MARCH 2022

Global perspectives:

HAEi MAGAZINE · ISSUE 1/2022

93 Member countries

Global perspectives:

Global Perspectives
Issue 1/2022
March 2022

Cover photo
HAEi announces upcoming 2022 HAEi Global Leadership Workshop in Germany, 6-9 October – read more on page 18.

Magazine staff
Henrik Balle Boysen, Executive Vice President and COO

Rikke Sørensen, Communication Design and Graphics Manager

Steen Bjerre, Communications Manager

Subscription
If you would like to subscribe to our magazine, please send an email to info@haei.org or register directly at haei.org

HAEi 2022 activities are supported by:

biocryst
CSL Behring
Pharming
Takeda

HAEi
HAE International

HAEi is registered as a non-profit organization in USA

HAEi is a global non-profit umbrella organization dedicated to working with a network of national HAE member organizations to raise awareness of HAE

DEAR HAEi FRIENDS,

Welcome to the first 2022 edition of Global Perspectives, the quarterly magazine that provides a truly comprehensive overview of what is happening in the global HAE community.

I would like to start this message by highlighting changes we are making to future HAEi sponsored gatherings. The steady growth in our community has made it impossible to find a venue large enough to accommodate the HAE Global Conferences we have held in the past. With this new reality in mind, the HAEi team went back to the drawing board with the idea of planning future in-person meetings that allow maximum participation and best serve the diverse situations and needs faced by HAEi friends throughout the world.

The relaxing of COVID-19 restrictions has enabled us to schedule our first HAEi Global Leadership Workshop that will take place in Frankfurt, Germany from 6 October to 9 October 2022. In addition, we are planning three HAEi Regional Conferences:

- 2023 HAEi Regional Conference APAC (Asia Pacific),
- 2023 HAEi Regional Conference EMEA (Europe, Middle East, and Africa), and
- 2024 HAEi Regional Conference Americas (North and South America)

More details about the new event offerings can be found on page 18.

As outlined in the article on page 15 – HAE Treatments on the Horizon – the interest in developing new HAE medicines is nothing short of extraordinary. This good news is cause for optimism, and our community wholeheartedly supports continued investment in next generation HAE therapies. Nevertheless, there are altogether too many of our Member Organizations that do not have adequate access to and reimbursement for the eight modern treatments that have already been approved by regulatory authorities. This reality motivates HAEi's burning desire for developing programs, training initiatives, tools, and services to help Member Organizations advocate for winning access to the modern HAE treatments. It is always worth mentioning that our kind, compassionate, and knowledgeable Regional Patient Advocates (RPAs) are always ready to help Member Organizations organize and implement a successful advocacy program. See page 6 for the latest reports from our RPA's.

HAEi is horrified and saddened by the situation being faced by our fellow HAE brothers and sisters in Ukraine. Some Ukrainians are seeking a safer environment by fleeing to neighboring countries. Page 23 includes practical information for those arriving in another country.

I wish all HAEi friends happy reading.

Warm regards,

Tony

Anthony J. Castaldo
President and CEO, HAEi

IN THIS ISSUE

IN THIS ISSUE OF GLOBAL PERSPECTIVES

NEWS FROM THE HAEi REGIONAL PATIENT ADVOCATES

HAEi has many fantastic tools and resources to support our Member Organizations and people with HAE. We are delighted to see the great uptake of the HAE TrackR app which allows patients to record their attacks as well as acute and prophylactic treatments. HAE TrackR is now available in 27 languages.

Our Regional Patient Advocates (RPAs) continue to focus on the global roll-out of HAEi Advocacy Academy, our comprehensive online educational platform. We are encouraged that many Member Organizations have voiced their opinion that the information contained in HAEi Advocacy Academy courses is invaluable and has helped them turn ideas into action.

HAEi designs its programs, services, and activities to meet the diverse needs of the global HAE community. We regularly obtain information and guidance from our Regional Advisory Groups (RAGs), which consist of Member Organization leaders in each region. The RPAs are now in the process of working with the RAGs on another round of information gathering, which will inform HAEi on ways to address our Member Organization's current unmet needs and challenges.

hae day :-) 2022 is fast approaching, and we look forward to everyone participating in this year's event, ***Stepping Up for the Global HAE Movement***.

The HAEi RPAs are always ready to help by providing their expertise and support. Please reach out to your RPA for any of your HAE related questions.

Fiona Wardman
Chief Regional Patient Advocate

JØRN SCHULTZ-BOYSEN
NORDICS, GERMANY, AUSTRIA AND SWITZERLAND

We are still working on bringing together the Regional Medical Advisory Panel for the region. Some doctors are on board, and for some countries, we are waiting for a confirmation of who should join. The first round of dialogue has already been ongoing. Still, it will be great to get the next countries on board to get the whole region activated in this activity and benefit from the great experience from all the involved persons.

Similarly, feedback from the Regional Advisory Groups is also starting to come in, which is excellent. This will enable us to benefit from the experience of the local organizations in the region and also use the ideas present for HAEi.

In my region, HAE TrackR has been made available in two more languages over the past period. It is now also ready in French and Finnish, adding to German, Norwegian, Swedish, and Danish. A huge thank you to the people in the Member Organizations who have helped with the translation of the app. As stated before, the HAE TrackR app is easy to use – and a safe way to store your data – and it will help the patient and physician in their dialogue on current and future treatment options. I can only urge everyone to check it out and start using it!

The Member Organizations have let their members know of the option to use the HAE TrackR app as well – this is really great! And again, a kind reminder for everyone that the HAE TrackR app is available in many languages, ready for you to use – and to make your everyday with storing your HAE treatments a lot easier. As with any other tool, you need to try it and get used to it, and we are certain that you will see the benefit once you do that.

Germany continues to be very active, amongst other things, on social media and releasing interesting podcasts regularly. The podcasts cover everyday issues, challenges, and opportunities on living with HAE.

Switzerland and Austria are planning the first physical meetings since the coronavirus outbreak. It will be exciting to meet again!

Finland is planning several online activities over the coming months. A lot of interesting information will be shared with the participants.

Norway, Sweden and Denmark are still leveraging from the patient meeting held in November 2021. At the same time, several exciting projects are about to kick-off, not least to benefit the younger part of the community. Also, local patient meetings are being planned.

