November 2026 · Issue 59

EHDN *News*

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK



Patrick Weydt and Åsa Petersén

Welcome!

Catherine Deeprose

The 59th issue of EHDN *News* brings updates from the EHDN Clinical Research Congress 2026 (EHDN CRC 2026), held in Kraków, Poland, 22–24 October. Bringing together more than 1,200 delegates from across the Huntington's disease (HD) community, this was our largest meeting to date and the second congress to present a combined EHDN and Enroll-HD programme, with clinical development firmly at the core. >>

The EHDN community is deeply shocked and saddened by the tragic news of 7 November from Kraków – a beautiful and peaceful city that so warmly hosted our community for the EHDN Clinical Research Congress.

EHDN
Clinical Research Congress
Kraków 2026

PHOTOS **RECORDINGS** **POSTERS**

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EHDN CRC 2026

EHDN Executive Committee Chair **Patrick Weydt** set the tone with an energising welcome, joined by **Cristina Sampaio, Danuta Lis**, and Polish regional official **Krzysztof Jan Klęczar**. Next, Deputy Chair **Åsa Petersén** introduced **Charlotte Spearing, Marianna Ellison-Klimontowicz, Greg Witkowski**, and **William Gray** for a powerful plenary session dedicated to family and patient perspectives. A series of sessions then took stock of the scientific and therapeutic landscape and the road ahead for the HD community.


Patrick Weydt


Cristina Sampaio


Danuta Lis


Krzysztof J. Klęczar


Marianna Ellison-Klimontowicz

Navigating the Therapeutic Pipeline

Swati Sathe and **Pavlina Stefanova-Konstantinova** welcomed **Anne Rosser** to provide an overview and update on experimental approaches, as well as the EHDN Advanced Therapies Working Group and collaborations. **Cristina Sampaio** followed with a close look at the specific opportunities and challenges facing HD therapeutic development over the next five years and beyond.


Åsa Petersén and Charlotte Spearing


Greg Witkowski


William Gray


Anne Rosser


Hugh Rickards


Jenna Heilman

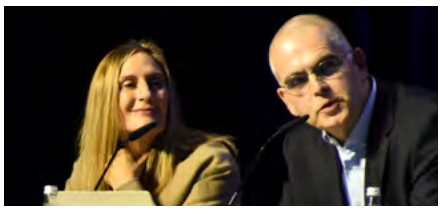

Ignacio Muñoz-Sanjuan


Josie Godfrey

Access and Affordability

Chaired by **Hugh Rickards** and **Jenna Heilman**, this session opened with an introduction to the aims and activities of the HEATED (Huntington's Equal Access to Effective Drugs) Task Force. **Ignacio Muñoz-Sanjuan** spoke on behalf of Factor-H, reminding us of the specific challenges Latin American countries face as the HD treatment pipeline progresses. **Josie Godfrey** expanded on these discussions from a policy perspective and outlined how the HD community can work together to address inherent access challenges.





Jenny Townhill and Ralf Reilmann



Jeffrey Long



Niels Skotte



William Griffiths



Hilary Wilkinson

Update on Ongoing Clinical Trials

Chaired by **Jenny Townhill** and **Ralf Reilmann**, a summary is included in Update: Clinical Trials in this issue. **Jeffrey Long** also contributed new insights into understanding the placebo response in randomised clinical trials.



Daniel Weintraub and Bernhard Landwehrmeyer



Elena Hernández Martínez de Lapiscina

Clinical Trial Progress and Regulatory Perspectives

Chaired by **Bernhard Landwehrmeyer** and **Daniel Weintraub**, this included regulatory perspectives on trial innovation and clinically meaningful outcomes by **Elena Hernández Martínez de Lapiscina**, followed by an update from Roche's **David Hawellek** on results and learnings from GENERATION HD2.



David Hawellek

Advanced Biomarkers



Rachael Scahill

Niels Skotte welcomed **William Griffiths** to speak about the potential role of lipids as biomarkers in HD. Alongside **Hilary Wilkinson**, he then presented on proenkephalin and neurofilament light chain as fluid biomarker candidates. Finally, **Rachael Scahill** provided an update on the ongoing longitudinal HD Young Adults Study (HD-YAS), tracking the early progression of HD compared to controls across comprehensive neurobiological and neuropsychiatric domains.



Jamie Hamilton and Ahmad Aziz



Matthew Roche

Efficacy Demonstration – Standards, Measures and Endpoints

Ahmad Aziz and **Jamie Hamilton** introduced **Matthew Roche,** who commenced by explaining key changes in how Unified Huntington's Disease Rating Scale (UHDRS) motor certification will be conducted in Enroll-HD.





