BPR1M492: A MOR/NOP Dual Agonist as a Safe Pain Killer

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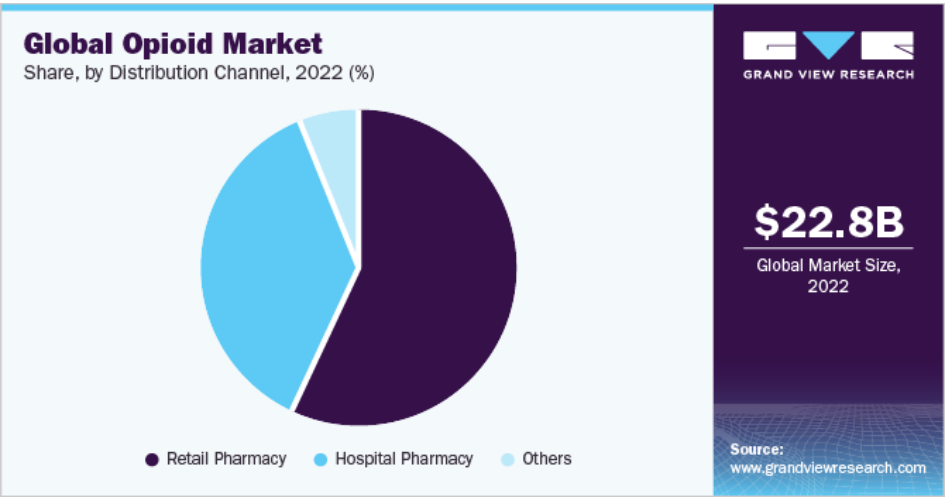
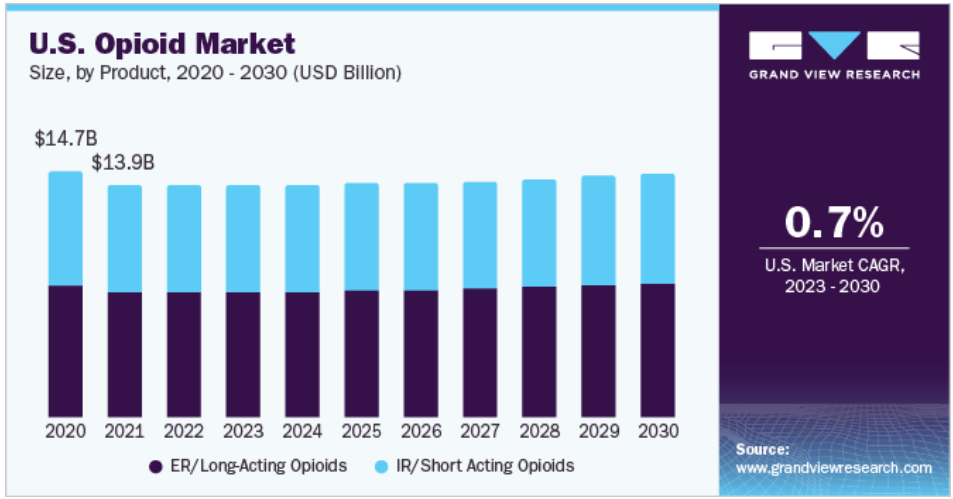
Opioid market size



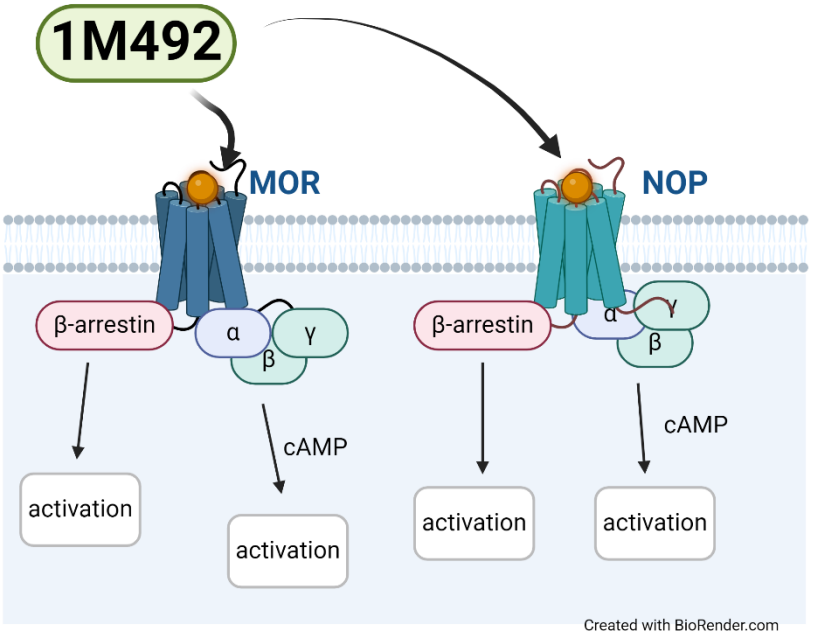


- The global **opioid market size** was valued at **USD 22.8 billion in 2022** and is anticipated to grow at a compound annual growth rate (CAGR) of 1.4% from 2023 to 2030. Increasing approval and the launch of new opioid medicines to treat patients with chronic pain are the factors expected to drive market growth.
- **Olinvyk** is an opioid agonist administrated intravenously to patients and costs around **USD 194 for a supply of 10 mL** .

