

Silurian Pharmaceuticals, Inc. to present at the Cystic Fibrosis Foundation Science Meeting,
Portland, OR

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 CFF Science Meeting, Portland, OR.

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 caused by HNE.

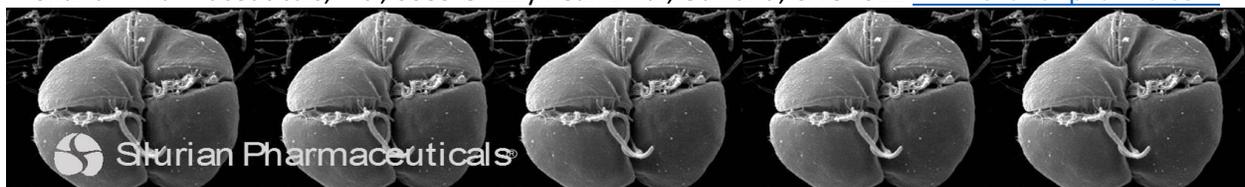
More so, it appears that brevenal's effect on mucociliary function is superior to currently used therapies in CF patients and can be used in combination with CFTR modulators.

The title of the current study is "Brevenal induces intracellular calcium release and activates extracellular chloride release via calcium-activated chloride channels, resulting in increased airway surface liquid in cystic fibrosis primary human bronchial epithelial cells"

We have shown that brevenal increases ASL secretion and abrogates increased TGF β 1-induced ASL absorption in CF human bronchial epithelial (HBE) cells; restores mucociliary transport (MCT) dose-dependently when nebulized in sheep with slowed mucus clearance due to aerosol challenge with an inhibitor of cystic fibrosis transmembrane conductance regulator (CFTR_{inh}-172) or CFTR_{inh}-172 with human neutrophil elastase (HNE); increases ASL and MCT CF HBE cells homozygous for F508del CFTR as assessed by one-micron resolution optical coherence tomography (μ OCT); and demonstrates an additive effect when used in combination with the CFTR potentiator, ivacaftor. Brevenal does not affect the epithelial sodium channel (ENaC) or CFTR, suggesting it may alter the function of other ion transporters to change ASL and MCT, and has the potential for synergistic effects when combined with known CFTR or ENaC modulators. Normal airways homeostatically regulate the volume of airway surface liquid (ASL) through both cAMP- and Ca²⁺-dependent regulation of ion and water transport. Brevenal treatment elicited a dose-dependent Ca²⁺ ion release. Also, brevenal resulted in extracellular chloride ion release. This activity was attenuated by chloride channel (CACC) inhibitor T16Ainh-A01, whereas chloride release was only partially attenuated by CFTR_{inh}-172.

Together, these findings demonstrate that Brevenal augments ASL secretion, and inflammatory-mediated ASL absorption, via Ca²⁺-dependent CaCC chloride release and that this effect is independent of CFTR.

Silurian Pharmaceuticals, Inc., 6085 Grizzly Peak Blvd., Oakland, CA 94611 www.silurianpharma.com





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.

Silurian Pharmaceuticals, Inc., 6085 Grizzly Peak Blvd., Oakland, CA 94611 www.silurianpharma.com