Work continues on a new HAEi patient guide which will soon be shared with our contact at the University Hospital in Reykjavik, Iceland. This patient guide will also be available for other Member Organizations to translate for the patients in their countries.

MARIA FERRON
THE MEDITERRANEAN, NORTH AFRICA AND THE BRITISH ISLES

I am happy to announce that Lanadelumab was recently approved to be used in hospitals in Portugal. Also, from Portugal, the HAE team has been working on setting up their 2022 actions plans which among others includes an HAE awareness campaign (supported with an HAEi poster), creating an activity for **hae day :-)** 2022, increasing the number of members of the national organization and improving their activity in social networks.

During mid-February, a meeting took place (pictures right) in Italy between the board of the Italian Network of Hereditary Angioedema (ITACA) and the board of HAE Italy (AAEE APS.ETS). The focus of the meeting was the definition of the action plan for the conjoint objective of increasing the functionality of all the HAE regional centers and a survey of the current weaknesses and strengths. In Italy, patients and HAE centers (doctors) have played an important role in spreading treatments and care for this disease. They would like to keep this collaboration to produce new tools and give patients and doctors more opportunities to manage and study HAE and other forms of angioedema.

On 26 February 2022, the 15th Conference on Rare Diseases took place in Morocco. The Alliance of Rare Diseases in Morocco (AMRM) organized two events:

A webinar with the support of Laboratories Roche and Laprophan under the theme "Patients facing rare diseases". This meeting was an opportunity to highlight once again the extent of these diseases as well as the difficulties that patients must overcome on a daily basis to live with their disease. Dr. Khadija Moussayer (President of the Alliance of Rare Diseases Morocco, President of the Moroccan Association of Autoimmune and Systemic Diseases (AMMAIS) and Vice-President of HAE Morocco (AMMAO) participate as a moderator while Imad El Aouni (President of AMMAO) spoke about HAE.

A hike in Benslimane with the support of the Jansen laboratory in support of rare diseases in general and one of the most severe, pulmonary arterial hypertensions, under the slogan "a step for a better breath".

Rare diseases pose a real problem in Morocco, as they are the cause of medical wandering that can last a lifetime. They are difficult to diagnose due to the lack of reference centers and the absence of systematic screening for certain rare diseases at birth. Their care is also problematic because of the non-accessibility of drugs in addition to the wandering of the patient during the care pathway.

CSL Behring has recently launched the patient support program CALMA TM in Spain. The program is for those patients using subcutaneous Berinert® 2000. The program facilitates the continuity and follow-up of patients in long-term prophylaxis and reduces the emotional burden of the disease.

Also in Spain, around 70 HAEi posters were distributed by health care professionals during the 1st National Scientific HAE workshop organized by the HAE and Dermo-Allergy CSURs (Reference Centers, Services and Units of the Spanish National Health System) in February at La Paz University Hospital in Madrid. HAE Spain (AEDAF) distributed more posters to health care professionals and patients (to hang in their hospitals, general practices, and emergency rooms) at their annual meeting on 26 March 2022.

Also, I would like to mention that I am working on providing National contact Ahmed Ali Abudahair from HAE Libya and Dr. Mariem Kebe from Mauritania with access to HAEi poster printings to distribute in their countries to find more HAE patients.

PATRICIA KARANI
SUB SAHARA AFRICA

In Namibia, a new HAE patient was diagnosed. We have been working with the physician to ensure that the patient receives the best possible care with the treatments presently available.

In Eritrea, a family with HAE has been found, and we are working to find a local physician with whom we engage to assist these patients with better management.

As for Kenya, Rare Disease Day was celebrated by HAE Kenya, being part of a panel of experts who discussed the journey and plight of patients living with rare diseases. I got a chance to talk about HAE and the burden of illness in my life. We had good discussions with representatives from the Ministry of Health, who assured us that they have set up a task force within the Ministry to try and come up with policies that will benefit patients with rare diseases. We also had representatives from KEMRI (Kenya Medical Research Institute), and they too highlighted the importance of researching rare diseases in Kenya.

I also participated in the KEMRI survey on rare diseases in Kenya. They try to forge out recommendations on rare diseases, more specifically in terms of access to healthcare services.

FERNANDA DE OLIVEIRA MARTINS
SOUTH AMERICA AND MEXICO

We are planning to apply the Baseline Burden of Illness Study in Mexico to understand the patient situation in the country better and support them better. The translation and adaptation of the questionnaire is being made by the leader of HAE Mexico.

The US HAEA has created a new Brady Book spring activity. The Spanish version has been shared with Member Organizations in South America and Mexico to be enjoyed by children in those countries as well.

Posting on social media continues, especially promoting activities organized by the Member Organizations to celebrate the rare disease day.

NATASA ANGJELESKA
SOUTH EASTERN EUROPE

The first preventive treatment started for one boy in North Macedonia, suffering from HAE attacks every four to five days. Thus far, the young patient responds to the new treatment very well, with no breakthrough attacks.

HAE Turkey has held a very successful meeting in Denizli with physicians and caregivers to come together with children and young patients and their families to share their HAE experiences. They discussed attacks experiences and got support from the psychologists who participated in the event.

I held meeting with a broader group of patients in Bosnia and Herzegovina. It was a very pleasant meeting, and I managed to respond to their questions regarding different HAE treatments available in general, specifically about the treatments available in North Macedonia. I also presented different awareness and advocacy activities we've undertaken in the past five to seven years in North Macedonia to make treatment available. Finally, we agreed on some concrete things to be implemented in the coming period.

Things started moving in Kosovo, as I held a meeting and exchanged many messages with a physician who treats two HAE patients. I'm also now communicating with a patient and a caregiver, trying to provide them with information about the disease, diagnostics, and treatment options. He was able to come to a medical examination in Skopje at Prof. Grivcheva who also scheduled laboratory testing to confirm the diagnosis. This patient has HAE type 2.

In December and January, I've participated in meetings with KalVista representatives to discuss clinical rollout in North Macedonia, Albania, and Kosovo. I held meetings with a representative from Exceed Orphan – distributer for Ruconest® and discussed availability options for patients in Albania, Bosnia and Herzegovina, and Montenegro.

In February, most of my activities were around organizing Rare Disease Day in North Macedonia as I was one of the speakers at the Rare Disease Day Meeting. I addressed the challenges in front of the Minister and Deputy Minister for Health, The First Lady/spouse of the President of North Macedonia, directors of different University Clinics, members of the Rare Disease Committee, patients, caregivers, pharma representatives, and media.

