Intranasal human abuse potential of PF614: A novel 'Next Generation' Trypsin Activated Abuse Protected (TAAP) opioid

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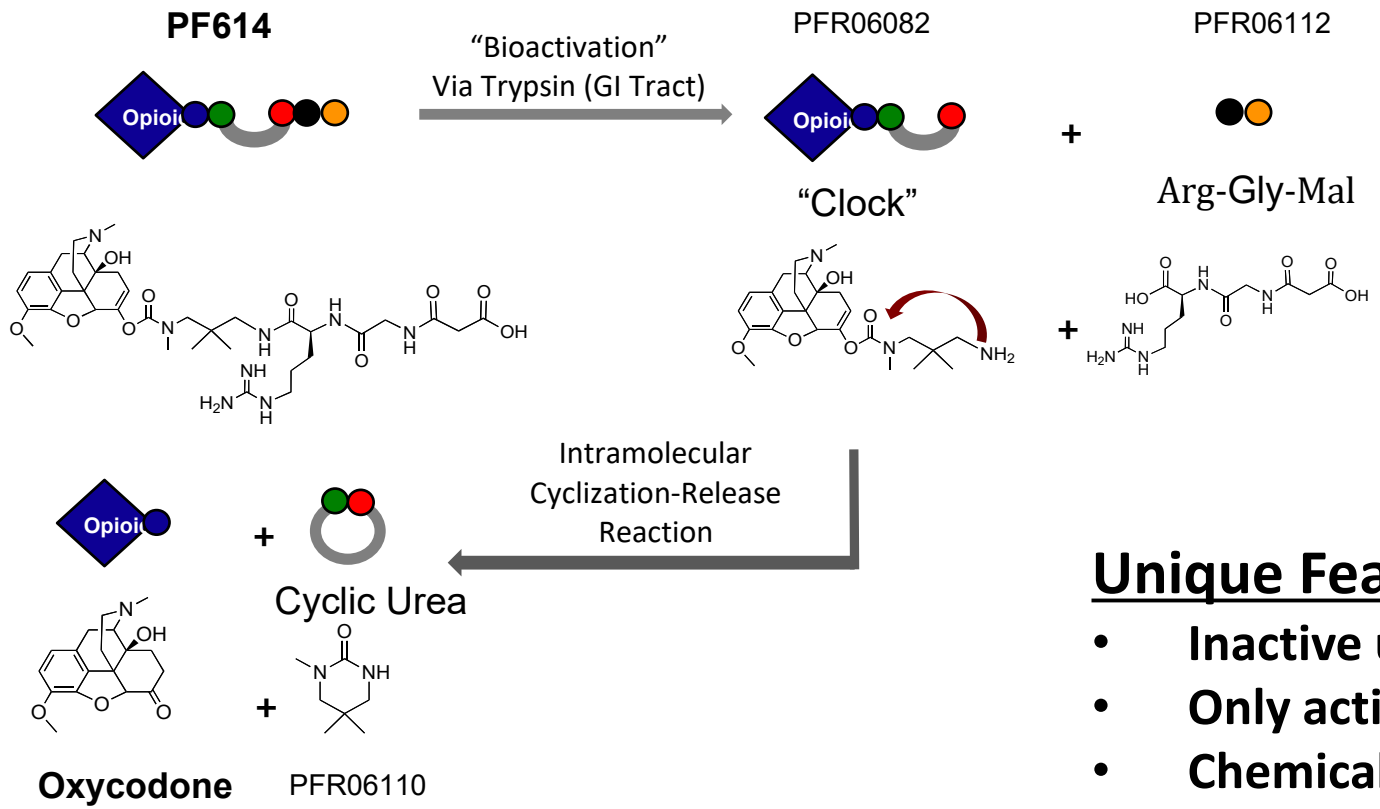
TAAP - Trypsin Activated Abuse Protection

Conversion of PF614 to Oxycodone



Previous Phase 1 study (Healthy Volunteers)