Angelika Caputo

Angelika Caputo presented on leveraging natural history data to contextualise and quantify treatment effects, and **Glenn Stebbins** concluded with a discussion of minimal clinically important difference, within-person important difference, and the implications for regulatory decision-making.



Glenn Stebbins

EHDN Business Meeting

Patrick Weydt opened with a reminder of the importance of self-governance, strategy, science, and community in EHDN, and the critical role of voting in EHDN elections. He confirmed the new Scientific and Bioethics Advisory Committee (voted on as a slate) and thanked the members stepping down for their hard work – Chiara Zuccato, Mayke Oosterloo, Niels Skotte, Willeke van Roon-Mom, Sandrine Betuing, Silvia Gines, and Jiří Klempíř.

Moving on to the Executive Committee, Patrick confirmed that Sandrine Humbert and Kathrin Reetz were stepping down, Åsa Petersén and Ed Wild had been re-elected, and that Mayke Oosterloo and Chiara Zuccato were elected as new members (see EHDN Elections 2026: Introducing the New Executive Committee Members in this issue).

Time was then taken to reflect on the valued contributions of our sadly missed friends and colleagues Tim McLean and Stephan von Hörsten to the HD community.

Updating on EHDN activities from 2024 to 2026, Patrick recapped on the scientific strategy 2023–2028, in which 2026 saw a dedicated focus on converting a strong pipeline and infrastructure into rigorous evidence, meaningful benefit, and equitable access in the HD field. Turning to Enroll-HD, he noted the unique strength of high-quality longitudinal data and biosamples in supporting trials and platform studies, as well as generating post-approval evidence.

EHDN endorsement and support of clinical trials require a solid scientific rationale, acceptable participant risk, an appropriate and feasible trial plan, and an acceptable burden on participants, families, and resources. Patrick noted that in 2026, the discontinuation of GENERATION HD2 and POINT-HD prompted the Network to rapidly convene communication and discussion.



The Lesley Jones Seed Fund Programme marked significant milestones in 2026, with >100 funds being awarded, representing >4 million Euros in research funding across 13 countries in Europe. Strategic Funding is a new initiative intended to support EHDN Working Groups and Task Forces in conducting discrete projects aligned with EHDN strategy and building critical mass and collaboration.

Working Groups and Task Forces represent the "engine room" of member-led science. A virtual forum in 2025 saw representation from 18 groups with over 70 participants. New groups were initiated in 2026, ensuring broad coverage of care and behaviour, biomarkers and methods, and therapies and access. The EHDN Think Tank continues to drive ideas through to implementation across advanced therapies, regulatory science and platform dialogue, placing value on turning discussion into action. Platform meetings represent another strength of the Network, with the recent Roche/tominersen event culminating in 324 registrations and 211 unique viewers.

The EHDN and MDS-ES Fellowship Programme facilitates the 6-week placement of early-career HD professionals from underserved regions in highly regarded HD clinics in Europe. Six fellowships were awarded in 2026, and the 2027 programme is currently open for applications.

Patrick summarised EHDN's value in connecting the HD community in the ways outlined above. Looking ahead to 2026 to 2028, he emphasised the importance of maintaining continuity while bringing new voices to the Executive Committee and Scientific and Bioethics Advisory Committee. For the 2023–2028 scientific strategy, it will be important to turn priorities into measurable outputs. EHDN will also need to prepare for effective therapies and make access part of that success. Finally, EHDN will strengthen the HD community by enabling progress through collaboration.



Get in Touch with the Think Tank!

EHDN's Think Tank brings together EHDN members and staff who are closely involved in supporting scientific research – including members of the Executive Committee, Central Coordination and the working groups – and it engages with the HD research community in three ways:

- Researchers may contact the Think Tank for help in identifying potential collaborators or funding opportunities, or to discuss scientific ideas
- The Think Tank welcomes suggestions of research topics, and has provided a contact form on its website via which these can be submitted
- The Think Tank may occasionally propose specific research topics that could be addressed by a dedicated task force working for a defined period of time

For more information about the Think Tank, please contact Kinga.Kolodziej@ehdn.org



Keynote Lectures



Alexandra Durr

Chaired by **Nayana Lahiri** and **Hoa Huu Phuc Nguyen**, **Alexandra Durr** delved into the complexities of genetic testing and argued that understanding the molecular basis of HD is essential to advancing treatment development.



Aaron Ciechanover

Aaron Ciechanover, recipient of the Nobel Prize in Chemistry in 2004, was introduced by **Hoa Huu Phuc Nguyen** and presented fascinating insights into how understanding the ubiquitin system became fundamental to modern medical science, including advances in understanding HD science.



