Results: Approximately 30 formulations designed for nasal delivery by POD technology were manufactured and then assessed using analytical chemistry techniques and device-compatibility testing. Twenty of the formulations were evaluated in rat and NHP PK models. Short-term stability tests and device compatibility testing were used to further narrow down formulations for additional PK studies. The lead formulation was tested to five months of stability with >99% assay, <1% total impurities, and positive device compatibility over the storage period. All formulations tested in NHP PK studies resulted in a Tmax of less than 53 minutes and a Cmax greater than 26 nanograms per milliliter (ng/mL). The lead formulation, selected for clinical development in the INP105-101 study, exhibited a Tmax of 17 minutes, similar to that reported for IM OLZ, and a Cmax of 71 ng/mL, approximately threefold higher than the reported Cmax in patients receiving 10 milligrams (mg) IM OLZ.

Conclusion: Impel NeuroPharma is developing a drug-device combination product that will administer powder OLZ to the vascular-rich, upper nasal space with a novel precision olfactory delivery (POD®) device. It is needle-free, easily administered by self or caregiver, and a potentially rapidly effective OLZ treatment to abort episodes of acute agitation in the low-intensity community clinic or emergency department setting. This series of preclinical development studies has led to the identification of a lead formulation to be tested in the INP105-101 proof-of-concept clinical study for further development.

9 Heroin Abstinence: A Case Report of Kratom in the Emergency Department and Beyond

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Introduction: Kratom, an herb that was traditionally used by Southeast Asians to boost energy, is increasingly being used in the United States. According to the American Kratom Association, an estimated two to three million chronic pain sufferers resort to kratom as a "safe," natural alternative to prescription opioids. Some of the reported beneficial effects include analgesic effects, muscle relaxation, and anti-inflammatory properties. In the drug addiction world however, kratom is being propagated as a legal alternative to getting high that is undetectable on routine drug screen. Kratom, or mitragynine, is a major psychoactive alkaloid. Several studies have found that kratom has stimulant effects in small doses but sedative effects in large doses, binding to mu and kappa receptors (Yusoff et al. 2014). Kratom causes cravings and an array of opioid-like withdrawal symptoms when users attempt to decrease usage. Withdrawal symptoms include restlessness, severe bone pain, muscle aches, tearing or runny nose, gastrointestinal (GI) symptoms, blurred vision, depression, irritability, and changes in mood. This case report documents one patient who used kratom as an alternative to heroin use. We also describe its subsequent addictive potential and the successful management of his withdrawal symptoms with an opioid detoxification protocol.

Case Presentation: Our patient was an adult Caucasian male with a past psychiatric history of depression and severe opioid use disorder identified by appropriate history- taking. The patient recounted that he had been using kratom for the prior two and a half years as a "legal alternative" to heroin, motivated by his partner. At the time of encounter, he reported "strong cravings" and withdrawal symptoms when he attempted to abstain from kratom. Urine drug screen was negative. A quick Clinical Opioid Withdrawal Scale (COWS) evaluation was noted to be 30, and inpatient detoxification was deemed appropriate. He admitted to using initially four capsules per day, which increased up to 30 capsules a day over the 30-month time period. He reported having spent a lot of money to feed his habit and noted weight loss and decreased appetite. He reported, "I felt high," and maintained that he had abstained from illicit heroine use. The patient admitted that he had not known kratom had addictive properties and reported that the withdrawal symptoms were more protracted – as long as two months post his last use when compared to that of heroin after being "hard stopped" during a brief incarceration. We used a COWS assessment and scoring to determine management of his withdrawal symptoms at initial presentation and over a short period of time. We measured vital signs, hepatic function, and management of withdrawal symptoms daily two hours after the delivery of daily buprenorphine and naloxone (using tapering protocol) for five days. We also administered clonidine at a dose of 0.1 milligrams (mg) by mouth every six hours (PO q6h), baclofen 10 mg PO for muscle spasms, chlorproamazine/ diphenhydramine 50mg as needed (PRN) for agitation, and ibuprofen 600mg PO q6h PRN for generalized joint pain. We monitored his symptomology by patient evaluation, daily vital signs, and a physician-guided questionnaire.

Results: Electrolytes, renal function and liver studies were found to be within normal limits; however, his heart rate was elevated at 100 beats per minute on day of admission. Blood pressure was 122/75 millimeters of mercury and temperature was 97.5° Fahrenheit with a body mass index of 21.5. Urine toxicology was negative for all drugs of abuse including methadone and opiates. The patient's pupils were constricted and there was profuse diaphoresis visible over his forehead. He also reported joint pain throughout his body, and he was unable to sit still. His eyes were tearing, he had uncontrollable yawning, and complained of "skin crawl." The patient denied having any GI symptoms such as diarrhea or nausea, and he also denied having tremors. No tremors were observed, although muscle twitching of his forearm and biceps was noted. His COWS score was noted to be 30 on day one, and considered moderately severe. HIS COWS score

reduced to five by day four. Of note, the COWs scale increased to 10 by day seven on 0mg of buprenorphine and naloxone.

