Next-generation potent painkiller with low side effects

Candidate drug for treating acute and severe chronic pain through opioid receptor conformational modulation

DBPR116: Opioid Receptor Allosteric Modifier

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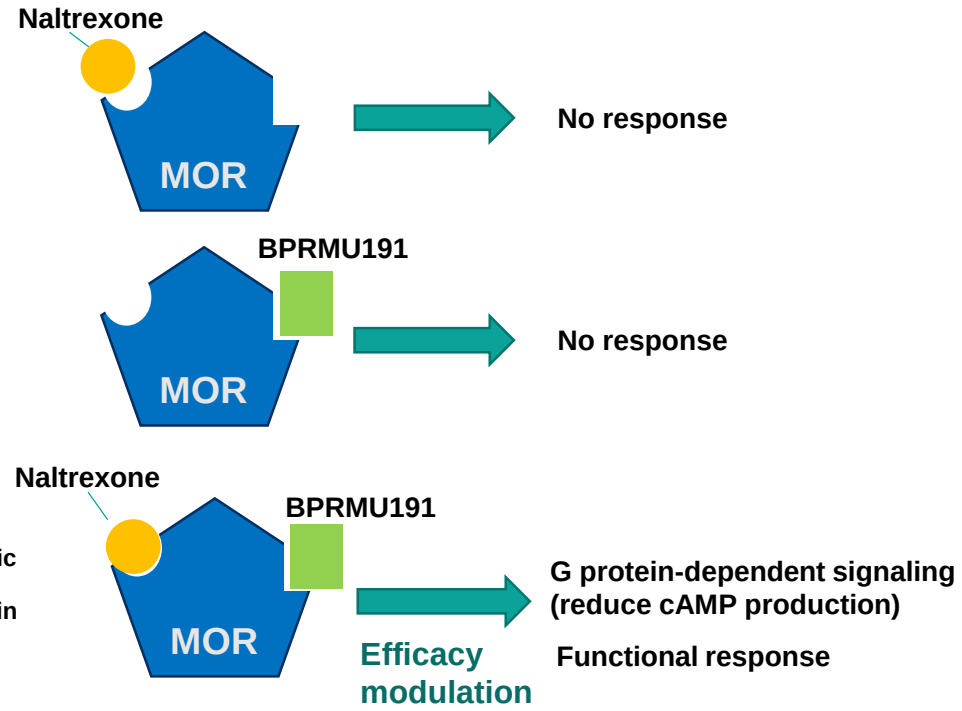
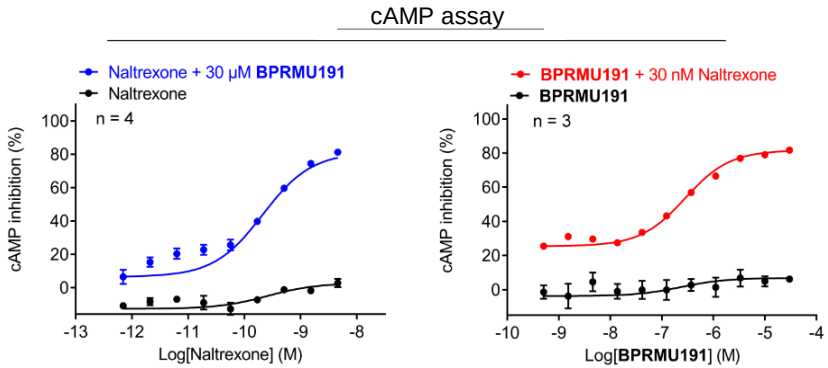
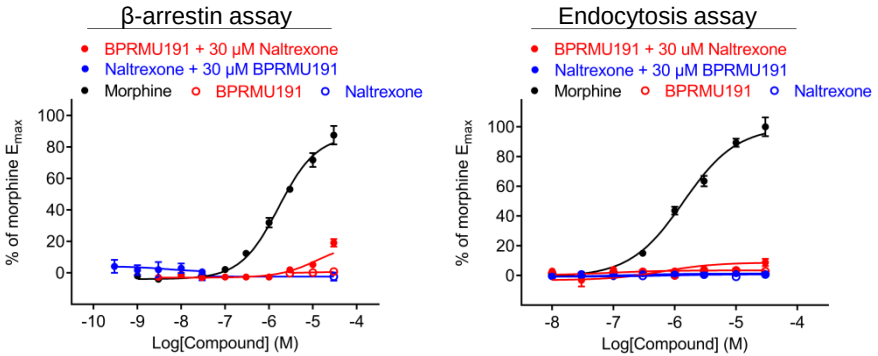
DBPR116 (a prodrug of BPRMU191) is a unique allosteric modulator of mu-opioid receptor (BPRMU191)

