Overview of Medivation and Dimebon

Sarah Noonberg M.D., Ph.D.
Director, Clinical Development
Medivation, Inc.

• Publicly-traded biopharmaceutical company
• Founded in 2003
• Headquarters in San Francisco
  – Offices in Chile and India
• Mission is to efficiently develop innovative therapies for serious diseases with significant unmet medical need.
• Current pipeline:
  – Dimebon in Huntington’s disease and Alzheimer’s disease
  – MDV3100 in prostate cancer
• www.medivation.com
History of Dimebon

- 1970’s: Developed in Russia as an antihistamine
- 1980’s: Approved in Russia to treat allergic conditions
- 1990’s: Neurologic properties discovered by Russian scientists
- 2003: Medivation was formed and Dimebon was in-licensed
- 2006: Clinical trial demonstrated tolerability in Huntington’s disease
- 2007: Clinical trial demonstrated benefit in Alzheimer’s disease
Major Activities in 2008

Phase 2 Trial of Dimebon in Patients with Mild-to-Moderate Huntington’s Disease (DIMOND)
- Safety/tolerability over 3 months of treatment
- Effect on Huntington’s disease symptoms
- Enrollment complete; initial results expected in July
- If results encouraging, phase 3 program to follow

Phase 3 Trial of Dimebon in Patients with Mild-to-Moderate Alzheimer’s Disease
- Effect on Alzheimer’s disease symptoms over 6 months of treatment
- Safety/tolerability
- Enrollment ongoing
Dimebon Has Potent Effects on Mitochondria


Human cell

So…

• What are mitochondria?
  – Small structures inside of cells that turn nutrients from food into fuel
  – Tiny “gas” stations that provide fuel to cells for normal function

• What do mitochondria have to do with Huntington’s disease?
  – Genetic defect is believed to interfere with normal mitochondrial function
  – Brain cells may not have enough energy to function properly

• How might Dimebon benefit Huntington’s disease patients?
  – Dimebon is believed to improve mitochondrial function
  – Improved mitochondrial function may translate into healthier brain cells and improved symptoms
Important Laboratory Effects of Dimebon

- Dimebon improves neuron survival under experimental conditions
  - Ionomycin (neurotoxin)
  - Low serum conditions (cellular stress)
  - β-amyloid (Alzheimer’s disease)

The Huntington’s Disease Fly Model

- Dimebon improves neuron survival in a fly model of Huntington’s disease
Dimebon Protected Photoreceptor Neurons

Number of Neurons

Dimebon Concentration in Food

Control
Low Dose
Therapeutic Dose
Important Clinical Effects of Dimebon

• Huntington’s disease:
  – Dimebon was generally well tolerated over 8 days of treatment
  – Results supported moving forward to the current Phase 2 study

• Alzheimer’s disease:
  – Dimebon improved thinking, behavior, and overall function after one year of treatment
  – General signs and symptoms were improved or stabilized in ~70% of patients
  – Benefits were seen as early as 3 months and were stable or increased over time
  – Dimebon was generally well tolerated
  – Results supported moving forward to the current confirmatory Phase 3 study
Similarities Between Alzheimer’s Disease and Huntington’s Disease

• Both diseases have similar progressive symptoms
  – Difficulty in thinking, changes in behavior, loss of independence

• Both diseases involve the accumulation of abnormal proteins in brain cells
  – β-amyloid vs. huntingtin protein

• Both diseases involve abnormalities in mitochondria function contributing to brain cell death

• Our hypothesis: Benefits demonstrated in Alzheimer’s disease will translate into benefits in Huntington’s disease
Looking Ahead in our HD Program

• In the coming days:
  – Completing dosing in the DIMOND study

• In the coming weeks:
  – Analyzing initial safety and efficacy data from the DIMOND study
  – Announcing initial results (expected in July)

• In the coming months:
  – Full analysis of the DIMOND study
  – If warranted, progressing to Phase 3 studies with Dimebon
Lastly….

Patients

Physicians

Caregivers

Study Personnel

Thank you