Nayana Lahiri and Hoa Huu Phuc Nguyen

Parallel Sessions



Daniel Zielonka and Danuta Lis

A series of parallel sessions held throughout the congress explored topics as diverse as glymphatic imaging, psychological interventions, social cognition, digital biomarkers, and artificial intelligence.

Additional highlights included **A Collaboration of Global Advocacy** presented by the Huntington's Disease Youth Organization, European Huntington Association, and International Huntington Association, and a panel discussion dedicated to **Clinical Trial Communications in Context** (chaired by **Emily Gantman** and **Ed Wild**, featuring **Charlotte Spearing, Mai-Lise Nguyen, Rachel Harding** and **David Anderson**).

The HD community joined EHDN in sharing updates throughout the congress via LinkedIn and other social media with **#EHDNCRC26**. Presentations are available on **EHDN** YouTube, and abstracts are available in an open-access supplement in the *Journal of Neurology, Neurosurgery and Psychiatry*. You can also view congress photos and posters online, and a full meeting report will be available shortly.





Sarah Gunn

End of Life Care Working Group

The End of Life Care Working Group is one of EHDN's latest initiatives. Led by Sarah Gunn (University of Leicester/UK National Health Service), Catherine Lyon (University of Leicester), and Dorine Boersema-Wijma (Huntington Center of Expertise Topaz Overduin/Leiden University Medical Center), the group is supported by EHDN Lanco Helen Finnegan Ford. The core aim is to adopt a collaborative, staged approach to improve understanding and care at the end of life for people with HD and also their family members – a critical but under-addressed part of the Huntington's journey. Find out more at ehdn.org/end-of-life-wg, and if you are interested in joining the first meeting, please register your interest at forms.gle/1MJnqvT49MixPip28.

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Gabriele Berti and Selene Capodarca

Art & HD Working Group

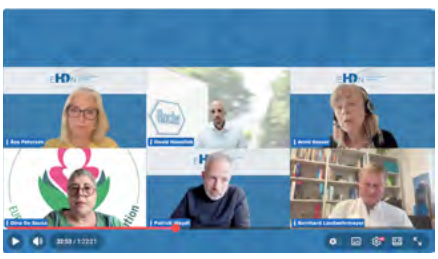
Led by Selene Capodarca (EHDN) and Melanie Clark (Edith Cowan University), the newly formed ART & HD Working Group integrates artistic and scientific approaches with the aim of establishing creative methodologies as rigorous scientific and clinical instruments. This is the first working group within EHDN to bring together researchers, clinicians, people with lived experience, artists, family associations and communication experts, with community members engaged as co-creators rather than as research participants. Find out more at ehdn.org/art-hd-wg. The group is supported by EHDN Lanco Adriana Kubis-Kubiak.

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EHDN Platform Meeting: Tominersen – GENERATION HD2 Results and Key Learnings

Following Roche's community letter announcing the discontinuation of GENERATION HD2 and EHDN's Executive Committee statement, EHDN hosted a platform meeting on 29 September 2026, where David Hawellek, Biomarker & Experimental Medicine Leader at Roche, discussed the results and key learnings from the study of tominersen. The expert panel included Patrick Weydt, Åsa Petersén, Anne Rosser, Bernhard Landwehrmeyer, and Dina De Sousa. The recording is available on EHDN YouTube, and the results of an evaluation of the platform meeting were included in a poster at EHDN CRC 2026.



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Roughly 40 participants joined the workshop in Yerevan, Armenia

Huntington's Disease and Hyperkinetic Movement Disorders Workshop, Armenia

Selene Capodarca, Enroll-HD Global Study Director



Selene Capodarca



Zaruhi Tavadyan

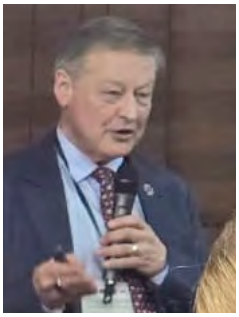


Hugh Rickards

I was thrilled to present at the Huntington's Disease and Hyperkinetic Movement Disorders workshop, held in Yerevan, Armenia, on 7 November 2026. This event was part of the MDS-ES Developing World Educational Program, organised by the International Parkinson Movement Disorders Society and Armenian Movement Disorder Group, and co-hosted by EHDN and the Armenian National Institute of Health (NIH).

Zaruhi Tavadyan (Armenian NIH, Parkinson's Disease and Movement Disorders Center, Somnus Neurology Clinic, Yerevan, Armenia), a former fellow of the EHDN & MDS-ES Huntington's Disease Fellowship Programme, led the organisation of the event. This built on the success of a workshop held in Dilijan in October 2024, and further extended her collaboration with fellowship host Hugh Rickards (Birmingham and Solihull Mental Health NHS Foundation Trust; University of Birmingham, UK).