I have assisted patients in Albania in establishing communication with a new patient, who unfortunately lost his twin brother due to HAE not being diagnosed on time. This sad occasion also had me urge the representative for Ruconest® for Albania to communicate with both physician and patient representatives to hear their needs for improved access to medications in the country.

Together with HAE Macedonia representatives, I held a meeting with HAE Greece to assist in some aspects of cooperation with pharma companies, submitting budget proposals, budgeting, etc. HAE Greece provided input in the form of a case study about registering patient organization course that is part of HAE Advocacy Academy now.

I continued sharing information about each patient's advantages when using the HAE TrackR app and asked more countries to translate the application to the local language to become more available to patients everywhere.

MICHAL RUTKOWSKI
CENTRAL EASTERN EUROPE, BENELUX AND THE MIDDLE EAST

I hope you have had an enjoyable holiday season and went energized into the new year with advocacy motivation. So many things have happened since the last edition of *Global Perspective*s magazine, and I am happy to share it all with you.

I was privileged to attend numerous virtual meetings with patients, caregivers, and health care professionals within the regional HAE community. A fixed point of my RPA activity is to organize and participate in the individual meetings with Member Organizations' patient leads to discuss the current situation on an ongoing basis and take appropriate actions to improve it. In recent months I have participated in meetings with patient/physician leads from Armenia, Belarus, Georgia, Hungary, Kazakhstan, the Netherlands, Russia, Poland, Ukraine. Moreover, I connected with Iranian patients and physicians with whom I hold regular meetings to identify their situation and immediate needs. Additionally, Regional Advisory Group meetings were held for Central Eastern Europe, Benelux, and the Middle East in January-February. In total, 13 Member Organizations participated in these meetings, including (but not limited to) countries such as Armenia, Georgia, Egypt, Iraq, Jordan, Kuwait, and Lebanon.

Also, I participated in meetings with CSL Behring, KalVista Pharmaceuticals, and Takeda, where we discussed the important things for the patients' community and prospects with modern treatment options.

Our Regional Medical Advisory Panels for the Middle East and for Central Eastern Europe and Benelux is growing, with the latest addition of two HAE expert physicians: Dr. Iman Nasr from the ACARE center at the allergy unit at the Royal Hospital in Muscat, Oman, and Dr. Elena Latysheva from the NRC Institute of Immunology FMBA Russia.

Together with other RPAs, I work to disseminate and provide our Member Organizations the HAEi resources:

- the HAE TrackR application that has been recently translated into Czech, Dutch, Lithuanian, Russian, and Slovak – currently, together with Member Organizations, we work on the translations into Armenian, Hungarian, and Kazakh,
- the HAEi Emergency Room Poster has been translated into Armenian and Georgian, and the production will start soon,
- the HAEi Advocacy Academy has been updated with a case study called "Working with Pharmaceuticals", where I try to share with our HAE community the experience HAE Poland has gained in successful and effective collaboration with our pharma partners over the years. I hope this case study will be useful for the advocacy activities of your organization.

Wonderful news has arrived from the city of Nur-Sultan (formerly Astana) in Kazakhstan, where three HAE patients have been treated with C1-INH esterase for the very first time. It is a huge success of the local HAE community, and I would like to congratulate HAE Kazakhstan and Dr. Elena Kovzel, who have played a significant role in this achievement. Hopefully, more patients in Kazakhstan will soon receive access to modern HAE therapies.

Together with HAEi Consultant Rashad Matraji, I focus on a detailed analysis of the current patients' situation in Jordan and identifying drug reimbursement options based on local legal regulations. We have also established initial contact with another local healthcare professional interested in HAE. Furthermore, we are working on a project to better understand the disease by patients, and I hope that in the next edition of Global Perspectives, I will be able to tell you more about it.

FIONA WARDMAN
ASIA PACIFIC

For the last few months, I have focused on catching up with the Member Organizations in the Asia Pacific region and South Africa via virtual means. It seems that everyone is looking forward to once again being able to meet face-to-face.

The latest tools and resources have been implemented throughout the countries, including Advocacy Academy, TrackR and the Emergency Room Poster in several languages (for the region), social media posts for TrackR and the latest Brady Club Activity books for children.

The second round of Regional Advisory Group (RAG) questions to gain further information from Member Organizations on their current unmet needs and challenges has been rolled out. I look forward to collating the answers and creating ways to achieve better outcomes for Member Organizations.

Australia and New Zealand have held hybrid patient and carers meetings. And Australia now has its first Angioedema Centre of Reference and Excellence (ACARE) in Melbourne, Victoria.

During the HAE Korea general meeting, I was invited to present on HAEi, advocacy, and available tools and resources for patients and patient groups. I also took part in the Asia Pacific Alliance of Rare Disease Organisations (APARDO) meeting as a panellist to discuss patients and patients' groups involved in the research and development of treatments.

The Burden of Illness survey outcomes for India was presented to Dr. Ankur Jindal from the Post Graduate Institute of Medical Education and Research (PGIMER) in Chandigarh, India. HAEi looks forward to publishing the data to assist access to modern treatments for patients in India.

HAE South Africa is going through an exciting growth period which has seen new projects and opportunities come their way. It's such a pleasure to watch the Member Organization expand and put their thoughts and plans into action. Stay tuned for more updates!

JAVIER SANTANA
CENTRAL AMERICA AND THE CARIBBEAN

In my region, there is still a shortage of medicines and treatments despite the efforts made by patient groups. In countries like Costa Rica, where in 2017 only about 18 patients had been identified, today about 80 people with HAE have been registered according to reports from allergy and immunology specialists who work hard to ensure that patients finally get the treatment they deserve.

Even though the Ministry of Health of Costa Rica approved the purchase of medicines for prevention and another for attacks to attend exclusively to children with HAE, hospitals are still waiting for modern and exclusive medicines after several months. On the other hand, representatives of pharmaceutical companies continue to make their efforts to introduce some modern treatments for HAE in Central America and the Virgin Islands.

New patients with HAE have been identified in Trinidad & Tobago, and it is hoped that we will be able to initiate a new representative group of patients with HAE here in the future.

