Efficacy, Safety, and Tolerability of JBT-101 in Systemic Lupus Erythematosus (ALE09)

# **Sponsor**

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

Noven New York City, NY A Randomized, Multiple-Dose, Open-Label, 4-Week Study to Characterize the Pharmacokinetics, Cumulative Irritation, Safety, and Tolerability of d-Amphetamine Transdermal System (d-ATS) in Adults Diagnosed with ADHD (N25-015)

Pfizer CRO: ICON New York, NY

Panel Approved Research Study

Pfizer CRO: ICON New York, NY

Panel Approved Research Study

Purdue CRO: PRA Raleigh, NC

A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel Group, Laboratory Classroom Study to Evaluate the Safety and Efficacy of PRC-063 Compared to Placebo in Children (6-12 years of age) with ADHD (063-015)

**Sponsor** 

<u>Description or Title</u>

of Clinical Drug Trial Protocol

Recro Pharma Malvern, PA A Phase 2, Randomized, Double-Blind,

Placebo- and Active-Controlled, Evaluation of the Efficacy and Safety

of DEX-IN Following Painful Outpatient

Procedures (REC-17-023)

Shire

CRO: PPD

San Diego, CA

Panel Approved Research Study

Shire

CRO: PPD San Diego, CA Panel Approved Research Study

Vertex Boston, MA A Phase 2 randomized, Double-Bind, Placebo-Controlled, 3-Arm, Parallel-Design Study of the Efficacy and Safety of VX-150 for Acute Pain Following Bunionectomy (VX16-150-103)

#### APPENDIX C

# CURRENTLY OPEN *(December 31, 2017)*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

Keith Heinzerling, M.D. UC Los Angeles Los Angeles, CA Phase 1 Safety-Interaction Study of Pomaglumetad Methionil for Methamphetamine Use Disorder

Steven Shoptaw, Ph.D. UCLA.
Los Angeles, CA

Varenicline for Methamphetamine Dependence

Steven Shoptaw, Ph.D. UCLA.
Los Angeles, CA

Phase I Safety Interaction Trial of Ibudilast with Methamphetamine

NIDA/NSC/NIH Bethesda, MD Phase 2, Multi-Center Trial of Lorcaserin for the Treatment of Cocaine Use Disorder (NIDA/VA CS #1033)

# **Investigator or Sponsor**

# Description or Title of Research Project

NIDA/NSC/NIH Bethesda, MD

Comparing Treatments for HIV-Infected Opioid Users in an Integrated Care Effectiveness Study (CHOICES) Scale-Up (NIDA CTN 0067)

NIDA
The EMMES Corp.
Rockville, MD

Extended-Release Naltrexone vs. Buprenorphine for Opioid Treatment (X:BOT) (0051)

NIDA/CTN Rockville, MD Accelerated Development of Additive Pharmacotherapy Treatment (ADAPT-2) for Methamphetamine Use Disorder (NIDA CTN 0068)

#### 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.