Enroll-HD Scientific Plan

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FINAL

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Scientific Plan Working Group Members:
Nellie Georgiou-Karistianis
Karen Anderson
Joe Giuliano
Blair Leavitt
Julie Stout
Cheryl Fitzer-Attas

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ENROLL-HD Scientific Planning Committee Membership

Co-Chairs: Karen Anderson and Julie Stout

Members:

Anne Rosser (UK)	Cardiff, UK
Karen Anderson (US)	Washington, D.C., USA
Monica Haddad (Brazil)	Sao Paulo, Brazil
Nellie Georgiou-Karistianis (Aus)	Melbourne, Australia
Blair Leavitt (Can)	Vancouver, Canada
Hugh Rickards (UK)	Birmingham, UK
Julie Stout (Aus)	Melbourne, Australia
James Gusella (US)	Boston, MA
Erik van Duijn (NE)	Leiden, Netherlands
Cheryl Fitzer-Attas (US)	CHDI, Princeton, NJ

Basic Science Advisors: Jeff Carroll (US), Ray Truant (Can)

Introduction

Enroll-HD is a global multi-center longitudinal observational study of Huntington's disease (HD). It will be open to participation for HD families in North America, Europe, Latin America, Australia/New Zealand and some countries in Asia. The overarching goal of Enroll-HD is to accelerate the discovery and development of new therapeutics for HD.

Enroll-HD is also a platform designed to facilitate HD clinical research around the world. The study provides access to clinical data and bio-specimens collected from participants. It encourages the use of data to better inform future clinical trials and to enable recruitment in clinical trials by accelerating the identification of potentially eligible participants.

Enroll-HD as a research platform will also consider the following strategies to help significantly advance knowledge in HD and develop new therapeutics:

1) Build and strengthen the platform and establish it as a stable entity while using it to train, motivate and build the existing HD networks in preparation for global clinical trials; and
2) Take advantage of the lessons learned from other observational studies in HD (COHORT, Registry, Predict, PHAROS, TRACK-HD) to significantly improve platform operations, and build on them for the future.

An important component of Enroll-HD, as a platform for HD clinical research, is the enabling of sub-studies and ancillary studies as defined below:

Sub-studies are non-interventional studies that are intended to be pre-approved as part of the Enroll-HD core protocol. They involve the development and validation of novel assessment tools or the gathering of additional data to better understand less common phenotypic presentations of HD. Additional sub-studies may be included in future versions of the protocol.

Ancillary studies may be observational or interventional and require separate IRB/EC approvals from the study institution. Ancillary studies may be performed at one site or multiple sites, but they are not part of the Enroll-HD core protocol. Ancillary studies may use data that has been gathered as part of the Enroll-HD protocol but are independent studies. Such studies may include for example testing of new imaging modalities or a new assessment, or the qualification of a new biomarker.

Enroll-HD will provide the necessary infrastructure to foster research discoveries that will make a lasting impact on improving knowledge on HD globally. The Leadership of Enroll-HD encourages investigators to "think big" and to pursue a research agenda based on relevance and impact. The Enroll-HD Scientific Planning Committee will encourage and support high quality research studies that meet this objective.

The Scientific Planning Committee (SPC) will be responsible for the review of all sub-studies and ancillary studies and will recommend high quality, relevant studies to the Steering Committee (SC) for final approval and inclusion in Enroll-HD platform. The process of how to apply for a sub-study or ancillary

study will be described in a separate document. The information below provides the scientific aims of Enroll-HD, as well as the purpose of the scientific plan, which will help guide the Scientific Planning Committee in its review of proposed studies.

Purpose of the Scientific Plan

The purpose of the Enroll-HD Scientific Plan is to:

1. Provide direction to the Scientific Planning Committee and Steering Committee for prioritization and decision making with to new projects;
2. To specify processes and mechanisms for submission of proposals, proposal review, and form making recommendations regarding proposal outcomes to the Steering Committee.; and,
3. To keep abreast of emerging trends, priorities, and research questions among the HD scientific community so that these can be used to guide potential applicants, and so that this information can be used in prioritizing proposals.

Aims of Enroll-HD

The overriding aim of Enroll-HD is to enable clinical research. The Enroll-HD Steering Committee and Sponsor state the following three aims, prioritized in order:

Specific Aim 1
To provide a platform to support the design and conduct of clinical trials by:

a. providing a resource to identify, develop and qualify novel assessment tools, clinical endpoints and biomarkers;
b. collecting longitudinal data to inform disease modeling; and,
c. facilitating the identification and rapid recruitment of clinical trial participants.

For example, this could include (but is not limited to) biomarker development and quantification, and validation of new clinical rating scales.

Specific Aim 2
To improve the understanding of how the phenotypic spectrum changes over time and the disease mechanisms of HD by:

a. collecting longitudinal natural history data covering the cognitive, behavioral and motor domains;
b. collecting data to identify genetic and environmental factors that may influence the HD phenotype and disease progression; and,

   c.   promoting studies that elucidate the pathogenesis of HD.

For example, this could include (but is not limited to) characterization of clinical phenotypes, identification of genetic and environmental modifiers of disease, or enabling a systems biology approach.

Specific Aim 3

To inform clinical decision making and improve health outcomes for the participant/family by:

   a.   assisting in the identification of beneficial interventions (e.g., clinical, pharmaco-therapeutic, non-pharmacological);
   b.   providing a platform for conducting health outcomes research; and,
   c.   promoting projects that offer exploratory data analysis that may improve the healthcare of affected individuals and their families.

For example, this could (but is not limited to) evidenced-based research for developing and confirming standards of care.