I have written a column on the situation of HAE patients in the Dominican Republic. The effort has developed discussion on the HAE issue, and I have been invited to have meetings in the future with government officials to discuss HAE and coordinate events to start educating about the disease. You will find the column here: https://encontexto.com.do/angioedema-hereditario-una-enfermedad-rara-que-amenaza-la-vida-de-pacientes-en-republica-dominicana.

In Puerto Rico, the Governor approved and signed 28 February as a national Rare Disease Day.

In Panama, a new law of rare disease has been approved by Parliament and is presently waiting for the signature of the President. This is excellent news because the law requires that patients receive their medications from a special fund administered exclusively by the Office of the President.

HAE TREATMENTS ON THE HORIZON

By President and CEO Anthony J. Castaldo, HAEi

The global HAE community has achieved something unprecedented for an ultra-rare condition: regulatory approval of eight different treatments. Remarkably, the pace of development for next-generation HAE medicines is nothing short of extraordinary. There is a very good reason why HAE continues to attract significant interest in new treatments. Our community has always understood that achieving a better quality of life for ourselves, our children, and grandchildren starts with participating in clinical trials.

Before going into details regarding each potential new medicine, we must first acknowledge that far too many of our Member Organizations do not have adequate access to and reimbursement for HAE medicines that have already been approved. Therefore, it is important to emphasize that HAEi's primary goal (as reflected in our programs, training initiatives, and services) is to provide Member Organizations with the tools necessary to win access to the modern treatments that are already available. Our kind, compassionate, and knowledgeable Regional Patient Advocates are the "boots on the ground" forces ready to apply their expertise and bring the full range of HAEi's resources to help Member Organizations organize and implement successful advocacy efforts.

At the same time, however, it is also sensible, and in our community's best long-term interests, to encourage investment in next-generation treatments by continuing to enroll in clinical trials.

Right now, nine companies are developing new HAE therapies. In all, there are thirteen treatments at various stages of clinical development that include:

- Five orally administered preparations – two for treating attacks and three for preventing HAE swelling,
- Two new monoclonal antibodies to be injected subcutaneously,
- A medicine for subcutaneous injection that has been developed using messenger RNA technology, and
- Five prospective gene therapies.

Before we get started with the details, I want to make it very clear that all of the information presented today has been derived solely from public sources such as websites and press releases. Please visit each company's website for updates and additional information on their individual HAE clinical development programs.

CSL Behring already has two approved HAE medicines: Berinert® for treating attacks and HAEGARDA®/ Berinert® 2000-3000 for attack prevention. The company is developing an HAE treatment called garadacimab, delivered once a month by subcutaneous injection. The medicine is a monoclonal antibody targeted to block Factor XIIa, which research shows is the fuel in human plasma that ignites an HAE attack. The results of a phase 2 trial announced in June 2020 revealed that garadacimab was well tolerated and reduced the average number of HAE attacks when compared to placebo by as much as 99% in one of the dosing levels being tested. According to Clinical Trials.gov, CSL Behring is now conducting a phase 3 clinical trial at 37 sites worldwide.

KalVista is developing three oral HAE treatments. The company's drug candidate for treating attacks when they occur, KVD-900, works by blocking kallikrein, which is a key component in the HAE attack biology. KalVista reported the results of their Phase 2 trial in February 2021 and noted that KVD-900, when compared to placebo, significantly reduced the use of rescue medicine and the time it takes for symptoms to begin resolving. On 8 March 2022, the company announced the initiation of KONFIDENT, a Phase 3 worldwide, double-blind, placebo-controlled crossover trial to evaluate the efficacy of two dose levels of KVD900 compared to placebo in 84 adults and adolescents during acute HAE attacks. According to KalVista, the study is being conducted at approximately 60 sites in 20 countries.

KalVista is also conducting KOMPLETE, a Phase 2 clinical trial of KVD824, a twice-daily oral preparation for preventing HAE attacks. The trial is a randomized, double-blind study evaluating the safety and effectiveness of twice-daily administration against placebo for 12 weeks at varying doses of 300 mg, 600 mg, and 900 mg. According to ClinicalTrials.gov, the trial will include 48 people with HAE types 1 and 2. It is being conducted at 30 clinical trial sites.

In addition, KalVista is in the early stages of researching a pill to inhibit Factor XIIa, which, as we mentioned earlier, is the protein that initiates HAE attacks.

Pharvaris is another company developing an oral form of HAE treatment called PHVS416. This medicine is designed to have the same biological effect as Icatibant, the generic name for a treatment most HAEi friends might also know under the brand name Firazyr®. According to a March 2022 presentation that is on the company's website, a phase 2 trial called RAPIDe-1 for treatment of HAE attacks with PHVS416 is looking to recruit 72 people with HAE types 1 and 2 from 30 clinical trial sites in the United States, Canada, Europe, Israel, and the United Kingdom.

In addition, Pharvaris has started another Phase 2 study of PHVS416 called CHAPTER-1 to test the medicine as an HAE preventive therapy. The company is looking to enroll 30 HAE patients across 24 sites in the United States, Canada, Europe, Israel, and the United Kingdom.

Pharvaris expects to report data on the effectiveness and safety from both the Rapide 1 and CHAPTER 1 trials is expected in the 4th quarter of 2022.

Ionis Pharmaceuticals announced (on 18 November 2021) a phase 3 study called OASIS-HAE designed to test the safety and effectiveness of a medicine called donidalorsen. This treatment will be given as either a monthly or bi-monthly subcutaneous injection to prevent HAE attacks. Ionis is looking to recruit 84 people with type 1 or type 2 HAE. In brief, this medicine works by employing messenger RNA to suppress pre-kallikrein, a protein that figures prominently in the biological cascade causing an HAE attack. In March 2021, the company announced the results of a Phase 2 study indicating that donidalorsen demonstrated a 90% reduction of HAE attacks in weeks one to 17 of the study, with a 97% reduction observed in weeks five to 17.

Astria Therapeutics is researching a STAR-0215, a monoclonal antibody to inhibit kallikrein given once every three months or longer. According to the company's website, Astria plans to file an Investigational New Drug application for STAR-0215 in mid-2022 and initiate a Phase 1 clinical trial with initial results anticipated by year-end 2022.

