(2S,4R)-5-(5'-CHLORO-2'-FLUOROBIPHENYL-4-YL)-4-(ETHOXYOXALYLAMINO)-2-HYDROXYMETHYL-2-METHYLPENTANOIC ACID AS NEPRILYSIN INHIBITOR

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

The present invention relates to a novel compound and a crystalline form thereof that are metabolized *in vivo* to form a compound having utility as a neprilysin-inhibitor. The invention also relates to pharmaceutical compositions comprising compound, processes for preparing this compound, and methods of using compound to treat diseases such as hypertension, heart failure, pulmonary hypertension, and renal disease.

STATE OF THE ART

Neprilysin (neutral endopeptidase, EC 3.4.24.11) (NEP), is an endothelial membrane bound Zn^{2+}metallopeptidase found in many organs and tissues, including the brain, kidneys, lungs, gastrointestinal tract, heart, and the peripheral vasculature. NEP degrades and inactivates a number of endogenous peptides, such as enkephalins, circulating bradykinin, angiotensin peptides, and natriuretic peptides, the latter of which have several effects including, for example, vasodilation and natriuresis/diuresis, as well as inhibition of cardiac hypertrophy and ventricular fibrosis. Thus, NEP plays an important role in blood pressure homeostasis and cardiovascular health.

NEP inhibitors, such as thiorphan, candoxatril, and candoxatrilat, have been studied as potential therapeutics. Compounds that inhibit both NEP and angiotensin-I converting enzyme (ACE) are also known, and include omapatrilat, gempatrilat, and sampatrilat. Referred to as vasopeptidase inhibitors, this latter class of compounds is described in Robl et al. (1999) *Exp. Opin. Ther. Patents* 9(12): 1665-1677.

Numerous NEP inhibitors are described in U.S. Patent Application Publication No. 2013/0109639 to Hughes, et al. One such compound is *(2S,4R)*-5-(5'-chloro-2'-fluorobiphenyl-4-yl)-2-hydroxymethyl-2-methyl-4-(oxalylamino)pentanoic acid, which has