Source: https://www.grandviewresearch.com/industry-analysis/opioids-market#

Mechanism of Action (MOA) of MOR/NOP dual agonist

Opioid analgesic: Treating moderate to severe pain with several side-effects.
Side effects: Respiratory suppression, constipation, tolerance, withdrawal symptom, dependence.
A compound targeting both mu opioid receptor (**MOR**) and nociceptin-orphanin FQ peptide (**NOP**) receptor can relieve pain and decrease numerous side effects.
Cebranopadol: A MOR/NOP dual agonist in NDA application. Treating neuropathic pain.
See: J. Pharm. Exp. Ther. 2014 (349) 535-548; DOI: https://doi.org/10.1124/jpet.114.213694



Pain relief, side-effects

MOR

NOP

Reduce side-effects

- Potent anti-nociceptive effect.
- Fewer adverse-effects, such as: Tolerance, **respiratory suppression**, cardiovascular function inhibition, **gastrointestinal function inhibition**, sedation, **dependence**, withdrawal symptom.
- To avoid drug abuse and addiction from MOA.

Summary of BPR1M492

(MOR/NOP dual agonist)

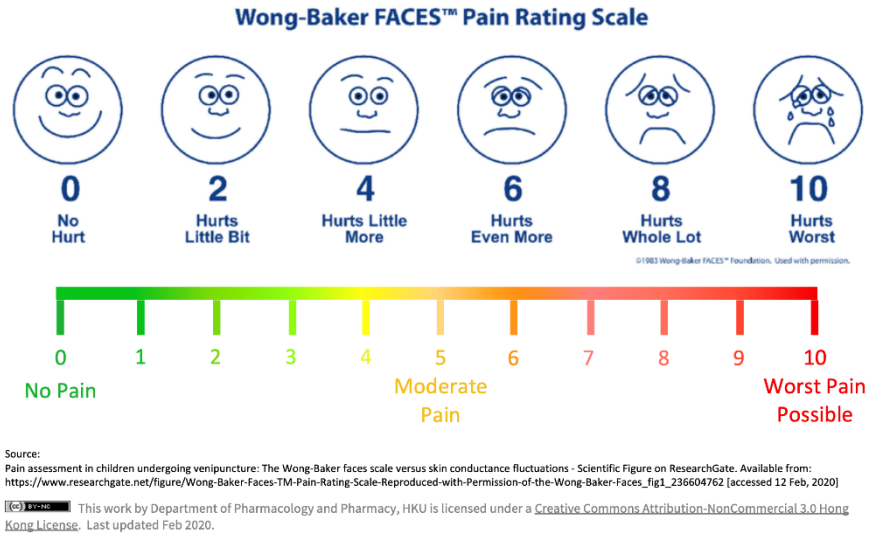
	TRV130	1M492	morphine
Antinociception (ED_{50}, mg/kg) (KH mice)	0.257	**0.027**	1.1
Onset time (min)	~10	**< 5**	~20
Postoperative pain (10 min; grams; von Frey)	~0.75	**~1.0**	~0.1
GI transit inhibition (ED_{50} and % E_{max})	0.56 µg/kg (~70%)	**3.4-fold 0.093 mg/kg (~70%)**	1.9-fold 2.07 mg/kg (~80%)
Sat'd blood oxygen rate (30 min; %)	70	**70**	69
Antinociceptive tolerance	**No**	**No**	Yes (7.2 mg/kg)
Maximum tolerated dose (KH mice)	**>195 ED_{50}**	**>1850 ED_{50}**	90 ED_{50}
Withdrawal symptom	+++	**+**	+++

TRV130 (Oliceridine): A biased MOR agonist entered the market since 2020. Treating postoperative pain.

Clinical indication

Indication: postoperative pain, pain of trauma, pain of burn injury, breakthrough pain. (FACES > 6)

Pain Rating Scale – Wong-Baker FACES™ & Visual Analogue Scale (VAS)



Source:
Pain assessment in children undergoing venipuncture: The Wong-Baker faces scale versus skin conductance fluctuations - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Wong-Baker-Faces-TM-Pain-Rating-Scale-Reproduced-with-Permission-of-the-Wong-Baker-Faces_fig1_236604762 [accessed 12 Feb, 2020]

https://pcpc.hku.hk/zh/product/pain-rating-scale-wong-baker-face-vas-zh/

Patients criteria: hospitalized patients, patients in the perioperative period.

Drug usage: SC injection, microneedle patches.

Product summary including IP and publication

Key Features:

- **A rapid period painkiller** - The onset of the antinociceptive effect of BPR1M492 was within **five minutes** after subcutaneous injection.
- **Slight affecting in the digestive system** - BPR1M492 caused less constipation (ED_{50} is 3.4-fold higher than antinociceptive ED_{50}).
- **High level of safety** - This drug caused low antinociceptive tolerance, and withdrawal symptom. This helps to protect patients from increasing the dose level and reduce the risk of drug usage (MTD > 1850 ED_{50}).

Intellectual Properties:

- **US provisional patent of BPR1M492 has been applied in August, 2024**..

Market Positioning:

- Currently, there is only one MOR/NOP dual agonist in NDA application. BPR1M492 is a novel analgesic with high safety and fewer adverse effects.

Business Opportunity:

- License and/or collaboration and sponsored research.