Huntington’s Disease Research Update

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HDSA Center of Excellence
University of South Carolina School of Medicine
HD Education Day
Raleigh, NC, April 6, 2019
The HDSA Mission:
To improve the lives of everyone affected by HD.

- Clinical care (Centers of Excellence)
- Advocacy
- Research
- Education
- Support groups/Social Workers
How does HDSA support research?

• We fund research grants

• We organize research communications

• We support clinical science

• We link individuals with clinical studies

• We help give families a voice in research

• We have scientists on staff
HD clinical studies and trials
HD Clinical Research: Enroll-HD

Enroll-HD is a global observational study open to people who have HD or who are at risk.

What’s involved?

• Annual visits (about 1-2 hours)
• Health questions (thinking, behaviors, feelings, lifestyle)
• Neurological exam
• Blood sample for genotyping and bio-banking
• Family history (optional)
• Travel support is available

More than 16,500 participants worldwide
What are the goals of Enroll-HD?

- To increase our understanding of HD in people by monitoring how symptoms appear and change over time
- To study the best clinical practices for HD care
- To improve the design of clinical trials to give us clear answers more quickly
- To accelerate the discovery and development of new therapeutics
How does Enroll-HD accelerate research?

• More people undergoing the exact same evaluations means greater likelihood to uncover new things about HD.

• More scientists around the world working on HD: the data is available to any scientist with a legitimate research project devoted to understanding HD.

• Research platform for future trials:
  – It lays out a “welcome mat” for researchers and pharmaceutical companies to study HD.
  – Enroll-HD creates a database of potential volunteers for future studies, including drug trials.

COME ON IN AND DO SOME RESEARCH!
HD Drug Pipeline

**Basic Research**
- Target Validation
- Lead Optimization
- Safety & Manufacturing

**Preclinical Research & Development**
- Phase I
- Phase II
- Phase III

**Clinical Development**
- FDA Approval

**Phase 3 being planned**
- Lundbeck/Tetrabenazine
- Teva/Deutetrebzenzine
- Teva/Pridopidine (PRIDE-HD)
- Teva/Laquimod (LEGATO)
- uniQURE/AAV5-miHtt
- Raptor/Cysteamine
- Pfizer/PDE10A (Amaryllis)
- UC-Davis/HD-Cell
- Ionis and Roche/ASO
- Ipsen/Triheptanoin
- Omeros/PDE10A inhibitor
- Vaccinex/anti-SEMA4D
- Azevan/V1aR antagonist
- Heinrich-Heine Univ/DBS
- Voyager/Sano/AAV1-shRNA
- Spark/AAV2-siRNA
- Shire and Sangamo/ZFPs
- SomBiotech/VMAT2
- WAVE/WVE-120101
- WAVE/WVE-120102
- BioMarin/Htt AON

**Recruitment Complete**
- Phase 3 being planned

**TERMINATED**
- EU only

**Ph2 on hold**
- EU only

**Recruiting**
- EU only

**2017 start; 2018 in USA**
- 2017 start; 2018 in USA
What are the phases of a clinical trial?

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who?</td>
<td>Patients</td>
<td>Patients</td>
</tr>
<tr>
<td>Patients or healthy</td>
<td>Patients</td>
<td>Patients</td>
</tr>
<tr>
<td>volunteers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>What?</td>
<td>Safety (dangerous side effects)</td>
<td>Other side effects &amp; body effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How many?</td>
<td>20-100</td>
<td>100-300</td>
</tr>
<tr>
<td></td>
<td></td>
<td>300-600 or more</td>
</tr>
</tbody>
</table>
# HD drug pipeline: completed and ongoing trials