Pharming NV is the manufacturer of Ruconest®, a recombinant C1-inhibitor concentrate approved for treating HAE attacks. In July 2021, the company announced plans to research, develop, manufacture, and commercialize a gene therapy called OTL-105. The concept for this therapy involves drawing blood from a person with HAE and then taking this blood to a laboratory where a "healthy" copy of the C1-inhibitor gene is inserted into the person's blood stem cells. Once this process is completed, the patient is infused with the stem cells containing the "working" C1-inhibitor gene.

BioMarin is developing a gene therapy for HAE called BMN 331. According to ClinicalTrials.gov, the company is conducting a Phase 1/2 Open-Label, Dose-Escalation Study to determine the safety, tolerability, and efficacy of BMN 331 in 34 people with HAE due to C1-inhibitor deficiency. People receiving this therapy will be followed for five years.

Intellia Therapeutics is pursuing a gene therapy for HAE using a technology called CRISPR-Cas 9 to knock out (which means to inactivate and stop) the gene that ultimately produces kallikrein. CRISPR-Cas 9 edits genes by removing, adding, or altering sections of the DNA sequence. According to Clinical Trials.gov, Intellia is running a multi-national Phase 1/2 study that will evaluate the safety, tolerability, and biological activity of its gene therapy medicine called NTLA-2002 in 55 adults with Type I or Type II HAE. In December 2021, Intellia reported that the first clinical trial dose of NTLA-2002 had been given to a person participating in the clinical trial.

Spark Therapeutics is another company researching gene therapy for HAE. According to the company's website, Spark is in the early stages of developing an investigational gene therapy for the treatment of HAE using liver-directed gene therapy for C1-Inhibitor replenishment.

RegenxBio is the fifth company developing an HAE gene therapy using AAV technology. In a November 2021 press release, RegenxBio said it continues to conduct research and pre-clinical studies to advance its gene therapy candidate for the treatment of HAE. The company's website shows that the HAE program is in the pre-clinical stage.

WORKING TOWARDS A BETTER FUTURE

The incredible and special "can do" and "will do" attitude of the global HAEi community has been noticed and has a lot to do with why there are so many new therapies being researched. There is little doubt that HAEi friends will continue our longstanding tradition of fiercely advocating for access to modern therapies while also enabling a better future for us and future generations through participation in clinical trials.

For more information, feel free to contact your Member Organization or HAEi's Clinical Trial Project Leader at clinicaltrials@haei.org.

HAE TREATMENT IN THE HORIZON

HAE TREATMENT SECTION UPDATED ON HAEi.ORG

On our website haei.org you will find information about available HAE treatments.

You can also read more about the current HAE treatment strategies that focus on medications to:

- Provide rapid relief during attacks (on-demand or acute treatment)
- Prevent symptoms in people with HAE who experience a high frequency of attacks (long-term prophylaxis)
- Prevent symptoms in people with HAE who undergo dental or surgical procedures, which may trigger an attack (preprocedural or short-term prophylaxis).

>> Read more on haei.org

2022 HAEI GLOBAL LEADERSHIP WORKSHOP

Announcing the

2022 HAEi Global Leadership Workshop

In light of worldwide actions to ease pandemic restrictions and allow face-to-face gatherings, HAEi is delighted to announce our upcoming 2022 HAEi Global Leadership Workshop, which will take place in Frankfurt am Main, Germany, 6-9 October 2022.

Please observe that this global leadership workshop is different from past HAE Global Conferences and is designed to bring on board members and leadership of our Member Organizations. The steady growth in our global community has made it impossible to get the community as a whole into one venue, and we are planning regional conferences that will accommodate members of your organizations that are not part of the leadership structure.

The 2022 HAEi Global Leadership Workshop theme is "Together Again", and we expect to welcome around 600-650 HAEi friends, including Patient Advocacy Leaders, HAE Physicians/Scientists, HAEi Youngsters Advisory Group, and industry sponsors. The workshop will follow the general format of past global conferences and will offer a track for the scientific community. In addition, pharmaceutical sponsors will have exhibition space dedicated to providing HAE-related information.

We will provide travel grants for the leaders of our Member Organizations. Travel grants will be allocated through the population-based formula used for the four previous HAEi global meetings.

As for the HAEi Regional Conferences where Member Organizations can bring patients and caregivers from their respective countries to a conference, our plan is this:

- **2023 HAEi Regional Conference APAC** (Asia Pacific)
- **2023 HAEi Regional Conference EMEA** (Europe, Middle East, and Africa)
- **2024 HAEi Regional Conference Americas** (North and South America)

We look forward to finally getting together again in October.

The youngsters are here with open arms

By Nanna Boysen and Victoria Schultz-Boysen, board members of HAE Scandinavia

HAE Scandinavia celebrated its 20th anniversary on 12-14 November 2021 in Copenhagen, Denmark. Considering the global COVID-19 challenges, we are beyond grateful that patients, caregivers, physicians, and pharma companies could get together again.

Not only did HAE Scandinavia celebrate its first two decades that weekend, but it was also the first conference where HAE Scandinavia arranged something special for young patients and young caregivers. We came up with the idea as we have been part of the HAEi Youngsters Community and have participated in various activities – Nanna is also a member of the HAEi Youngsters Advisory Group.

We have found a lot of support, understanding and new lifelong friendships in the global HAE community. We hope to bring a lot of what we have experienced into the Scandinavian organization and help other young patients with HAE feel more connected. The 2021 HAE Scandinavia Conference was a great start, and we are all looking forward to the next time we can meet.

Nanna:
Being an HAE patient myself, I know that HAE comes with many challenges, but we do also gain a lot of strength. We all have our own stories and experiences of how HAE has affected our lives. I have been misdiagnosed by doctors and nurses and given the wrong treatment. For a long time during my childhood, I was afraid of being different from other children and therefore tried to hide my HAE. This meant that I didn't like to go far away from home and my parents in case of an HAE attack. I feared not being close to medication because my friends would no longer just see me but also my HAE, which made me uncomfortable and want to avoid these situations when I could.

Today I am thankful for being able to treat myself as I'm not afraid of showing my HAE anymore. I have gained a lot more confidence with my HAE due to advocating for it and meeting so many young people with the same diagnosis! These are only a few examples of what I have experienced and felt as an HAE patient. We all know HAE comes with many feelings, thoughts, and questions. Therefore, I believe that a youngsters support network for HAE Scandinavia could help answer some of the questions and make young patients and caregivers feel understood.