100 mg PF614 bioequivalent to 40 mg OxyContin

T_{max} = 6 hr (vs. 2-3 hr OxyContin)

$t_{1/2}$ = 12 hr (vs. 4.4 hr OxyContin)

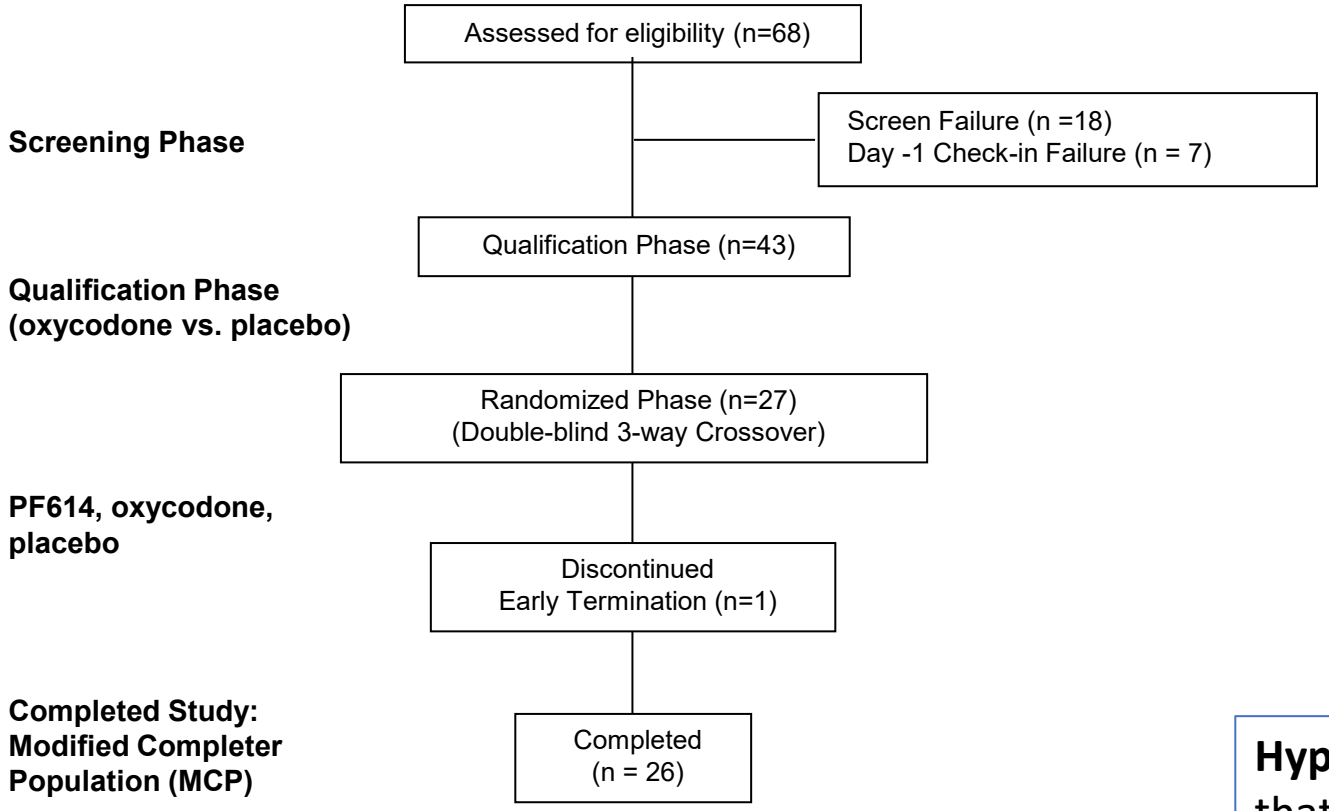
Unique Features:

- **Inactive until swallowed**
- **Only activated by trypsin (enzyme) in GI tract**
- **Chemical modification (not an ADF formulation)**
- **Not altered by manipulation**

PF614-103

Intranasal Human Abuse Potential Study: PF614, oxycodone, placebo

CONSORT Study Design



Screening Visit : standard physical exam, review of Inclusion / Exclusion criteria, Informed Consent

