**Brain injury treatment**

- **Compounds with a novel mechanism-of-action for the treatment of acute brain injury**

**Strong chemistry pipeline composed of analogues from three structural classes**

<table>
<thead>
<tr>
<th>Compd A series</th>
<th>Prodrugs of A, novel structures</th>
<th>Expected increased brain permeability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compd B series</td>
<td>5 times higher affinity than Compd A, Novel structures, unrelated to A</td>
<td>Crystal structure data with compound</td>
</tr>
<tr>
<td>Compd C series</td>
<td>Novel structures, unrelated to A</td>
<td>Expected high brain permeability</td>
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</tbody>
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**Compd A works as a neuroprotective agent**

- Reduced infarct size as determined from Cresyl Violet staining
- Reduced motor performance deficit (Day 3) in mice treated with Compd A 12 hours after the injury

**Background: Compound class & brain expression pattern**

- Cmpd A-specific binding sites in the mammalian brain as measured by 1H-Cmpd A autoradiography

**Primary method: The photothrombotic mouse model of focal ischemic stroke & traumatic brain injury (TBI)**

- **Non-invasive**
- **5 min anesthesia**
- **Predefined region of ischemia**
- **High validity:** Produces infarct sizes comparable to those seen in 60% of human strokes
- **Mixed model of TBI & ischemic stroke**

**Unique Selling Points**

- Brain-penetrable neuroprotective small-molecule compound
- Effective when administered up to 12 hours after the injury
- Novel targeted mechanism-of-action (first-in-class), novel binding site and striking subtype selectivity
- No drugs exist against target for other indications; first small-molecule ligands for target
- Other indications are envisaged based on the identified target

**Commercial Perspectives**

Acute brain injury is a major world-wide health issue with very limited medical treatment options. It includes traumatic brain injury (caused by, for example, road accidents or a blow to the head) and ischemic stroke. Uniquely, our compound can be given hours after the injury, also by non-invasive routes. Ischemic stroke is the third leading cause of death worldwide and the leading cause of adult disability. The only pharmacological treatment available for ischemic stroke is tissue plasminogen activator (t-PA) which is, however, only useful for a small subset of patients.

**Technology Description**

- Cmpd A rapidly enters the brain after systemic administration and targets an intracellular, multi-functional enzyme involved in higher brain functions
- Interaction with enzyme happens via a novel binding site
- Cmpd A is easily water-soluble, stable and brain-selective
- Cmpd A is non-sedative and is well-tolerated in rodents
- Extensive target validation has been performed (still unpublished)
- Structure-based drug design possibilities for further compound development due to recent crystal structure with Cmpd A analogue

**Current state**

Cmpd A: Proof-of-concept in several brain injury models. A scale-up synthesis use has been developed. Prodrug design is ongoing. Further dose & timing studies in young and old mice.

**2nd generation compounds:** In vitro studies to select candidates for in vivo testing and further mechanism-of-action studies.

**The Inventors**

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**Technology Seeking:** Funding/Investors, Licensee, Partner/Research Collaboration

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