<table>
<thead>
<tr>
<th></th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teva/Deutetrabenazine</td>
<td></td>
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<tr>
<td>Teva/Pridopidine (PRIDE-HD)</td>
<td></td>
<td></td>
<td></td>
<td>Phase 3 on hold</td>
</tr>
<tr>
<td>Teva/Laquimimod (LEGATO)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azevan/V1aR antagonist (Stair)</td>
<td></td>
<td></td>
<td>Failed to meet endpoint</td>
<td></td>
</tr>
<tr>
<td>Vaccinex/anti-SEMA4D (Signal)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ionis and Roche/ASO</td>
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</tr>
<tr>
<td>WAVE/WVE-120101</td>
<td></td>
<td>Recruiting (Canada, EU, US)</td>
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</tr>
<tr>
<td>WAVE/WVE-120102</td>
<td></td>
<td>Recruiting (Canada, EU, US)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Huntingtin lowering
- Recruitment complete, Phase 2
- Recruitment complete, Phase 2
- Phase 1b/2a Complete
HD drug pipeline: **Austedo** approved by FDA!

**Deutetrabenazine**

- Oral drug that controls movements; similar to tetrabenazine
- In the Phase III trial called FIRST-HD it showed benefits for chorea and day to day function
- Longer lasting = fewer side effects than tetrabenazine
HD drug trials: ongoing, not currently recruiting

Phase 1

Pridopidine

• An oral medication to stabilize dopamine, a neurotransmitter that controls movement and mood

Phase 2

• Did not improve movements, but improved total functional capacity, a measure of how people function in their daily lives

Phase 3

• The Phase III study is currently on hold

FDA Approval

<table>
<thead>
<tr>
<th>OCCUPATION</th>
<th>0 = unable</th>
<th>1 = marginal work only</th>
<th>2 = reduced capacity for usual job</th>
<th>3 = normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>FINANCES</td>
<td>0 = unable</td>
<td>1 = major assistance</td>
<td>2 = slight assistance</td>
<td>3 = normal</td>
</tr>
<tr>
<td>DOMESTIC CHORES</td>
<td>0 = unable</td>
<td>1 = impaired</td>
<td>2 = normal</td>
<td></td>
</tr>
<tr>
<td>ADL</td>
<td>0 = total care</td>
<td>1 = gross tasks only</td>
<td>2 = minimal impairment</td>
<td>3 = normal</td>
</tr>
<tr>
<td>CARE LEVEL</td>
<td>0 = full time skilled nursing</td>
<td>1 = home or chronic care</td>
<td>2 = home</td>
<td></td>
</tr>
</tbody>
</table>
HD drug trials: ongoing, not currently recruiting

- An oral medication targeting brain inflammation
- Looking mainly at effects on movements but also other symptoms
- In August 2018 this trial unfortunately did not meet its primary endpoint – it did not improve motor symptoms
- However, brain volume shrinkage was slowed somewhat
HD drug trials: just finished recruiting

VA1R antagonist (SRX246)

- A 2x daily oral medication to treat irritability in HD
- Blocks vasopressin receptor 1a which plays a role in anxiety and aggression
- Test in early symptomatic HD patients (108 patients)
- Trial began May 2016 and finished recruiting in Sept 2018
HD drug trials: enrollment completed

Phase 1  Phase 2  Phase 3  FDA Approval

VX15

- An antibody given as a monthly IV infusion
- Could modulate brain inflammation and increase growth and health of nerve cells
- 9/19/17 webinar presentation: VX15 an effect on the volume of the brain as measured by MRI and other imaging
- Enrollment completed in January 2019
HD research: examples of other recruiting studies

- Worldwide: HD-Clarity, donation of HD samples to accelerate the development of therapies
- Nationwide: phone interview about adult’s experience talking to adolescents at risk for HD
- Nationwide: 5 research surveys currently recruiting on HDSA’s website
- Columbia University: exercise coaching sessions to improve HD symptoms
- Massachusetts General Hospital: brain imaging (PET scan) to understand genetic changes in HD
New look, new features and extended call center hours (9-6 EST)

>3,500 individual profiles signed up

Most up to date database of North American HD research opportunities
Create a Profile

Profile type (Required)
- Select Profile type

Who is this Profile For?
- Myself
- Family Member
- Friend
- My Patient

Address
- Type address or location
- Enter the address of the person interested in possible study opportunities

Create a Profile Name
- 
- From this account you can manage a profile for yourself and also for others you care about

Continue

Request a Contact

or call toll-free
1-866-890-6612
To review your results with a Clinical Trial Navigator, connect with study teams, learn more about the clinical trial process, and stay updated on new trials.