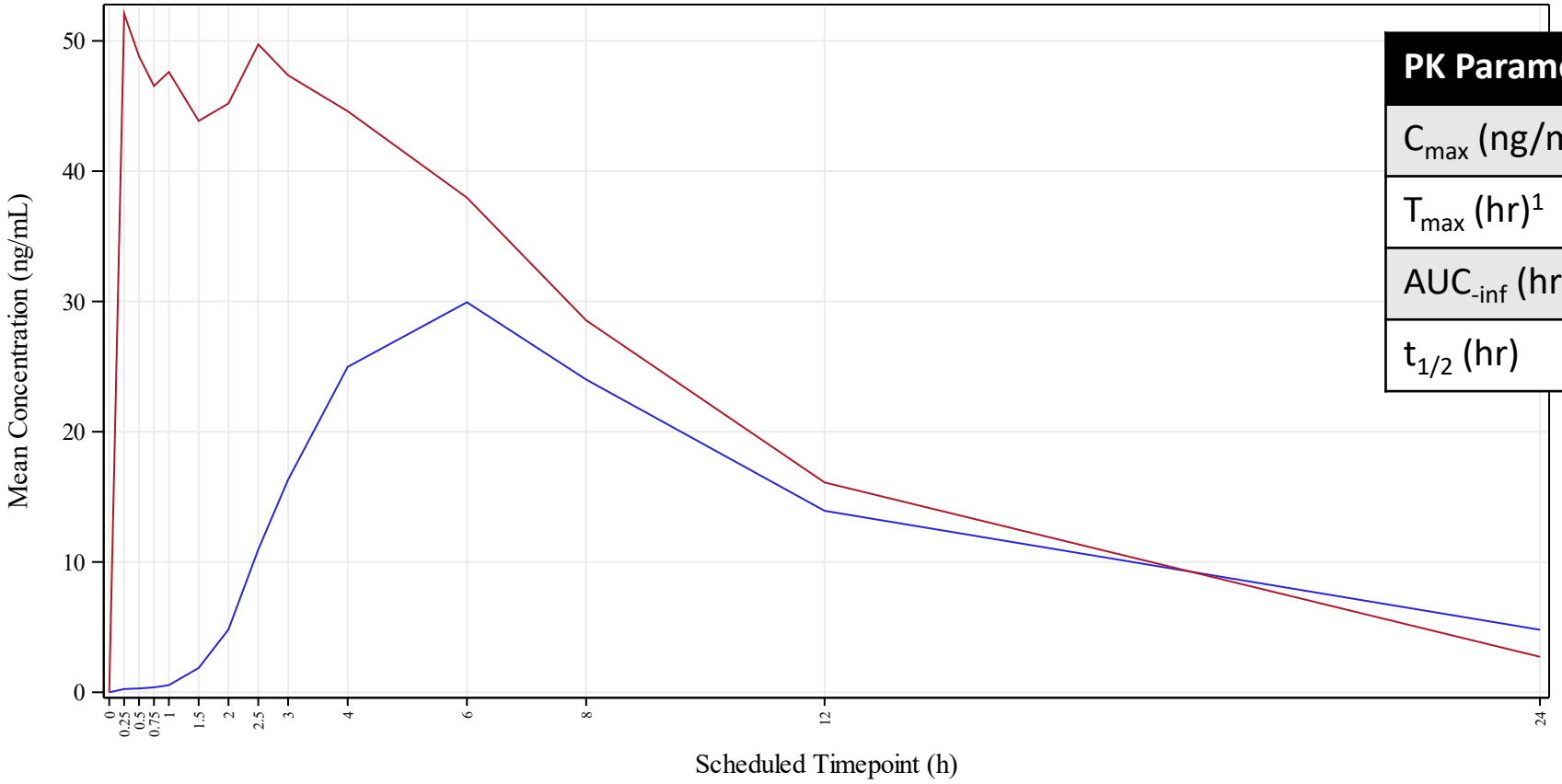
Qualification Phase: Naloxone Challenge Test (confirm non-dependent on opioids); double-blind crushed oxycodone HCl IR (40 mg) vs. placebo drug discrimination test