> *'On a personal note, this was a truly meaningful opportunity to connect with the HD community in Armenia.'*
>
> ***Selene Capodarca***



Bernhard Landwehrmeyer

EHDN was also represented by Bernhard Landwehrmeyer (Ulm University Hospital, Germany). Additional speakers included Michele Matarazzo (HM CINAC, Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain), Matej Skorvanek (Pavol Jozef Šafárik University and University Hospital, Košice, Slovakia), and Marika Megrelishvili (Department of Clinical Neurology, Tbilisi State Medical University; Simon Khechinashvili University Hospital, Tbilisi, Georgia).

The high-quality scientific presentations were accompanied by stimulating discussions on how EHDN can support education and research in the region. A particular focus was the Enroll-HD platform and the significant value of its rich longitudinal data and biosamples for the region's growing research community.

On a personal note, this was a truly meaningful opportunity to connect with the HD community in Armenia, and I look forward to building on this collaboration in our shared mission to advance HD science and care.

Lesley Jones Seed Fund: Latest Awards

EHDN has recently awarded seed funding to two exciting new projects.



Manuel Seefelder

Manuel Seefelder (Ulm University) has been awarded funding to develop DNA aptamers using the SELEX method that selectively distinguish between the two forms of HAP40 – one bound to Huntingtin (HTT) and one free-floating – allowing them to be studied separately for the first time. This matters because HAP40 is among HTT's most abundant partners in the brain, both proteins decline in HD, and the role of the unbound form has never been investigated.



Rosanna Parlato

Rosanna Parlato (Heidelberg University) has been awarded funding to investigate glycans – sugar structures on proteins and cells – which play key roles in neuronal function but have never been systematically studied in HD. Using HD mouse models and human stem cell-derived brain tissue, she will map glycan changes across different cell types to uncover their role in disease progression and explore their potential as biomarkers and treatment targets.



Flaviano Giorgini



Kinga Kolodziej

The Lesley Jones Seed Fund programme is intended to support pilot studies that will eventually kickstart larger projects. The next deadline for applications is 1 March 2027.

More information about the programme and how to apply is available here or you can contact Flaviano Giorgini (flaviano.giorgini@ehdn.org) or Kinga Kołodziej (kinga.kolodziej@ehdn.org) for further information.



Lunch at Bottino, West Chelsea, NYC, June 2, 2022 – Photo: Animesh Ray

In Memoriam: Ethan Signer

We are profoundly saddened by the passing of **Dr Ethan R. Signer**, a pioneering molecular biologist and dedicated advocate for families impacted by HD.

A founding scientist at CHDI Foundation (and before that, the Hereditary Disease Foundation), Ethan's legacy extends beyond publications, programmes, and the many individuals he mentored to encompass the collective strength of our community today. His commitment to rigorous, collaborative science will live on in all of us as we continue our shared mission to advance HD research and care.

Ethan will be deeply missed by his family, friends, colleagues, collaborators, and the HD community.



Juliana Bronzova and Fionnuala Margreiter



Asun Martínez

Update: Fellowship, Education and Funding

Fionnuala Margreiter, Grants & Collaborations Manager,
Juliana Bronzova, Science Director

EHDN and European Academy of Neurology (EAN) Initiatives

Engagement with EAN at their congress in June highlighted the importance of contributing early to congress planning through scientific panels, committees and educational structures. EHDN is encouraging members to become more involved in these groups so that HD expertise is represented in future calls for topics, courses and workshops. Similarly, EHDN members could be involved in the MDS Regional Sections and Education Committees to help bring HD topics for discussion and planning of joint training activities/workshops.

> *'Fellows enjoyed learning more about EHDN and Enroll-HD activities and how they could remain engaged beyond their placements.'*
>
> ***Fionnuala, Juliana and Asun***

EHDN & MDS-ES Huntington's Disease Fellowship Programme (written with Asun Martínez)

Two of the 2026 fellows have completed their placement in Spain in recent months. The other five fellows started their placement in October to coincide with participation in EHDN CRC 2026. This was an important opportunity to strengthen links between fellowship participants and the wider EHDN community, and included an evening networking event and a dedicated fellowship meeting. Fellows enjoyed learning more about EHDN and Enroll-HD activities and how they could remain engaged beyond their placements. A joint poster by the fellowship team with the 2025 and 2026 fellows was also presented.

