PD Expert Briefing:

What’s in the Parkinson’s Pipeline

Presented by:
David G. Standaert, M.D., Ph.D.
Professor of Neurology
Director, Center for Neurodegeneration and Experimental Therapeutics
University of Alabama at Birmingham

Will begin: Tuesday, April 20, 2010 at 1:00 PM ET
Welcoming Remarks

Robin Elliott
Executive Director
Parkinson’s Disease Foundation
What’s in the Parkinson’s Pipeline

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PD Pipeline: What are we looking for?
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Symptomatic Treatments
• Goal is to correct or suppress specific symptoms
• Some good existing treatments of this kind
• Examples
  – levodopa
  – ropinerole
  – pramipexole
PD Pipeline: What are we looking for?

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Neuroprotective Treatments
- Goal is to slow or prevent progression of PD
- No proven therapies in this category yet
- Need is increasing:
  - 2008: 1,500,000
  - 2050: 4,000,000

Estimated PD cases in the US
The pathway to therapy discovery

**Empiric Strategies**

- Simple Systems:
  - Receptor
  - Proteins
  - Cell Models

**Complex Systems:**
- Non-mammalian models
- Small mammals
- Non-human primates

**Target-driven Strategies**

- Human Trials:
  - Safety and Tolerability
  - Proof of Principal
  - Efficacy Studies
Model Systems
Where do they come from?

• Based on ideas about what causes PD

• Genetics – a revolution in PD
  – Dominant Genes for PD
    • Alpha-synuclein – aggregates in all cases of PD
    • LRRK2 – most common genetic cause, 1% of cases
  – Recessive Genes
    • Parkin, PINK1, DJ1

• Environmental causes
  – Oxidative stress
  – Pesticides and toxins
Non-Mammalian Models

- Based on PD genetics
- Low-cost, rapid tool for screening

Yeast
Flies
Worms

Wikimedia Commons
Mammalian Models

- Rodents – lower cost, faster
- Non-human primates – expensive, but the most authentic model

http://commons.wikimedia.org/wiki/File:Gibraltar_Barbary_Macaque.jpg
How good are our models?

• For **symptomatic therapies** the existing models are very good, and predict success with good reliability

• For **neuroprotective therapies** none of the existing models is known to have predictive power
The drug development pipeline

- Preclinical: Discovery and Validation
- Clinical Trials: Phase I, Phase II, Phase III
- Post-market: Phase IV
Recent Arrivals: newest drugs for PD

- Extended release dopamine agonists
  - ropinerole ER (Requip® XL)
  - pramipexole ER (Mirapex® ER)
- Rotigotine (Neupro® patch)
- Rasagiline (Azilect®)
- Rivastigmine (Exelon® patch)
Phase IV: Postmarket

• Rasagiline in combination with DA agonists
• Naltrexone for impulse control disorders
• Rivastigmine for cognitive impairment
• Lubiprostone for constipation
• Donepezil for dementia
Phase III: “Pivotal” Trials

- Symptomatic
  - IPX066 – levodopa formulation
  - levodopa intestinal gel (Duodopa®)
  - istradefylline – A2a antagonist
  - safinamide (MAO inhibitor, Na+ channels)
  - pimavanserin (for psychosis)
  - pitolisant (for excessive sleepiness)

- Neuroprotective
  - CoQ10
  - Creatine
Phase I/II: Safety/Efficacy

• Symptomatic
  – AFQ056 (mGluR5 antagonist)
  – pardoprunox (dopamine agonist)
  – fipamezole (adrenergic antagonist)
  – Prosavin® (gene therapy)

• Neuroprotective
  – CERE 120® (gene therapy, neurturin)
  – STEADY PD (isradipine)
  – SURE-PD (inosine/urate)
  – PYM50028 (Cogane®)
Preclinical: Discovery and Validation

• Anti-Synuclein strategies
  – Reducing production
  – Increasing clearance
  – Preventing aggregation
• LRRK2 kinase inhibitors
• Anti-inflammatory treatments for PD
• Growth factors and neuro-regenerative approaches
So what’s likely to emerge from the pipeline next?
So what’s likely to emerge from the pipeline next?

“It’s tough making predictions, especially about the future.”

Yogi Berra
Pipeline Forecast

• Immediate future:
  – Symptomatic drugs for non-motor symptoms – fatigue, constipation, memory loss
  – Dopaminergic treatments – levodopa formulations, dopamine agonists
  – Other symptomatic therapies
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• Near term:
  – Neuroprotective therapies of modest effect – CoQ, creatine, isradipine
  – Gene therapy, growth factors
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• Longer term: potent protective and restorative treatments
  – Anti-synuclein
  – LRRK2 kinase inhibitors
  – Anti-inflammatory treatments
Questions and Answers
Closing Remarks

Robin Elliott
Executive Director
Parkinson’s Disease Foundation
The archive for this *PD ExpertBriefing* will be available on

**Tuesday, April 27**

Please visit [www.pdf.org](http://www.pdf.org) for more information.
Fatigue, Sleep Disorders and Parkinson's Disease
Joseph Friedman, M.D.
Clinical Professor of Neurology
Brown University
Tuesday, June 1, 2010 at 1 PM ET
Do You Have Questions About Parkinson’s Disease?

We can help.

Call Monday through Friday, 9 AM to 6 PM ET
Submit your questions online and hear back in 8 to ten days.

(800) 457-6676

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