Intranasal and Oral Human Abuse Potential (HAP) Studies with PF614: A Novel Trypsin Activated Abuse Protected (TAAP) Oxycodone Prodrug

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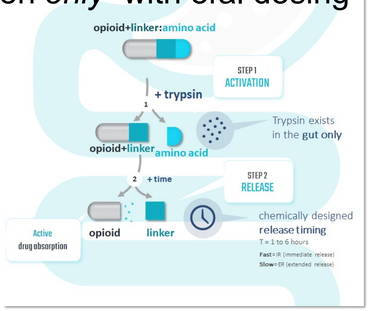
Introduction

Ensysce's "Next Generation" opioids use a chemical approach to reduce abuse (**TAAP™**) and overdose (**MPAR®**). **TAAP prodrugs represent novel products that are inactive until swallowed and activated by trypsin in the small intestine. They deter abuse by chemically controlling the rate of release, and reducing release by all non-oral modes of administration.** PF614 is an oxycodone-derived TAAP prodrug, designed to reduce abuse through its trypsin based extended-release profile.

Ensysce's TAAP Technology Platforms are Driven by *Chemistry*, and not by *Formulation*

TAAP™ Trypsin Activated Abuse Protection — Activation *only* with oral dosing



Two Step Activation

1. **Swallow**: trypsin 'turns on' activation
2. **Chemically controlled release** for immediate and extended-release products.

PF614 is Bioequivalent to OxyContin® but with advantages.

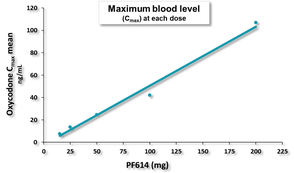
	PF614		OxyContin
Efficacy		=	
Pain Relief (half-life hr)	12.7	>	7.6
Safety		=	
Can dissolve in water[2]	✓		X
Difficult to manipulate	✓		X
Snorting/injecting undesirable	✓		X
Overdose Protection Possible	✓		X

Methods

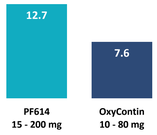
Study Populations:
Non-dependent recreational drug users who were prequalified to identify oxycodone vs. placebo tablets (oral) or crushed tablets (nasal) before enrollment into 3-way or 5-way crossover studies

Study Endpoints:
Key endpoints for both oral and intranasal studies:
'Drug Liking' and 'Take Drug Again'
were evaluated for up to 24 hr after dosing.

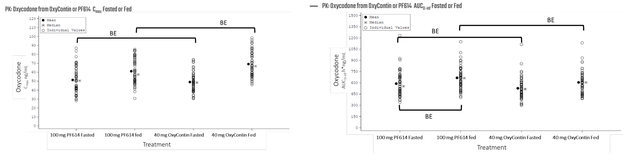
PF614 delivers oxycodone efficiently (linear PK)



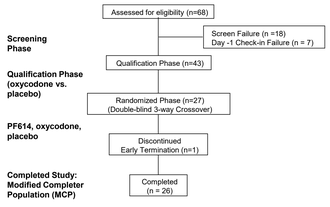
Longer half-life than OxyContin



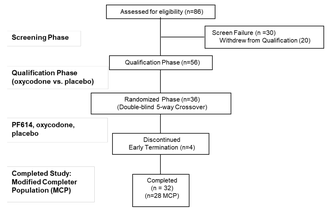
PF614 shows bioequivalence to OxyContin



Intranasal HAP study design



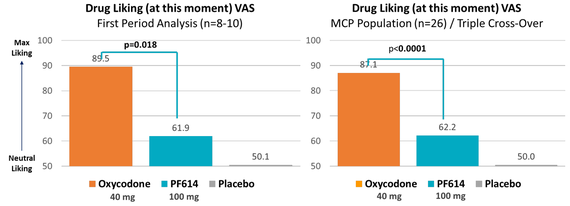
Oral HAP study design



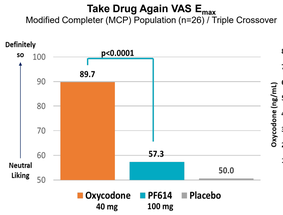
Results

Intranasal HAP study

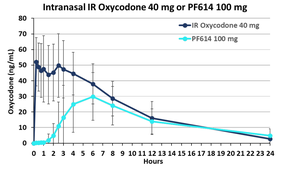
Drug Liking at the Moment



Take Drug Again

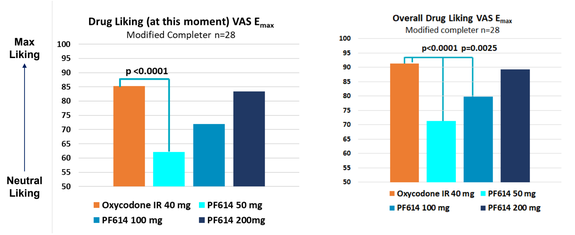


Nasal PK

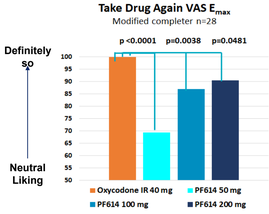


Oral HAP study

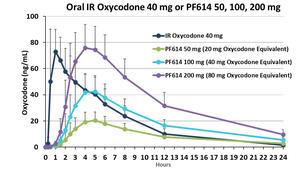
Drug Liking at the Moment / Overall



Take Drug Again



Oral PK



Conclusions

- Both **intranasal** and **oral** PF614 showed significantly less abuse potential than IR oxycodone.
- Intranasal PF614 had significantly lower VAS scores for 'Drug Liking at this moment' and 'Take Drug Again' than crushed IR oxycodone.
- Oral PF614 required a significantly longer median time to reach peak effect for "Drug Liking" than oxycodone at all three dose levels.
- Intravenous (IV) abuse deterrent studies have not been required by the FDA since IV administered PF614 will never be exposed to trypsin and hence will pass out of the body in an inactive form.
- PF614 could represent a new class of 'Next Generation of Opioids' that require trypsin activation, have reduced abuse potential, and cannot be manipulated to release an immediate-onset drug load.