Genetic Counselling Workshop at Factor-H Conference

EHDN recently collaborated with Factor-H in providing a genetic counselling workshop at the



2026 Latin American Huntington's Disease Conference in Medellín, Colombia. Through support from Spanish-speaking expert in medical genetics, Claudia Perandones, and ongoing knowledge-sharing activities, the initiative helped strengthen education and professional development opportunities for the HD community across Latin America. EHDN's Asun Martínez also co-hosted a very successful session with the lay community during the conference.

Update: Clinical Trials

Jenny Townhill, EHDN Clinical Trial Director; Director, Enroll-HD External Partnerships

Key updates since the July newsletter are provided below for EHDN-endorsed trials with a particular focus on presentations at EHDN CRC 2026; please refer to Table 1 for a summary of all ongoing endorsed research. An expanded description of EHDN-endorsed trials and studies (completed and in progress) and details of the EHDN endorsement process are published on the EHDN website.

Alnylam Therapeutics: ALN-HTT02 (brezosiran) is an RNA interference (RNAi) therapeutic. Administered intrathecally, it targets exon 1 of HTT messenger ribonucleic acid (mRNA) to reduce HTT protein levels. At EHDN CRC 2026, **Sarah Tabrizi** presented interim data from the ongoing phase 1b trial in HD-ISS stage 2 and early-stage 3 participants, suggesting dose-dependent HTT-lowering and an encouraging safety profile. Five single-ascending doses have been studied to date, with no dose-dependent increases in central nervous system (CNS) inflammatory markers, cerebrospinal fluid (CSF) neurofilament light chain (NfL), or ventricular size. Participants can opt to join the open-label extension receiving brezosiran every six months, allowing the further evaluation of safety and potential efficacy trends. A larger placebo-controlled study is planned for 2027; further details will be shared by Alnylam in due course.



Sarah Tabrizi



Beth Borowsky

Novartis Pharmaceuticals: The current phase 3 INVEST-HD trial progresses the global expansion of the study investigating the safety and efficacy of the small-molecule votoplam (previously PTC-518). **Beth Borowsky** discussed the phase 2 votoplam study results at EHDN CRC 2026. This included data from the phase 2 long-term extension (LTE) study, in which an interim analysis of 24-month data showed a safe, well-tolerated clinical profile with no evidence of treatment-induced NfL spikes or mean increases. Group-level NfL changes in the HD-ISS stage 2 and early-stage 3 groups did not show the increases typically observed in natural history studies. Dose-dependent decreases in mHTT were found at 12 months compared to placebo and continued to 24 months. Previously reported favourable changes on the cUHDRS at 12 months were sustained at 24 months compared to a propensity score-matched (PSM) control cohort from Enroll-HD.



Skyhawk Therapeutics has four studies of the investigational, once-daily oral small-molecule SKY-0515: three trials and an open-label extension. The phase 1/2 trial has completed, and the final 15-month data were reported in a press release on 15 September 2026.

At EHDN CRC 2026, **Meghan Miller** presented these data in more detail. Up to 15 months, SKY-0515 appeared safe and well tolerated. Preliminary data suggested dose-dependent effects, CNS penetrance, and lowering of HTT and postmeiotic segregation increased 1 (PMS1) mRNA in blood (~62% lowering of HTT and ~26% lowering of PMS1 in the high-dose group), while CSF and plasma NfL remained stable. Comparisons with an overlap-weighted natural history external control suggested favourable outcomes for SKY-0515 at 15 months on cUHDRS and its components, and subdomains of the UHDRS® Total Motor Score.



Meghan Miller

FALCON-HD, the phase 2/3 trial in Australia and New Zealand, has completed enrolment of 144 participants and is ongoing. The open-label extension has enrolled participants from the phase 1/2 trial and will be open to eligible participants as they complete FALCO N-HD. The EHDN-endorsed worldwide FALCON-HD phase 2/3 study is recruiting at around 21 sites globally

(target recruitment 400–600 participants), with more sites in Latin America, Europe and North America expected to open soon (see ct.gov).

uniQure: In September, uniQure announced submission of a Biologics License Application (BLA) to the US FDA and a Marketing Authorisation Application (MAA) to the UK MHRA for AMT-130 (ifezuntirgene inilparvovec). The FDA has subsequently accepted the BLA and granted priority review, with a target decision date of 1 May 2027.

The BLA and MAA applications were supported by the 36-month data reported in September 2025 (N = 12) compared with a PSM control from the Enroll-HD natural history study (Enroll-HD A: PDS6).

