ACR16 for the Treatment of Huntington’s Disease

Joakim Tedroff, M.D, Ph.D.

Pittsburgh, June 7, 2008
ACR16 for Huntington’s disease

• ACR16 is a small molecule belong to a pharmacological class called ’dopaminergic stabilizers’
• Dopaminerigic stabilizers are compounds that can enhance or inhibit activity depending on the initial level of activity
• ACR16 has a broad neuropharmacological activity potential

• ACR16 is still an expermental therapeutic.
• It has undergone limited clinical testing in patients and the results have been encouraging
ACR16- a dopamine stabilizer

**Neuroleptic**

- High
- Normal
- Low

**ACR16**

- High
- Normal
- Low
Reduction of dopamine receptors with the progression of Huntington’s disease

3 months          1 year  2 years
What does ACR16 do?

- **Cerebral cortex** to **Striatum**
  - Strengthening of cortical control of the basal ganglia

- **Striatum** to **Thalamus**
  - Mild inhibition of dopamine

- **Thalamus** to **Cerebral cortex**

**Diagram labels:**
- Subst. nigra/VTA
- Behavior
- Sensory input
Huntington’s disease - many symptoms

- Motor symptoms
- Neuropsychiatric symptoms
- Disruption of mental processing
HD - many symptoms a challenge

- Motor symptoms
- Neuropsychiatric symptoms
- Disruption of mental processing

- Chorea, dystonia (involuntary movements)
- Problems with eye movements
- Problems with voluntary control of movement (balance, gait, slowness, clumsiness, speech difficulties, swallowing problems etc.)
HD - many symptoms a challenge

- Motor symptoms
- Neuropsychiatric symptoms
- Disruption of mental processing

- Mood symptoms (depression, anxiety, apathy, mania, irritability)
- Psychosis
HD- many symptoms a challenge

- Motor symptoms
- Neuropsychiatric symptoms
- Disruption of mental processing
  - Thought processing problems
  - Forgetfulness
ACR16 been tested in Huntington’s disease

✔ So far a limited number clinical trials have been conducted and the results have been encouraging;

✔ It seems ACR16 has a clinical profile corresponding to findings in pharmacological experiments
Effects of ACR16 on voluntary movement in Huntington’s disease patients

Modified motor score (mMS) change vs. baseline after 14/28 days of treatment. Mean ± SEM, subjects displaying mMS > 10 at baseline.
* p < 0.05 vs. baseline  ** p< 0.01 vs. baseline  # p < 0.05 ACR16 vs. Placebo

Corresponds to about 1 year of progression
ACR16 - effects on gait function

Patients with gait improvement:
11/28 patients ACR16
3/30 patients placebo

# P < 0.05 vs placebo
ACR16 - effects on anxiety and depression

Change from baseline

* P < 0.05 vs baseline
What is the place for ACR16 in Huntington’s disease?

- Well tolerated with minimal tradeoff for the patient
- To improve voluntary control of movement
- To improve neurosychiatric symptoms and possibly also cognitive performance

To reduce the overall burden of having HD
What is ongoing?

- A double-blind placebo controlled study in Europe
- 420 patients
- Treatment groups:
  - 45 mg q.d.
  - 45 mg b.i.d.
  - Placebo
- 6 months duration
- This trial is currently enrolling
North American ACR16 trial

- 3 months treatment duration
- 4 dose groups including placebo
- Eligible patients:
  - HD diagnosed clinically or with a genetic test
  - General good physical health
  - HD motor symptoms of a certain magnitude
  - Treatment with neuroleptics or tetrabenazine not allowed
  - Some other concomitant medications also not allowed
Thank you for listening