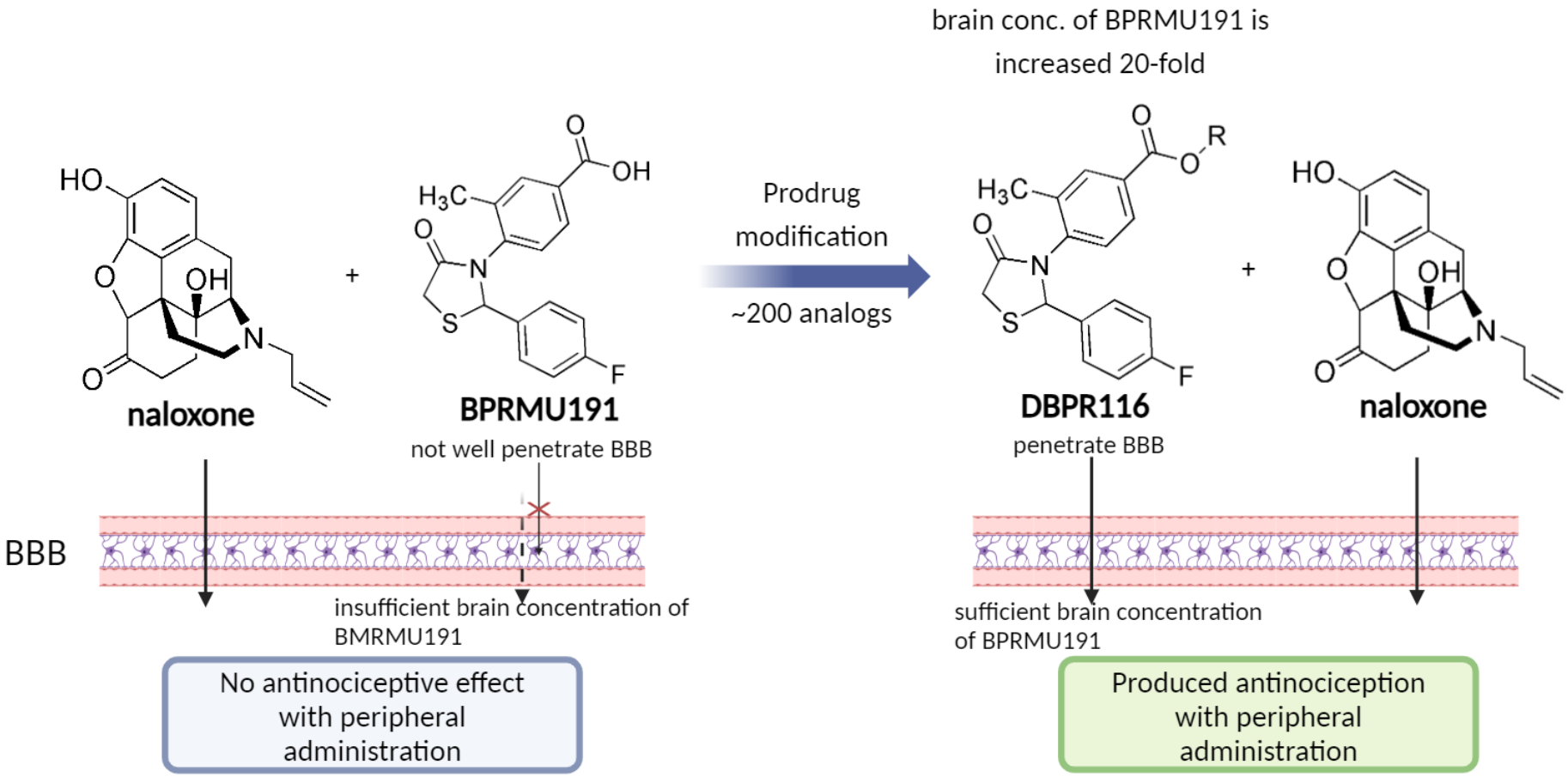
- **Project Name** DBPR116 (A prodrug of BPRMU191)
- **Target Class** mu-opioid receptor
- **Compound Class** antagonist to agonist allosteric modifier (AAM)
- **Comparator** AAM: none
  allosteric modifier: BMS986121&BMS986122
  (Bristol-Myers Squibb Company)
  opioid: Morphine, Buprenorphine, Fentanyl, Methadone
- **Market** $15~20 billion/year
- **Therapeutics Area** pain
- **Indication** renal colic, acute pancreatitis, angina, chronic neuropathic pain, chronic regional complex pain syndrome, cancer pain







DBPR116 is a prodrug of BPRMU191



Summary of animal pharmacology

	DBPR116 +1 mg/kg naltrexone	Morphine
ED_{50} (mg/kg)	11.9 (mMOR), 2.4 (hMOR)	1.9 (mMOR), 1.1 (hMOR)
AUC (min x sec)	200-600	450-750
Threshold (gram)	0.7-0.9	0.2-0.3
Tolerance	no	no
Threshold (gram)	0.5-0.7	0.2-0.7
Tolerance	no	< 6 days
GI inhibition (%)	+	+++
Decrease in Respiratory frequency (%)	++	+++
Addiction	+	+++

Acute thermal pain (Tail-Flick test) Cancer pain (Von Frey test) ddC-induced neuropathic pain (Von Frey test)

The primary advantages and market differentiation of DBPR116

- DBPR116 (a prodrug of BPRMU191) is a novel “First-in-Class” AAM which can combine effectively with MOR antagonist (such as naloxone or naltrexone) and produce impressive anti-nociception effects in multiple pain models (mice)

- DBPR116/naltrexone combination also exhibit better tolerance in cancer pain and efficacy in neuropathic pain models

- AAM/MOR antagonist combination also exhibited significant less adverse effects (compare to morphine) on:
  - ✓Constipation
  - ✓Addiction
  - ✓Tolerance