Contact Information

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Fact Sheet

GIBH130

A Therapy for Stopping Alzheimer's Disease

Innovation in the DDP

Candidate 130 as an Anti-Neuro-Inflammatory Agent for the treatment of AD

Product Description

GIBH-130 is a new drug for the treatment of Alzheimer's disease (AD). Drug 130 blocks neuro-inflammation by targeting active microglia cells in the brain, thereby reducing their ability to secrete inflammatory cytokines and destructive proteases, resulting in the preservation of the extra cellular matrix (ECM). Preservation of the ECM is key strategy for stopping the progression of neuronal death in AD.

Indication and Market

Alzheimer's disease is an irreversible, progressive brain disease that slowly destroys memory and cognitive skills of patients with even the ability to carry out the simple tasks being lost. Approximately 100 million people worldwide are living with Alzheimer's disease and the number is still increasing as the global population ages. In 2012, the direct costs of caring for those with AD and other dementias in the West totaled an estimated $200 billion. Unfortunately, there are only a few approved AD drugs, such donepezil and memantine, which provide minimal symptomatic relief, but do not stop or slow disease progression. Thus, new therapies exhibiting improved efficacy and more importantly, drugs that demonstrate disease modification will hold a strong position in the global AD market and estimated to be $10 to 20 billion.

Product Rationale

Insufficient understanding of the pathogenesis of AD has made the development of disease-modifying drugs challenging. With the recent failure of several, late-stage clinical drugs aimed at reducing beta-amyloidal deposition, there is now an urgent need to pursue new drugs that target other mechanisms of AD disease. Inspired by the importance of microglia driven inflammation in the progression of AD, our drug discovery approach has been oriented at identifying novel inhibitors/antagonists of microglia activation. Increasing evidence has demonstrated that neuro-inflammation and the concomitant degradation of the ECM is key driver in both early and late stages of AD. Internal data in standard AD models show that blocking inflammation in the brain and protecting the ECM, dramatically attenuates neuronal synaptic dysfunction and behavioral alterations.

Preclinical Development

Preclinical studies demonstrate that GIBH-130 is able to effectively block spatial learning and working memory impairments in both the β-amyloid induced and APP/PS1 double transgenic mouse models of AD in a dose dependent manner with EC50 values of less than 2.5mg/kg. The overall in vivo efficacy of drug 130 is better than first line marketed anti-AD drugs donepezil and memantine. Compound 130 is orally bioavailable (F = 74.9%, T1/2 = 4.3 h) and is readily CNS permeable.

Intellectual Property

To protect the potential commercial value of our novel, neuro-inflammatory inhibitors, GIBH has filed patent applications for the intellectual property rights for the medical use of these compounds including GIBH-130 for the treatment of Alzheimer's disease and other neuro-inflammatory related diseases such as stroke in China. Patent applications have also been filed in United States and European Union. Patents include 200910030051.8.

Product

GIBH-130 is a novel inhibitor of neuro-inflammation, BBB penetrable and metabolically stable.

Indication

Primary: Alzheimer's disease

Secondary: Stroke and dementia

Design

Compound 130 has been formulated as a tablet suitable for oral dosing.

Development Status

Clinical Candidate: Preclinical proof-of-concept in industry-standard models of AD established. Both acute and chronic safety evaluation in rodents completed. IND filing is to be initiated in 2013 for AD.

Commercialization Strategy

Partner in China is South China Center for Innovative Pharmaceuticals (SCCIP). Other commercial partners are being sought for development and marketing in the EU and North America.

Drug like properties of 130

Druglikeness	Rule of five	None violation
	CLogP	2.163
PD	Activity in vitro	IC_{50} = 1.74nM
	Activity in vivo	Better than donepezil and memantine
PK	F	74.91%
	$T_{1/2}$	4.32 ± 2.62 h
	BBB penetration	AUC(Brain/Plasma) = 0.21
	Metabolism	Stable in rat
Safety	Acute toxicity	MTD > 2000 mg/kg