Novel Hepatitis C Protease Inhibitor

Executive Summary
Hepatitis C virus (HCV) infects 150-200 million people worldwide. Americans account for 4.1 million of the people affected with hepatitis C. There are six hepatitis C genotypes; the most common genotype in the United States, Japan, and Europe is genotype 1. At present, the most commonly prescribed drug used to treat HCV is pegylated interferon, which affects patients’ immune responses, but HCV research is now focused on attacking the virus directly through the inhibition of viral proteins’ essential activities. There are several proteins, which may be inhibited, but one particularly promising target is the NS3/NS4A complex. This complex forms a potent serine protease, which cleaves several of the viral polyprotein’s peptide bonds. If an inhibitor molecule can bind to the NS3/NS4A complex active site, a catalytic triad, the formation of infectious virions can be prevented.

Sixteen potential drug candidates have been identified. These were identified through modifying the functional groups of a known HCV protease inhibitor, boceprevir. The functional groups were modified to choose the combinations that would likely give the highest binding affinity, which corresponds to a low value of $K_d$ and highest HNE/HCV. These drug candidates were tested for their binding strength using DockingServer. One candidate, (3S)-3-[[1R,2S,5S]-3-[(2R)-2-[(tert-butylcarbamoyl)amino]-2-cyclohexylacetyl]-6,6-dimethyl-3-azabicyclo[3.1.0]hexan-2-yl]formamido)-4-cyclobutyl-2-oxobutanamide, was determined to be have a better inhibition coefficient and also a better selectivity against human neutrophil elastase than boceprevir.

In addition, in part 2, we evaluated the manufacturing and commercialization of SCH 503034 (Boceprevir). It was found that the manufacturing and commercialization efforts from preclinical trials to plant implementation will take approximately 13.5 to 14 years. Six years will be spent in preclinical trials, four years will be spent in clinical trials, and it will then take approximately 3.5 to 4 years to build a manufacturing plant, install equipment, and train employees.

It was found that the cost of preclinical research, clinical trials, and manufacturing plant implementation will most likely be $528 million. The manufacturing cost of boceprevir will most likely be $96 million if approximately 7.5 million pills are to be produced per year, with the major contributing factor to manufacturing cost being raw materials. In order to break even in one year each pill could cost $83.71, even though this rate seems high the monthly cost to a patient infected with HCV would be approximately 40% lower with boceprevir than it would be with current treatments, which leaves a high margin for profit.