There has never been a greater need for safe and effective analgesics...

- Conventional opioids and nonsteroidal analgesics (NSAIDs) carry significant risks of addiction and adverse side effects.

- Side effects lower quality of life and drive medical costs; thousands of patients are tragically dying from opioid overdose, stroke and heart attacks.

- Our novel pH-sensitive compound (NFEPP) selectively acts at sites of inflammation where tissue is acidic but not elsewhere in the body (e.g., brain) and hence is devoid of addiction risk and other side effects.

- The pain market is projected to increase by 50% in North America in 5 years.
NFEPP: First-in-Class Analgesic that Could Replace Opioids and NSAIDs

- Similar potency as opioids, NSAIDs and local anesthetics in inflammatory and cancer pain
- No addictive potential due to selective targeting of acidic pain sites outside of the brain; no side effects such as nausea, constipation, respiratory depression, cognitive and locomotor impairment
- Compelling pre-clinical data in multiple pain models and independent laboratories
- Potential anti-inflammatory and anti-cancer effects

"the non-addictive pain killer that lacks side effects"

Pharmacology & Therapeutics 2020;210:107519
Trends Pharmacol Sciences 2013;34:303
pHarm Therapeutics: First-in-Class Analgesic Selective for Site of Pain Origin

- pH-sensitive NFEPP selectively acts at sites of inflammation/injury (low pH) but not elsewhere in the body (normal pH, e.g. brain)
- US patent 14/239,461
- Ready for IND-enabling studies
- Potential phase I/II clinical trial in orthopedic surgery in 3-5 years
NFEPP has multiple indications in the growth pain market (red circles)

Pathological opioid receptor

addiction + side effects

protonated fentanyl binds MOR

mu opioid receptor

fentanyl

NFEPP is only protonated in acidic tissues (inflamed)

	\[
\text{pK}_a = 6.8 \\
\text{F}^+ \text{ at R1 or R2}
\]

inflammation + cancer pain models

Pre-clinical validation

Spahn et al. Science 2017
NFEPP: External and Cross-Species Validation
NFEPP has multiple indications in the growth pain market (red circles).

Visceral inflammatory pain

NFEPP has similar potency to fentanyl for inflammatory and cancer pain.

Replicated in 3 other models:
- Arthritis inflammatory pain
- Cancer inflammatory pain
- Post-operative inflammatory pain

NFEPP has multiple indications in the growth pain market (red circles).

Fentanyl directly produces addictive behaviour (addiction reward).

NFEPP induces no addictive behavior but pain relief (analgesia reward).

Massaly et al. Pain 2020

Spahn et al. Science 2017
Safety Data: Monitoring Major Opioid Side Effects in GI tract and Lungs

Oral gavaged contrast CT scans showing Fentanyl but not NFEPP paralyzes GI motility

Fentanyl has major side effects but not NFEPP

*Degro et al Pain 2023
Jimenez-Vargas et al Gut 2022*
NFEPP has multiple indications in the growth pain market (red circles). Degro et al. PAIN 2023

NFEPP inhibits human pain nerves only in acidic inflamed tissues.

Degro et al. PAIN 2023
Projected Pain Management Drug Market

NFEPP has multiple indications in the growth pain market (red circles)