Silurian Pharmaceuticals

Silurian Pharmaceuticals, Inc. to present at the American Thoracic Society, Washington, DC

Silurian will present recent results of its drug Brevenal for the treatment of defective mucociliary clearance and the prevention of exacerbations in Cystic Fibrosis, at the ATS, Washington, DC.

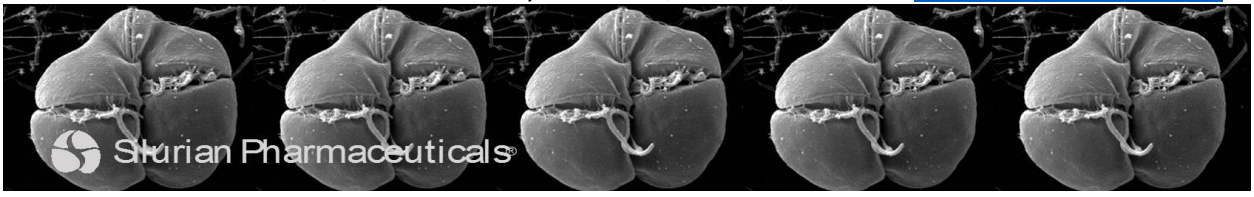
Brevenal is a promising new therapy for patients with cystic fibrosis. Low doses reverse the inhibition of airway mucociliary function caused by CFTR inhibitor 172 and human neutrophil elastase (HNE) in sheep. It also alleviates bronchoconstriction caused by HNE. This demonstrates that brevenal's activity is independent of CFTR, as well as it addresses the downstream pulmonary complications cause by HNE.

More so, it appears that brevenal's effect on mucociliary function is superior to currently used therapies in CF patients and can be used in combination with CFTR modulators.

The title of the current study is "Dose of aerosol brevenal but not ivacaftor the corrected slowed mucus transport caused by CFTRinh-172 + Human Neutrophil Elastase (HNE) challenge block HNE induced bronchoconstriction in sheep"

Sheep challenged with CFTRinh-172 (CFTRinh) show slowed mucus clearance, which can be corrected by aerosol ivacaftor or brevenal. However, challenge with CFTRinh does not cause bronchoconstriction. If human neutrophil elastase (HNE) is combined with CFTRinh, not only is mucus transport slowed, but the sheep bronchoconstrict. This challenge model replicates clinical observations in CF patients during exacerbations, where there is airway obstruction in the presence of increased levels of HNE. CF patients treated with ivacaftor show improved FEV_1 and reduction in the number of exacerbations. Whether this improvement is secondary to improved mucus clearance or a direct effect on airway tone is not clear. We hypothesized that if the effect of ivacaftor on FEV_1 was related to its direct ability to improve mucus clearance, then doses of ivacaftor that correct acute slowed mucus transport resulting from CFTRinh+HNE challenge should block the bronchoconstriction caused by HNE. For comparison, we performed these studies with brevenal, not known to have direct effect on CFTR function, which has also been shown to inhibit CFTRinh+HNE slowing of mucus transport. Challenge with CFTRinh+HNE produced a slowing of TMV which reached a maximum by 4h (53% of baseline, n=4) and remained depressed for 12h (52%). Aerosol ivacaftor given at 4h restored TMV at 5h to 88% (n=4) and TMV remained elevated for 12h (92%). Brevenal produced an equivalent response at 5h (91%) and 12h (91%), respectively (n=4). In contrast, ivacaftor had no effect on the increase in RL caused by airway challenge with HNE (22% protection, n=4), whereas brevenal provided 80% protection (n=6).

In conclusion, Ivacaftor, a CFTR potentiator, was effective at reversing CFTRinh induced acute slowed mucus clearance. Ivacaftor was not effective at reversing CFTRinh+HNE induced bronchoconstriction. Unlike ivacaftor, brevenal, provides improvement in both airway clearance and bronchoconstriction. The finding that ivacaftor and brevenal have different responses to correction of slowed mucus transport



and bronchoconstriction in an inflamed airway suggest that measures of airway function may not adequately reflect improved airway clearance.

About Silurian Pharmaceuticals, Inc.

Silurian Pharmaceuticals, Inc. is dedicated to the development of new approaches for the treatment of pulmonary disorders in CF and COPD. Silurian harnesses the discovery of the novel polyketides from Marine organisms.