The global HAE community and the HAEi Youngsters Community is where I felt most at ease. Talking to other youngsters my age and sharing my experiences made me feel a part of something. Knowing that others are going through similar challenges gives me a whole new perspective on HAE. Meeting with youngsters helps one better understand and manage HAE. Through sharing my experiences, I managed to build on my confidence and understand that it helps to talk instead of keeping things to yourself.

I can only speak for myself here, but these are the positive things about HAE. Being a patient doesn't seem so bad when you have support, treatments, and a community. I really hope that in Scandinavia, we can build a better environment for young patients and caregivers to share their experiences, feelings, thoughts, questions and support each other in learning more about HAE. I want to work with HAE Scandinavia to build a youngster-friendly environment where youngsters can meet, feel understood, and feel safe, so no one feels alone with this disease, and to make HAE our superpower!

Victoria:
I have always been surrounded by HAE patients who have been very passionate about HAE and wanted to make a change for all HAE patients worldwide. That inspired me, and it became very natural for me to stand up and make a difference as well. I joined the international HAEi Youngsters Community as a caregiver, and I have learned so much about HAE and what it is like to be young and live with such a life-threatening disease as HAE.

Over time, the HAE Youngsters Community has grown into a strong and rewarding forum where everyone can freely share their thoughts, feelings, hopes, dreams, as well as ups and downs with HAE. There is always plenty of understanding and sound advice to receive.

I have gotten to know so many amazing people, created friendships for life, gained more knowledge about different countries and cultures, and of course, I have learned so much more about HAE. I have also become aware of how I, as a caregiver, can give the best support possible and keep calm even in intense situations. At the same time, I have learned so much more about myself as a human being. I have been inspired to be the best support person possible by all the awesome and strong people I know with HAE and their caregivers. They are all true fighters, and I'm deeply fascinated by the joy of life shining from within them and their ability to fight for a better future with HAE.

I really hope that our first meeting for young patients and caregivers in Scandinavia will be the beginning of a very bright and exciting future for the HAE Scandinavia community for young people. By getting to know each other better, we can create an environment that enables turning HAE into our strength.

I wish for a Scandinavian community where we completely understand each other, give and receive good advice, get new ideas together and have fun! I really wish that for Scandinavia because I think it would be truly amazing! It is so important to know that you are not alone – we are here with open arms and hope to see more Scandinavian youngsters in the future :)

Thank you for reading – you can find more information on the HAE Scandinavia website, **haescan.org**, and on Instagram, @haescandinavia

HELP FOR HAE BROTHERS AND SISTERS IN UKRAINE

HELP FOR HAE BROTHERS AND SISTERS IN UKRAINE

HAEi recognizes the horrific situation in Ukraine, and we stand in support and solidarity with our fellow HAE brothers and sisters in Ukraine.

We understand that many Ukrainians are forced to flee to neighboring countries for safety. Therefore, our advice to people with HAE and their caretakers arriving in another country is to reach out to the HAE Member Organization for advice on HAE knowledgeable physicians and hospitals for assistance.

Also, HAEi has several resources that can be helpful to someone arriving in a new country.

MEMBER COUNTRY PAGES

On our website, haei.org, each of our member countries are represented and you can find contact information to the organizations, links to their social media platforms, and information about available treatments, HAE knowledgable physicians and hospitals in each specifc country.

>> haei.org/about-haei/globally

REGIONAL PATIENT ADVOCATES

The HAEi Regional Patient Advocates are ready to help. You can find their contact information on the HAEi website.

>> haei.org/about-haei/meet-the-rpas

HAE COMPANION APP

The HAE Companion app provides an easy way to access and store the HAEi emergency card electronically.

HAE Companion also links to contact information on ACARE centers (Angioedema Centers of Reference and Excellence) as well as HAE knowledgeable hospitals and physicians worldwide. Using Google Maps or Apple Map, the app indicates directions and distance to the nearest place.

The app is available on both Apple's App Store and Google Play for the Android platform.

>> haei.org/apps

HAEi EMERGENCY CARD

The HAEi emergency card contains clear and straightforward information about HAE and treatment required during an attack. The emergency card is available in many languages on the HAEi website and through our HAE Companion app.

>> https://haei.org/resources/emergency-cards

hae day :-) 2022

– *stepping up for the global HAE movement*

2021 was an exceptional year for **hae day :-)** as it was the 10th year that the global HAE community came together, with 16 May as the focus for HAE awareness-raising efforts. And now we're doing it again!

This year the theme is ***Stepping up for the Global HAE Movement***, and the activity challenge will run from 1 April until 31 May.

"We look forward to seeing the different ways our community will be Stepping Up for the Global HAE Movement in 2022", says Anthony J. Castaldo, HAEi President & CEO. "It's amazing what we can achieve when we step up together."

We encourage everyone to participate in physical and overall wellbeing activities. Any activity reported on haeday.org will be converted into steps, and the total will power us around the World.

The haeday.org website offers lots of helpful information about the campaign, inspiration for activities and how you can get involved.

When sharing **hae day :-)** information on social media, please use the hashtags #active4hae #haeday so we can find you!

In 2021, we generated 168 million steps, enough to walk more than three times around the Earth's circumference.

Will you be Stepping Up for the Global HAE Movement in 2022?

We encourage everyone to report their physical and wellbeing activities by *Stepping Up for the Global HAE Movement* on haeday.org

POWERFUL FREE RESOURCES FOR MEMBER COUNTRIES

FREE HAEi SERVICES KEEP GROWING IN NUMBERS

By Ole Frølich, HAEi Enterprise Technology Manager

Over the last few years, HAEi has introduced several free services to support our Member Organizations.

HAEi HOSTED WEBSITES

We are currently working on free websites for HAE Georgia, HAE Finland, and HAE Japan. When these three are launched, we have a total of 64 hosted websites. In addition, we introduce a two-factor login to the hosted websites to ensure an even higher degree of security.

Member Organizations interested in a free HAEi hosted website can get more information at **haei.org/resources/haei-hosted-websites**. Please do not hesitate to get in touch with us for an online demonstration.

FREE WEBSITES FOR
64 COUNTRIES

HAE TRACKR

We are very happy that the HAE community is embracing **HAE TrackR**. There are users in 21 countries, and the app is available in a rapidly growing number of languages. **HAE TrackR** is an easy way to help you manage your HAE by tracking your attacks and treatments.

