



### Contact Information

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## Fact Sheet

# GIBH1014

A Therapy for Blocking Inflammation and Pain

# GIBH's Drug Candidate 1014 for the Treatment of Post Operative Pain

## Product Description

GIBH-1014 is a new class of COX-2 selective inhibitor (CSI) that could fulfill an unmet medical need in inflammation and pain. Compound 1014, contains a chromene pharmacophore and possesses distinct physicochemical properties (i.e. non-sulfonamide, low molecular weight acid, appreciable aqueous solubility, and facile synthesis). Drug 1014 has unique intrinsic ADME properties, especially a relatively low volume of distribution resulting in higher concentrations of drug at sites of inflammation.

## Indication and Market

There are about 53 million surgeries performed in the United States each year that require drugs for post-operative pain, and over half of these patients still experience inadequate pain relief. The treatment of moderate to severe acute pain is dominated by opioids. While they offer excellent pain relief, they

come with undesirable side effects and abuse potential. The future market is highly receptive to better tolerated analgesics with opioid-sparing effects. The post-operative pain market is growing steadily and is expected to exceed \$6.5 billion in the U.S, E.U. and Japan by 2018.

## Product Rationale

Acute Pain: Celecoxib is the only CSI available in the United States and, thus, there is an unmet need for a novel and safer CSI that would confer improved efficacy in acute pain. GIBH-1014 provides the opportunity to fulfill this unmet need. In pre-clinical rodent models, compound 1014 conferred anti-inflammatory efficacy comparable to celecoxib, but conferred superior efficacy in reducing acute pain (hyperalgesia). Another unique property of 1014 compared with NSAIDs and coxibs is its mitigated effect at therapeutic doses on lowering renal blood flow in volume-depleted animals. A superior renal profile would differentiate

1014 from other CSIs and provide a huge market potential in chronic use indications, notably in patients with compromised renal function.

Cancer: Many studies have shown the efficacy of CSIs in animal models of cancer prevention. Mechanistically, COX-2 has been shown to be very important in all stages of oncogenesis. A case in point is that the FDA approved celebrex for use in patients with familial adenomatous polyposis (FAP). Also, many studies have shown the efficacy of CSIs in animal models of cancer treatment. COX-2 is highly expressed in tumor and stromal cells and PGE<sub>2</sub>, a major product of COX-2-mediated arachidonic acid metabolism, is a contributing component of angiogenesis. GIBH-1014 is currently being evaluated in animal models of cancer prevention and treatment.

## Preclinical Development

Compound 1014, was shown to be potent, efficacious, and selective both in vitro and in vivo.

Drug 1014 is active against recombinant COX-2 (IC<sub>50</sub> 14 nM), but inactive against the COX-1 enzyme (IC<sub>50</sub> >100 uM). The drug was shown to be efficacious in the rat carrageenan air pouch model (ED<sub>50</sub> = 0.34 mg/kg), the rat carrageenan footpad edema model (ED<sub>50</sub> = 3.0 mg/kg) and the rat hyperalgesia model (ED<sub>50</sub> = 2.2 mg/kg). The compound has a high degree of aqueous solubility, which affords the potential for parenteral formulation.

## Intellectual Property

GIBH has filed intellectual property rights for composition of matter, production and medical use of compound 1014 for the treatment of acute and chronic pain as well as various cancers including lung, colon and pancreatic tumors. Patents include 201210202059.X, 201210468591.6, 201210525326.7 and 201210528349.3.

## Product

GIBH-1014 is a low molecular weight (340 daltons), water soluble, S-isomer, benzopyran chromene carboxylate.

## Indication

Primary: Acute Pain

Secondary: Lung Cancer and Chronic Pain (if renal sparing in humans)

## Design

Compound 1014, is being formulated as a tablet suitable for oral dosing.

## Development Status

Lead optimization: Preclinical proof-of-concept in industry-standard models of acute pain and inflammation established. Candidate selection of the drug is scheduled for early 2013 and IND filing is to be initiated in 2014 for acute post-operative pain.

## Commercialization Strategy

Commercial partners are being sought for development and marketing in the EU and North America.

## Proof of Concept in Model of Inflammation and Pain