Later in September, uniQure reported 48-month data (N = 12) and updated 36-month data (N = 15) from the ongoing phase 1/2 studies. Outcomes were compared with PSM controls from an updated Enroll-HD dataset (Enroll-HD B: PDS7). Disease progression, assessed using the cUHDRS, was slowed by 80% at 36 months (nominally statistically significant) and 44% at 48 months (not statistically significant). Disease progression was slowed significantly at both 36 (67%) and 48 months (61%) for Total Functional Capacity (TFC). For the high-dose group, mean CSF NfL was 6% below baseline at 36 months (N = 14) and 4% above baseline at 48 months (N = 11).

Use of the updated Enroll-HD dataset presented challenges in comparing outcomes between the topline 36-month (September 2025), the updated 36-month, and the 48-month analyses. Therefore, a post-hoc analysis to further examine treatment effects at 48 months was conducted using PDS6 (Enroll-HD A). This showed slowing of disease of 54% on cUHDRS and 68% on TFC (both nominally statistically significant).


David Margolin

At EHDN CRC 2026, **David Margolin** presented 36-month data on Quantitative Motor (Q-Motor) dominant-hand speeded finger tapping – inter-onset interval and inter-peak interval – for the high-dose AMT-130 group (N = 17) compared with a propensity score weighted (PSW) external control arm from the TRACK-HD and TRACK-ON natural history studies. The Q-Motor measures favoured AMT-130 vs PSW control (non-significant). Differences between groups increased over time, with the greatest separation at 3 years compared with baseline.

Vico Therapeutics: At EHDN CRC 2026, **Scott Schobel** presented an update on the phase 1/2a study of VO659, an experimental antisense oligonucleotide (ASO) that binds directly to the CAG repeat. VO659 is designed to target several drivers of HD pathophysiology, including HTT1a and RAN protein, while sparing wild-type HTT. Data from cohorts 1–3 (10–40 mg


Scott Schobel



every 4 weeks) suggest that VO659 is generally well tolerated and achieved a significant, dose-dependent reduction in CSF mHTT levels, with no sustained elevation of NfL. Dosing is ongoing under a revised protocol (cohorts 4–5) to evaluate less frequent, long-term administration aiming to reduce inflammatory risk. Cohort 4 data (as of 1 October 2026) suggest VO659 is suitable for long-term dosing from a safety and tolerability perspective. Planned interim analyses will inform dose regimens for long-term study.

Table 1: Current EHDN Endorsed Trials

Registration ID	Sponsor	Trial name	Phase	Investigational Product	Mode of Action	Delivery	Treatment Goal	Target Enrolment	Location(s)	Status
NCT06585449	Alnylam Pharmaceuticals	ALN-HTT02-001	1	ALN-HTT02	HTT lowering; siRNA	Intrathecal	Disease modification	66	Canada, Germany, UK	Recruiting
ISRCTN87426672	Cardiff University	DEVISE-HD	4	Sertraline	Selective serotonin reuptake inhibitor	Oral	Feasibility	40	UK	Recruiting
NCT05686551	Hoffmann-La Roche	GENERATION HD2	2/OLE*	Tominersen	HTT lowering; ASO	Intrathecal	Disease modification	301 (actual)	Argentina, Australia, Austria, Canada, Denmark, France, Germany, Italy, New Zealand, Poland, Portugal, Spain, Switzerland, UK, USA	Active, not recruiting
NCT07246941	Hoffmann-La Roche	POINT-HD	1	RO7764733	mHTT lowering, ASO (SNP directed)	Intrathecal	Disease modification	40	Argentina, Australasia, Europe	Active, not recruiting
NCT07326709	Novartis Pharmaceuticals	INVEST-HD	3	Votoplam	HTT lowering, splicing modifier	Oral	Disease modification	770	Global	Recruiting
NCT07378644	Skyhawk Therapeutics	FALCON-HD	2/3	SKY-0515	HTT & PMS1 lowering, splicing modifier	Oral	Disease modification	400	Argentina, Brazil, Canada, Chile, Colombia, Georgia, Germany, Mexico, Peru, Poland, Spain, UK	Recruiting
NCT05243017	UniQure Biopharma B.V.	HD GeneTRX2	1b/2	AMT-130	HTT lowering; miRNA AAV-delivered gene therapy	Surgical, intrastriatal	Disease modification	15	Poland, UK	Active, not recruiting
NCT05822908	Vico Therapeutics	VO659-CT01	1/2, open-label	VO659	HTT lowering; allele-preferential ASO	Intrathecal	Disease modification	68 (SCA1, SCA3 and HD)	Denmark, France, Germany, Israel, Netherlands, UK	Recruiting

Note. AAV = adeno-associated virus; ASO = antisense oligonucleotide; HD = Huntington's disease; HTT = huntingtin; mHTT = mutant huntingtin; PMS1 = postmeiotic segregation increased 1; SCA1 = spinocerebellar ataxia type 1; SCA3 = spinocerebellar ataxia type 3; SiRNA = small interfering ribonucleic acid; SNP = single nucleotide polymorphism



Update: Moving Towards Enroll-HD 2.0

Olivia Handley, Enroll-HD Global Platform Director



The amendment to Enroll-HD (protocol version 2.0) will ensure the study meets current scientific needs and supports the next generation of clinical trials and research within the promising landscape of HD therapeutic development. While the study objectives remain unchanged, the study design will place greater focus on earlier-stage HD and use the Huntington's Disease Integrated Staging System (HD-ISS; see the November 2025 issue) to guide recruitment.