Randomized Phase: Double-blind, randomized, triple cross-over evaluation of PF614 (100 mg) vs. crushed oxycodone HCl IR (40 mg) & placebo

Hypothesis: only the small portion of insufflated PF614 that is swallowed will activate in the GI tract

PF614-103 Human Abuse Potential

Pharmacokinetics: Mean Plasma Oxycodone (ng/mL)



PK Parameters	Oxycodone	PF614
C_{max} (ng/mL)	67.0 ± 15.6	33.7 ± 19.2
T_{max} (hr)[1]	1.3	6.1
AUC_{-inf} (hr*ng/mL)	559 ± 185	381 ± 189
$t_{1/2}$ (hr)	4.4 ± 1.3	6.6 ± 1.7

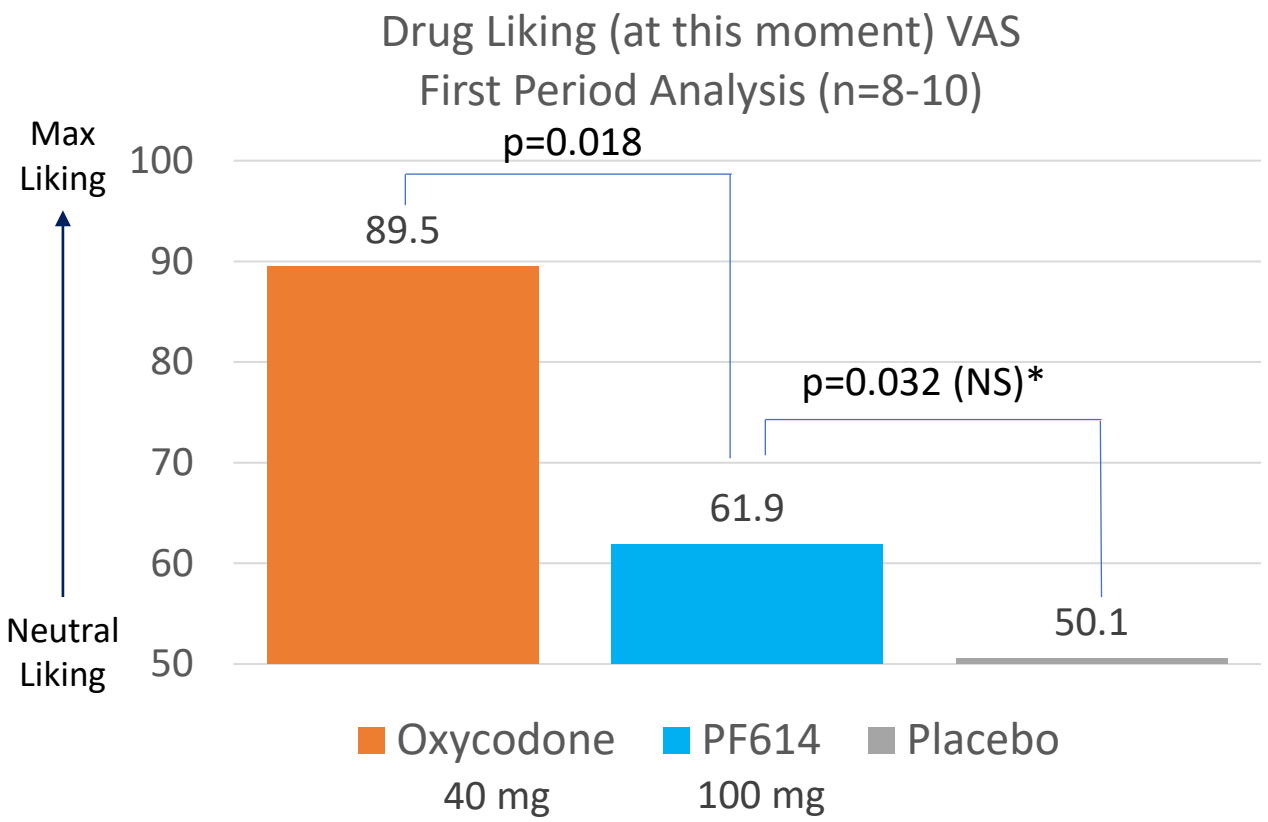
[1]Median value; other values are Mean ± SD

