Abstract

A new drug (S-1226) to treat asthma incorporating a novel formulation combining the potent bronchodilator carbon dioxide (CO₂) delivered to the lung as a gas in combination with a synthetic lung surfactant, perfluorocyclooctyl bromide (PFOB) co-delivered as an aerosol.

S-1226 is being developed by academic co-founders through the Canadian based biotech start-up SolAeroMed Inc.

S-1226:
- Effective: treats methacholine and allergen induced bronchoconstriction in sheep and rat models of asthma
- Safe: Phase I clinical trial showed minimal adverse effects at all dosing levels (4%, 8%, 12% CO₂)
- Currently in Phase II clinical trial – allergen induced asthma subjects
- Mechanism of action:
  - A relaxing effect of CO₂ on constricted airway smooth muscle
  - The ability of the gaseous component to rapidly penetrate closed airways
  - The ability to lubricate mucous plugs thus enhancing mucous clearance
- S-1226 and salbutamol do not compete for the same receptors
- Aims to complement rather than replace current treatments and is likely to be used when conventional bronchodilators are ineffective in opening closed airways

A novel portable delivery device is currently under development
- Anticipated future roles for S-1226:
  - Treating exacerbations of COPD and CF
  - A combination therapy to enhance delivery and effectiveness of other respiratory drugs

Medical Need for a New Asthma Drug

Asthma:
- Affects 300 million individuals worldwide; 400 million expected by 2025
- Worldwide 250,000 asthma deaths every year
- $8.9 billion problem in asthma when conventional emergency treatments don’t work
- Out of 3.9 million emergency hospital visits per year worldwide:
  - 85% sent home after 3 hours ($51.2 billion)
  - 15% use 1.8 million hospital bed-days ($5.8 billion)
- Short-acting β₂-agonists are the most common front-line emergency treatment
- Only one short acting bronchodilator (salbutamol)
- One-fifth to one-third of patients do not respond well
- Tachyphylaxis and toxicity have been demonstrated
- Major challenge for treating acute asthma is to open occluded airways rapidly enough to re-establish ventilation and allow delivery of O₂ and conventional medication to airways

Background to the New Treatment: S-1226™

In severe asthma the airways are blocked by a combination of bronchoconstriction and mucous plugs rendering personal inhalers ineffective

A new type of treatment is required that has both bronchodilator and biophysical properties (mucous plug penetration and clearance)

This led to the discovery of S-1226, a new class of short-acting bronchodilators by University of Calgary scientists

SolAeroMed Inc. was formed to progress R&D and support commercial development of S-1226
- Patents have been issued in the USA and Europe

Novel Asthma Drug S-1226™

S-1226 consists of 3mL Perfluorobroncholytic synthetic surfactant nebulized with CO₂-enriched air (4-12% CO₂, 20% O₂) with balanced N₂.
- Delivered as an aerosol/vapour/gas mixture
- New mechanism of action
- Both CO₂ and Perfluorobroncholytic are well-described and safe
- Both CO₂, and Perfluorobroncholytic have previously been approved by FDA, EMA, HC

Pre-Clinical Studies

Sheep Model of Asthma

![Sheep Model of Asthma](image)

**Perflubron**

**CO₂ enriched air**

**Figure 1**

**Figure 2**

![Figure 1](image)

![Figure 2](image)

**Mucolytic (In Vitro)**

![Mucolytic (In Vitro)](image)

**Figure 3**

**Perflubron delivered at a mean ratio of 41.5% (aerosol vapour)**

**Aerosol droplets have a 2.4 µm mass median aerodynamic diameter with 2.9 geometric standard deviation**

**Summary and Future Directions**

- Development of a personal rescue device to be used by patients as an emergency technique when away from the hospital setting
- First-in-class product; pharmacological and biophysical
- Platform technology for delivery of other drugs

**Clinical Studies**

<table>
<thead>
<tr>
<th>Phase I</th>
<th>S-1226 at 4%, 8%, and 12% CO₂</th>
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<tr>
<td>Completion</td>
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<th>S-1226 at 8% CO₂</th>
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<td>Drug Administration and Characterization</td>
<td>WestMed Circular® II Hybrid nebulizer system</td>
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**First-in-class product; pharmacological and biophysical**

**Platform technology for delivery of other drugs**

**New mechanism of action**

**Rapidly dilated airways (in vivo)**

**Enhances mucous plug clearance (in vitro)**

**Expected: Q3 2015**

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**S-1226:**
- Rapidly dilated airways (in vivo)
- Enhances mucous plug clearance (in vitro)
- New mechanism of action
- First-in-class product; pharmacological and biophysical
- Platform technology for delivery of other drugs