Visit **haei.org/apps** for more about the **HAE TrackR** app.

FREE APP IN
27 LANGUAGES

HAEi CONNECT

HAEi Connect, our user-friendly patient membership database and communications platform, is currently implemented by 32 Member Organizations with more to follow in 2022.

See more about HAEi Connect at **haei.org/connect**, and please let us know if you would like to test the system for your country.

FREE MEMBER DATABASES IN
32 COUNTRIES

OTHER HAEi RESOURCES

We would also like to call attention to **HAEi Advocacy Academy** and the **HAE Companion** app.

The **HAE Companion** app contains digital versions of our Emergency Cards in multiple languages and a list of ACARE centers, hospitals, physicians, and Member Organizations with contact information for the user to seek help in any given country. Find more information at **haei.org/apps**.

On **haei.org/academy** you will find information on **HAEi Advocacy Academy** – at the moment we have 12 courses in the Open-Access section and 18 courses in the Member Organization Exclusive Access area – all free of charge.

WEBSITE HOSTING: MAKE YOUR ORGANIZATION VISIBLE

- Freedom to add content and pages
- Choose from five different templates
- Supports right-to-left (RTL) text direction
- Always updated
- Daily backup
- Training for editors
- Your domain name
- Secure https://
- And it's free

Want to make your organization visible: Visit haei.org

POWERFUL FREE RESOURCES FOR MEMBER COUNTRIES

SECURE ONLINE MEMBERSHIP DATABASE AND COMMUNICATIONS PLATFORM FOR THE HAEi MEMBER ORGANIZATIONS

- User-friendly platform for collecting and storing member information
- Secure data quality by frequent automatic profile update reminders
- Easy email communication to individuals, groups or all members that enables member organizations to send targeted information to members e.g. clinical trials information, newsletters, surveys
- Cloud based solution with high security
- Compliant with EU General Data protection regulation (GDPR)
- New features can be added by HAEi on request
- Many custom fields available

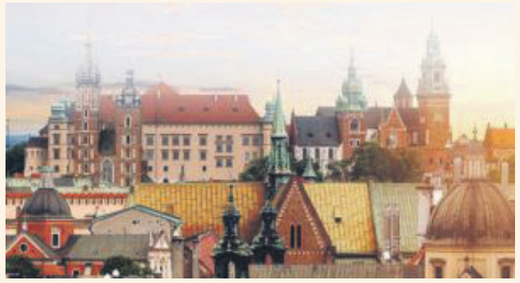
Want to know more: **Visit haei.org**

TRACK YOUR HAE WITH THE HAEi HAE TRACKR APP

- Easy-to-use electronic diary to track HAE
- Free – and product and company neutral
- Enables sharing data with your physician
- Protects your data and privacy
- Endorsed by the ACARE network
- Works on computer, tablet, or smartphone

Presently the **HAE TrackR** app is available in Arabic, Chinese (Hong Kong), Chinese (Taiwan), Chinese, Croatian, Czech, Danish, Dutch, English, Finnish, French, Georgian, German, Greek, Macedonian, Norwegian, Polish, Portuguese, Portuguese Brazil, Romanian, Russian, Serbian, Slovak, Spanish, Swedish, Turkish, Ukrainian – more languages will be added over time.

Start using HAE TrackR today: **app.haetrackr.org**




SUCCESSFUL HAEi VIRTUAL REGIONAL WORKSHOPS

By Deborah Corcoran, HAEi Chief Specialist Projects and Research

During 2020 and 2021, HAEi held four Virtual Regional Workshops covering the the following regions:

- South Eastern Europe
- Central Eastern Europe & Benelux
- South America & Mexico and Central America & the Caribbean
- The Middle East, North Africa, and Sub Sahara Africa

"Due to the coronavirus pandemic, HAEi continued to bring the community together by transforming its regional workshops into virtual events", says Fiona Wardman, Chief Regional Patient Advocate, HAEi. "Our Regional Patient Advocates worked with the Member Organizations and the HAEi Operations team in putting together engaging content tailored to the needs of each region."

The workshops featured video talks by HAEi Leadership, Regional Patient Advocates, expert physicians/scientists, and our member organizations. All the videos were subtitled in English and the languages of the regions.

"We are delighted with the great success of these virtual regional workshops despite the challenges of not being able to meet in person," says Fiona Wardman.

OUR VIRTUAL REGIONAL WORKSHOPS IN NUMBERS

DEDICATED WEBPAGES FOR REGIONAL WORKSHOP VIEWED

> 4,300 TIMES

110 VIDEO

PRESENTATIONS TO CHOOSE FROM

VIDOES WATCHED BY PEOPLE FROM

93 COUNTRIES

VIDEOS WATCHED

> 4,150 TIMES

TOTALING AROUND

250 HOURS

OR MORE THAN 10 DAYS OF VIEWING IN TOTAL

OUR MEMBER ORGANIZATIONS' FEEDBACK

96% agreed or strongly agreed that their regional workshop provided specific ideas they could use in advocacy and provided information useful to the needs of their HAE community

96% would watch and would recommend that their members watch Regional Workshop videos in the future

All of the tracks were rated useful and Member Organizations found the videos from experts to be especially useful

>> HAEi.ORG/VIRTUAL_WORKSHOPS

Visit the virtual workshops – subtitled into many languages!

PATIENT STORY

Zoltán Maros, Hungary:

THE THINGS WE GOT ARE NOT GUARANTEED

When I was a child, there was a tradition in Hungary that children would get a bunny for Easter. I was four years old when my first attack came – around Easter – my parents thought I was allergic to rabbits. However, it was clearly not as allergic medicines did not work. My tonsils were removed around the same age as the doctors thought they could have something to do with my disease. Also, at some point during my early childhood, I fell off my bike, and the doctor said that I had broken my arm. Plaster was put on, but after a few days, it didn't fit any longer since the swelling of the arm had gone down.

In fact, these were your first experiences with HAE. How long did it take until you were diagnosed, and how did it happen?

As I remember, I had other swelling before being diagnosed. Sometimes it was scary when my face, my mouth or my eyes got swollen, but most of my attacks were in the extremities – uncomfortable but nothing more. What was the worst was that my parents and I did not know why it was happening to me, which was both puzzling and quite frustrating.