The main changes include:

- Assigning participants to one of several cohorts, with assessments and procedures tailored to each cohort
- Targeted recruitment of specific populations using the HD-ISS
- Expansion of biosample collection activities
- Inclusion of two substudies available at selected sites for eligible participants

Key Study Documents

The amendment protocol was finalised in September 2026 and is currently undergoing signature approval. Significant progress has been made in developing the main participant informed consent form, while additional consent templates for substudies are nearing finalisation. Finalised versions of participant-facing materials are being delivered on an ongoing basis, including recruitment materials, participant-facing assessments, and procedural guidance outlining participation requirements. A new study site agreement template (with accompanying pricing schedule) is fully drafted and undergoing review.

Infrastructure

During protocol development, the Enroll-HD operations team assessed the infrastructure requirements needed to support the planned changes. Below are some of the major new and modified systems and services being implemented to support the updated study:

- New electronic data capture (EDC) system to
  - Support the transition of participants from Enroll-HD 1.0 to 2.0
  - Host additional substudies
  - Enable the continuation of HDClarity within the Enroll-HD EDC platform environment
  - Present new/modified EDC case report forms in a new visit schedule
  - Enable EDC-supported cohort assignment
  - Enable expanded biosamples collection activities
  - Deliver new and improved connectivity to other interfaces, such as the biorepository and electronic patient-reported outcomes (ePRO) platform
- Functionality within the ePRO platform to allow participants to enter patient-reported outcome data directly via a secure portal (either at home or at a visit using a tablet or similar device)
- Video-conferencing provider to allow participants, including companions, to join remote visits
- Sophisticated learning management system to assign, deliver, track and evidence a wide range of protocol-specific training for study site staff. This will serve as a repository to track and manage training compliance, and will enable swift and reliable course updates to be implemented
- New and/or modified assessments and accompanying translations requiring licenses/permissions
- Imaging biorepository for iEnroll-HD

Enroll-HD 2.0 represents a major expansion of the study, aligning its design and infrastructure with the evolving needs of the HD research community. Significant progress continues across protocol finalisation, study infrastructure, and operational readiness. At the time of writing, the timing of the first site transition remains subject to change, and we will communicate timelines directly to sites as key milestones are achieved over the coming months.

> *'We are excited to work in partnership with the Enroll-HD community to build a strong foundation that will support future HD research and enable the next generation of clinical trials.'*
>
> **Olivia Handley**

The Enroll-HD operations team continues to make strong progress towards delivering a smooth transition to the updated study. We are excited to work in partnership with the Enroll-HD community to build a strong foundation that will support future HD research and enable the next generation of clinical trials.

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HDClarity

Update: HDClarity

Gail Owen, Principal Research Associate, University College London, UK

HDClarity contributes to one of the primary aims of the Enroll-HD platform by providing CSF, plasma and serum samples that can be shared with researchers to identify and evaluate biomarkers for HD. All HDClarity study sites and participants must be taking part in Enroll-HD, as this ensures that the samples can be linked to Enroll-HD participant data collected at the annual study visits.

HDClarity sites must have teams with the expertise to perform lumbar punctures, or spinal taps, the procedure used to collect CSF. They must also have well-equipped laboratories that can process the samples according to a detailed manual and within a limited timeframe. This ensures participant comfort and sample quality.

We are very proud that HDClarity sites have now been opened in 11 countries, almost half of the 23 territories that are active in Enroll-HD. Samples were donated by our first Portuguese participants this year at the Gulbenkian Institute of Molecular Medicine – adding to those from other countries, including Germany, Italy, Spain, France, the UK, the USA, and Canada. Samples are also shipped to the central biorepository from the Southern Hemisphere and travel over 11,000 miles from both the North and South Islands of New Zealand. We are very excited that we will soon be adding Australia to this list when Monash University joins the HDClarity study. And, just like Enroll-HD, the ongoing success of the study depends entirely on these teams and the amazing participants around the world who volunteer their time to become a part of HD research.