Conclusion: Kratom possesses properties that can be successfully used as an alternative to heroin use. Nonetheless, there is a potential for abuse, which results in severe opioid- like withdrawal symptoms when the user attempts abstinence. Patients require increasing amounts of kratom as they develop tolerance. Kratom withdrawal symptoms can be successfully managed with opioid detox protocol or buprenorphine/naloxone protocol over a period of five days, although symptoms noticeably last longer. Pharmaceutical companies should explore safe, physician-guided administration of kratom to reduce heroin use and add to our repertoire of methadone or buprenorphine in managing opioid use disorders.

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10 A Case Report and Postulated Systematic Approach to the Evaluation of Emotionalism Post Stroke in a Crisis Unit

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Introduction: Emotionalism post stroke, when inadequately addressed, can cause distress to patients including embarrassment, confusion, possible caregiver complaints, and an overall decrease in health-related quality of life (Badhan, et al, 2014). Also known as pathological laughing and crying (PLC), emotionalism post stroke refers to the involuntary and neurologic pseudo-bulbar affect (PBA). It often leads to uncontrolled and exaggerated expressions of inappropriate, emotionally charged outbursts such as laughing and/or crying (Parvizi, et al, 2001). This "emotional lability" is usually seen in patients with neurological disorders, in particular stroke, and was first described in the literature in 1872. While the exact mechanism can be debated, studies suggest a lesion in the upper brainstem leading to involuntary triggering of the facio-respiratory patterns associated with laughter and crying that involve the motor cortices (Parvizi, et al. 2001) or the cerebellum (Sak, Wilson, 1924). However, with recent studies reporting the prevalence of depression as high as 29% post stroke (Ayerbe, et al, 2013), identifying differences between post-stroke depression and PBA in the emergency setting is crucial for appropriate treatment and disposition. A critical component of patient history with regard to PLC is the lack of inciting stimulus in reports of numerous episodes of pathological crying. This study aims to outline a systematic approach to evaluate and manage patients with PLC in the emergency department (ED).

Case Presentation: The patient was a 74-year-old Caucasian male with no formal PPH and PMH of T2D, HLD, HTN, who was brought by his wife to the ED with complaints of excessive crying and a reported verbalization of suicidal ideation. Upon interview, patient stated that he had been having "crying spells" in excess of emotional stimulus for the prior three months, increasing in severity. He denied neuro-vegetative symptoms of depression. Patient also denied recent stressors. He admitted to a transient ischemic attack five months prior to his presentation. He stated there were no neurological deficits at the time of encounter except for a noted decreased sense of taste. The patient admitted to having suicidal ideations (SI) but without intent, plan, or means. He determined that he had intermittent SI in the context of observing, "Doesn't everyone think about that sometimes?" He did not report details of his SI as he determined they were passive and vague thoughts of what it would be like to be dead. He denied past or recent suicide attempts or self-injurious behavior. The patient reported he had met with his primary care physician who advised him to go to the ED for further evaluation. The patient and his wife, also in her 70s, reported they thought the ED could prescribe medications and were not seeking hospitalization. His wife stated that the patient had been "crying at the drop of a hat." She noted that this was not usual for him and denied any recent stressors, or past episodes. She further stated, "I was at my wit's end and I feel like something is wrong with him." Patient stated the breaking point was his inability to attend an important engagement due to a dis-inhibited "crying spell" that lasted > 10 minutes. He and his wife reported frustration. The patient also reported, "I can't take it. Please help me." Patient affect was depressed, with intermittent "episodes of crying." We placed him on hold and re-evaluate status.

Method: Patient consent for this study was obtained. A literature search was performed in PubMed and JAMA Psychiatry for articles published on pathological laughing and crying since 1900, using multiple combinations of the search terms, which included the following: post stroke crying syndrome, emotionalism post stroke, involuntary emotional expression, and post stroke neurological disorders. The development of evidence approach and drafting of systemic approach.

Results: On observation, the patient had depressed affect and intermittent episodes of crying without provocation. He repeatedly denied being depressed and denied neuro-vegetative symptoms of depression despite his affect. Psychological review of systems was negative. Vital signs, complete blood count, and electrolytes were within normal limits. Collateral information was obtained and old chart review revealed mild to moderate small-vessel ischemic changes, including a semi-ovale infarct five months prior to presentation. His wife stated she wanted help for his presumed depression. Clinical pathway for the evaluation of emotionalism post stroke in the crisis unit