All of your information is secure.

Huntington’s Disease Society of America
Answer Questions

1. What is the date of birth of the HD impacted individual?
   - Month
   - Year

2. What is the gender of the HD impacted individual?
   - Male
   - Female
   - Prefer not to answer

3. Please select the most appropriate diagnosis:
   - Juvenile Huntington’s Disease
   - Adult onset Huntington’s Disease
   - Undiagnosed (asymptomatic and gene positive)
   - Undiagnosed (exhibiting symptoms and gene positive)
   - At risk for developing HD (genetic status unknown)
   - Gene negative
   - Spouse or caregiver of an individual with HD
   - Other condition not listed

Request a Consultation

or call toll-free
1-866-890-6612

To review your results with a Clinical Trial Navigator, connect with study teams, learn more about the clinical trial process, and stay updated on new trials.
### Personalized Trial Info Now at Your Fingertips

Call 1-866-890-6612 or [Request a Consultation](#) to identify clinical trials that match your diagnosis, treatment history and location.

<table>
<thead>
<tr>
<th>Clinical Studies (9)</th>
<th>Registries (1)</th>
<th>Biomarker and Imaging Studies (5)</th>
<th>Quality of Life Studies (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title</strong></td>
<td><strong>Phase</strong></td>
<td><strong>Interventions</strong></td>
<td><strong>Drugs</strong></td>
</tr>
<tr>
<td>VX15/2003 Treatment for Huntington’s Disease</td>
<td>2</td>
<td>Immunotherapy</td>
<td>YX15/2003</td>
</tr>
<tr>
<td>Tolerability, Safety, and Activity of SRX246 in Irritable Subjects With Huntington’s Disease</td>
<td>1/2</td>
<td>Vasopressin Antagonist</td>
<td>SRX-246</td>
</tr>
<tr>
<td>Safety and Tolerability of WVE-120102 in Patients With Huntington’s Disease (PRECISION-HD2)</td>
<td>1/2</td>
<td>Huntington lowering antisense oligonucleotide</td>
<td>WVE-120102</td>
</tr>
<tr>
<td>Safety and Tolerability of WVE-120191 in Patients With Huntington’s Disease (PRECISION-HD1)</td>
<td>1/2</td>
<td>Huntington lowering antisense oligonucleotide</td>
<td>WVE-120191</td>
</tr>
<tr>
<td>The Effects of Cognition on Balance and Gait in Huntington’s disease</td>
<td>0</td>
<td>Cognitive Behavioral Therapy, Cognitive Tests, Observational/Monitoring</td>
<td>Not Specified</td>
</tr>
<tr>
<td>Cooperative Huntington’s Observational Research Trial</td>
<td>Not Specified</td>
<td>Other</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>Efficacy of tDCS for Improving Gait in HD</td>
<td>Not Specified</td>
<td>Cognitive Behavioral Therapy, Cognitive Tests, Observational/Monitoring</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>Evaluating Wearable Sensors For Objective Measurement of Movement Disorder Symptoms – A Pilot Study</td>
<td>Not Specified</td>
<td>Data Collection, Device</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>

### Columbia University Medical Center

Paula Wasserman, Study Coordinator
Phone Number: 212-855-4957
Fax Number: 212-503-2329
Email: pw2332@columbia.edu

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*Note: The image contains a screenshot of a website interface with trial information.*
The only way to fill this bottle with a treatment for Huntington’s disease is if families enroll in clinical trials.

Please visit www.HDTrialFinder.org to enroll in a trial near you.