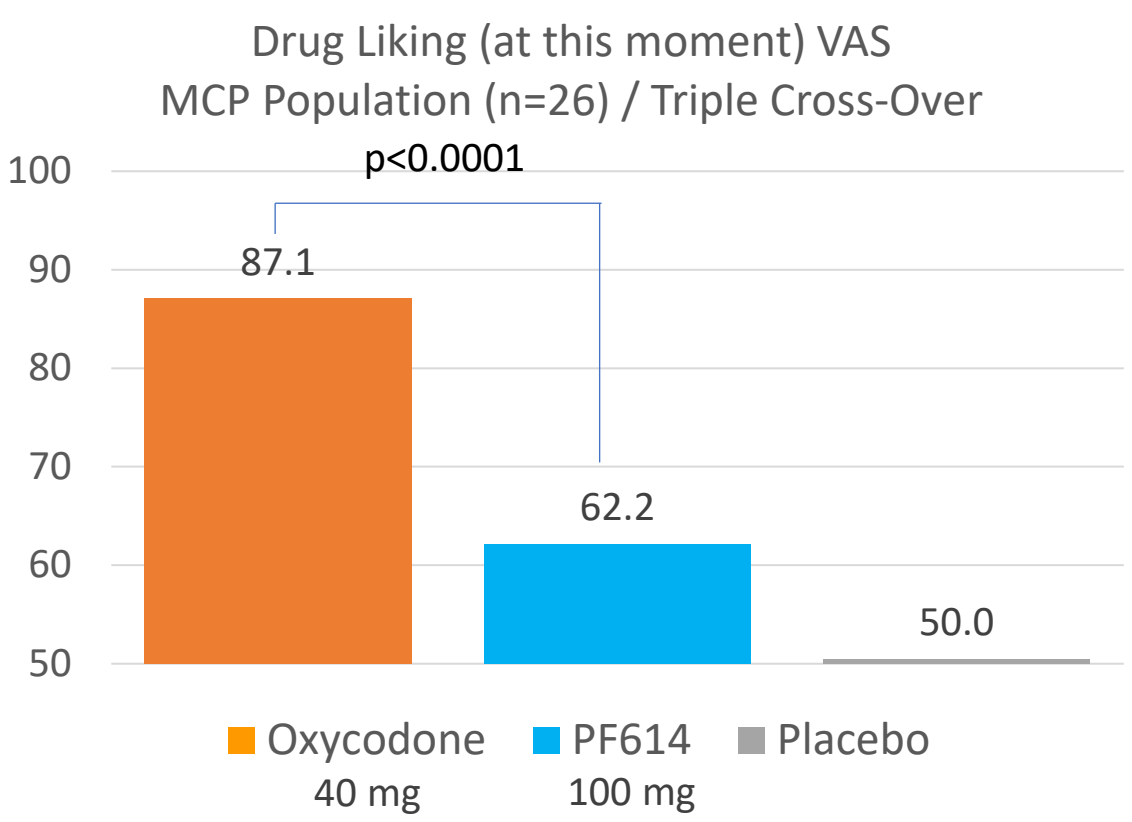
Hypothesis Confirmed:
Following insufflation, only the small portion of PF614 that is swallowed will activate in the GI tract

Crushed Oxycodone HCl IR tablet (40 mg) PF614 (100 mg)

