CFTR potentiators and correctors and bifunctional (corrector/potentiator) compounds for treatment of Cystic Fibrosis

Tech ID: 20824 / UC Case 2008-050-0

FULL DESCRIPTION

UCSF investigators have isolated set of compounds to treat cystic fibrosis (CF). The compounds are anticipated to treat the underlying defects in patients with the delta F508 mutation of the CFTR gene, which is present in around 90% of the CF cases. Small molecule therapy directed toward correcting the deltaF508 defects in cellular processing and channel gating of CFTR is thought to hold considerable promise.

A panel of novel potentiators (which restore gating defects) and correctors (which restore protein folding and plasma membrane trafficking) are available for licensing. Several of the potentiators identified are very potent (some at submicromolar potency) in restoring the gating defect in both deltaF508 mutants and other CFTR gating mutants, including G551D. They have also identified several highly effective (micromolar potency) correctors of the deltaF508 mutant protein. When used in combination, these compounds may correct the defects caused by the deltaF508 mutation in the CFTR gene.

Additionally, the investigator is currently developing a bifunctional compound capable of both potentiation and corrector activity, with promising results. It is thought that both activities are required to fully address the protein folding/trafficking and gating defects present in this mutation, which is the most prevalent (90%/US/66% world population). A single molecule that can address both defects in the deltaF508 mutation could provide a simplified approach that would be easier to study in clinical trials. The investigators believe the bifunctional compounds could be manufactured as either oral tablet or inhaled aerosol formulation.

PUBLICATIONS


RELATED MATERIALS

deltaF508 and G551D cystic fibrosis transmembrane conductance regulator chloride-channel gating.


PATENT INFORMATION

UCSF has a large portfolio of both US and foreign patent applications covering the use of these compounds for treatment of CF. Below are some selected patent application publications:

PATENT STATUS

<table>
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<th>Country</th>
<th>Type</th>
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<tr>
<td>United States Of America</td>
<td>Issued Patent</td>
<td>8,389,736</td>
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ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- SALT-SPARING UREA TRANSPORT INHIBITOR DIURETICS FOR TREATMENT OF CARDIOVASCULAR AND RENAL DISORDERS
- Potent TMEM16A Small Molecule Treatment for Inflammatory and Reactive Airway Diseases, Asthma, Hypertension, Pain and Cancer
- Novel Small Molecule Drug for the Treatment of Constipation and Oxalate Kidney Stones
- Small Molecule Pendrin Inhibitors for Treatment of Inflammatory Airway Diseases and Diuretic Resistance
- Immunotherapy for Treatment of Neuromyelitis Optica (NMO)