> *'Samples were donated by our first Portuguese participants this year at the Gulbenkian Institute of Molecular Medicine – adding to those from other countries, including Germany, Italy, Spain, France, the UK, the USA, and Canada.'*
>
> **Gail Owen**

For further information about requesting HDClarity samples for research, please see information at enroll-hd.org/for-researchers/access-data-biosamples/. The current HDClarity protocol and lab manual and a full list of participating sites are available at hdclarity.net, and the UCL Central Coordination team are always happy to answer any questions about the study (hdclarity-cc@enroll-hd.org).

EHDN Elections 2026: Introducing the New Executive Committee Members

Biennial elections for the EHDN Executive Committee and Scientific and Bioethics Advisory Committee ran from 1 June to 19 October 2026, in accordance with the EHDN Constitution.

The Executive Committee governs EHDN, directs and oversees its activities, and sets the Network's strategic direction, as outlined in Article 4 of the EHDN Constitution. In 2026, four positions were filled, with votes cast for individual candidates. Voter turnout was encouragingly higher than in recent years, and we look forward to building on this further in future voting cycles.

At EHDN CRC 2026, Executive Chair Patrick Weydt thanked the EHDN membership for voting and announced that Åsa Petersén and Ed Wild were re-elected, and that Mayke Oosterloo and Chiara Zuccato would be joining the Executive Committee as newly appointed members. Here, in their own words, Mayke and Chiara reflect on what these appointments mean to them.



Mayke Oosterloo

Assistant Professor
Maastricht University,
Netherlands

"I am a neurologist specialising in Huntington's disease at Maastricht University Medical Centre in the Netherlands, where I lead the Huntington's Disease Expertise Centre. I have been actively involved in the EHDN for several years, including as a member of the Scientific and Bioethics Advisory Committee.

I am honoured to join the Executive Committee and sincerely thank everyone who placed their trust in me. I hope to bring my clinical and research experience, strengthen collaboration between researchers, healthcare professionals and patients, and contribute to translating scientific advances into meaningful improvements in care for Huntington's disease families."



Chiara Zuccato

Associate Professor of Pharmacology
University of Milan, Italy

"I am a basic scientist at the University of Milan. My research focuses on identifying the determinants of synaptic dysfunction to develop new strategies against cognitive decline in HD. Throughout my career, I have actively engaged with patient associations, fostering dialogue among researchers, clinicians, and HD families.

After four years on the EHDN Scientific and Bioethics Advisory Committee, joining the Executive Committee is a privilege. I am deeply grateful for this opportunity.

I believe that research can only make a real difference if it walks hand in hand with patients. I will leverage my expertise to create the 'HD Young Scientists Network', connecting young researchers working on HD in Europe, and promote a dedicated EHDN conference session in which the young scientists and families can meet."



Patrick commented, "Welcoming Mayke and Chiara to the Executive Committee, alongside the re-election of Åsa and Ed, is one of the highlights of the congress. We are bearing witness to just how dynamic the HD field has become, and EHDN CRC 2026 captured this momentum exceptionally well – a growing and connected community, a rich therapeutic pipeline, strong science across the translational spectrum, and an expanding infrastructure for clinical research. Together, the Executive Committee will ensure EHDN continues to provide the forum, networks, and communication channels needed to turn that progress into meaningful advances for people and families impacted by HD."

> *'Welcoming Mayke and Chiara to the Executive Committee, alongside the re-election of Åsa and Ed, is one of the highlights of EHDN CRC 2026.'*
>
> ***Patrick Weydt***

Full details of the Executive Committee and Scientific and Bioethics Advisory Committee membership as of 22 October 2026 are available on the EHDN webpage. The next EHDN elections will take place in 2028, and members will be kept informed as the process gets underway.



Dates for Your Diary

- **10–11 December 2026:** VII International Conference of the Portuguese Society of Genetics takes place in Coimbra, India.
- **1 March 2027:** Applications close for the Lesley Jones Seed Fund programme.
- **12–14 March 2027:** Huntington's Disease Youth Organization's International Young Adults Congress takes place in Barcelona, Spain. Registration is now open.
- **12–15 June 2027:** The 60th European Human Genetics Conference takes place in Rotterdam, the Netherlands. Registration is available for in-person or virtual attendance and will open in February 2027.
- **26–30 October 2027:** The American Society of Human Genetics Annual Meeting takes place in Nashville, Tennessee. Further details to follow.
- **14–18 November 2027:** The HSG Clinical Research Congress takes place in Nashville, Tennessee.
- **5–7 October 2028:** The next **EHDN Clinical Research Congress** takes place in Copenhagen, Denmark. Save the date!

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