PF614-103 Human Abuse Potential

Drug Liking Visual Analog Scale (VAS), E_{max} / Primary Endpoint

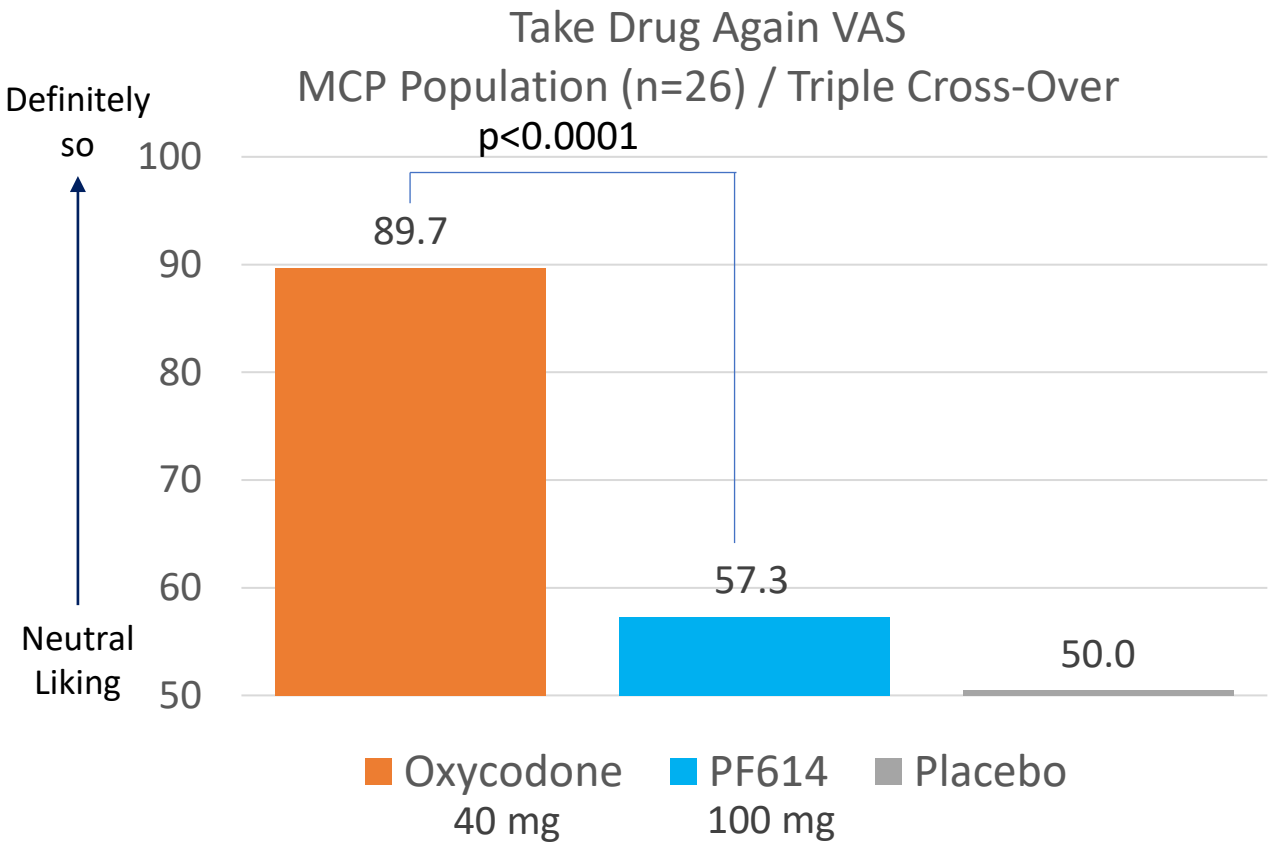




*One-way analysis; p<0.025 required for statistical significance

PF614-103 Human Abuse Potential

Take Drug Again (VAS), E_{max} / Key Secondary Endpoint



Conclusions:

- Intranasal PF614 showed significantly less abuse potential than ***bio-equivalent*** doses of crushed IR oxycodone HCl especially with lack of desire to "Take Drug Again."

- PF614 could represent a new class of "**Next Generation Opioids"** that:
  - require trypsin activation, and
  - cannot be manipulated to release an immediate-onset drug load