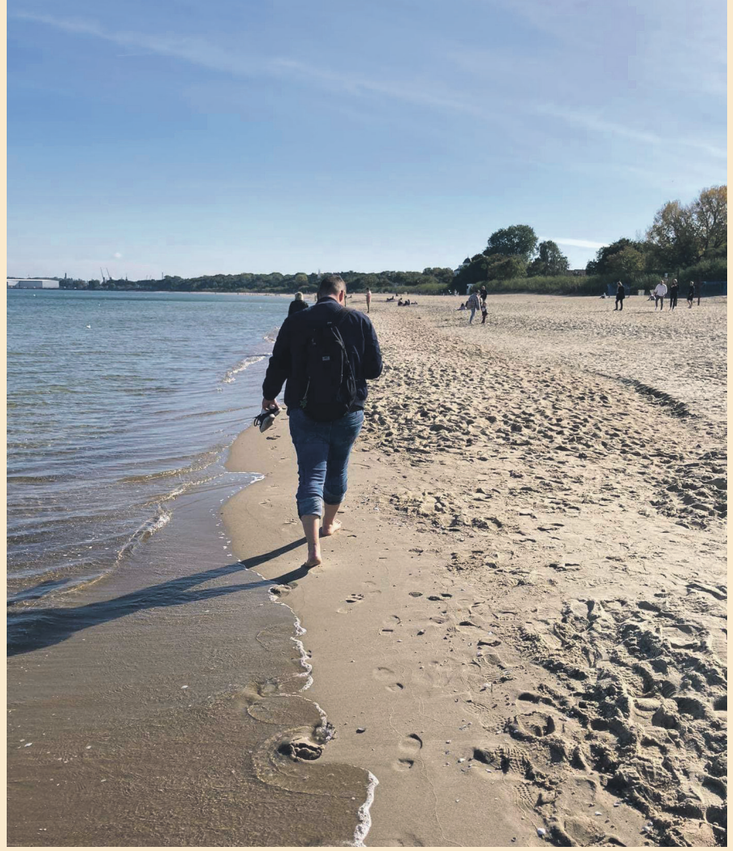
As I had an attack almost every month, my parents tried to find out what disease I was suffering from. We were lucky because my father's colleague – who later became my boss – had a good friend from the university. At that time, this friend's wife was an allergist at the children's hospital at Szeged, and she somehow found out that it might be HAE. The necessary blood tests were made, and I officially became an HAE patient when they came back.

How would you describe the first part of your life as an HAE patient? For instance, did your condition keep you from doing things your friends did or did you stick to your sport or other favorite activity despite having HAE?

I'm almost 40 now, and I can say that I have had a very satisfying childhood full of fun – and adolescence as well. I did not miss days from school too much, I had great friendships, and I did not have to skip meeting with them. I did sports like football, handball, volleyball,

ZOLTÁN'S STORY IN BRIEF

- **Born:** 1982 in Baja, Hungary; now living in Budapest, Hungary – married, no children yet.
- **Education:** Software Engineer from the University of Szeged, Hungary
- **Occupation:** System Test Architect at NNG, a Hungarian company providing navigation software for the automotive, enterprise, wireless and personal navigation industries
- **HAE symptoms registered:** 1986
- **Diagnosed:** 1991
- **Other HAE patients in his family:** None



basketball – and later in high school, I took part in rowing and canoe training. There were times when I went to parties every weekend and did whatever I just wanted. I learned my limits as a grown-up and had as much fun as I just could. Yes, there were attacks, and I had to rest for a few days, but they did not stigmatize my youth.

There are no other HAE patients in your family?

After my diagnosis, my parents and I went to the clinic in Szeged for a few years. Here they did blood tests and sent us the results, but that was really all they could do. Finally, after a few years, they found the HAE Center led by Professor Henriette Farkas, and we could level up. At the center in Budapest, my family was tested – not just blood tests but genetic tests too. We learned from those tests that I have Type I HAE and that I'm the only one with this condition in the family.

Being the only one with HAE in your family, would you say that you have met understanding from people around you, that is family members, friends at school, working relations?

Before I was diagnosed, my close family was worried and scared as we did not know why I had these attacks. Just a few of my friends knew about my disease, but as we never met when I had an attack, they didn't know how it was to live with this disease. However, these friends did understand that my attacks could be severe, so they were supportive. Mainly as all my episodes just needed a few days away from normal life, I did not have to scare anybody too much with my swellings.

Later, when I learned self-injection, my future wife learned it with me. It was very calming for me, and sometimes she asks me if she can do the injection because she wants to help. In high school and later at work, I have often been telling people that I'm an X-man as I have a DNA mutation – you know, a bit of a funny way to tell others about my condition, right?

Would you say that your condition influences your choices in life?

I'm happy to say that my condition does not influence my choices because I have access to modern medication all the time. So if we go on a vacation or there are more challenging times at work or maybe longer nights because of team building, I have the medication with me, and I can treat myself. That gives me the security I need.

Are you involved with HAE awareness work?

After we located the HAE Center in Budapest, we discovered that there are yearly patient meetings where I could meet people like me. At first, it was strange to be in a room full of other patients and their relatives, but then I wanted to know more.

Because it is a rare disease, not much was to be found – apart from a mention in one episode of the TV series "Dr. House". There were websites of a few patient organizations around the world, but I didn't find HAEi at that point.

It has been 12 years since I became Secretary of the Hungarian Patient Association, and since then, a new world has opened to me. I have had the opportunity to visit all the Global Conferences organized by HAEi, and so far, I have attended three regional conferences in Poland, not to mention participating in the C1-Inhibitor Deficiency Workshops in Budapest.

Attending an HAE Global Conference or other larger HAE gatherings is very comforting. It is also inspiring to meet people from all around the world and talk about something we have in common despite it being a disease. Also, it is an excellent opportunity to rethink what you have compared to how other countries are dealing with HAE. And it is good to hear interesting – sometimes sad – stories from other patients. I really like to meet new people and make new friends from other countries. Even if you only meet once or a few times, there is a hidden bond, and you will always have something to talk about and inspire each other with.

If you should advise a newly diagnosed patient from Hungary, what would you say?

Firstly, I'd say that now you are diagnosed and have access to proper medication through the HAE Center in Budapest. Therefore, you are in good hands but do not be satisfied. You have a lot of work to do: go to the check-ups, check your medication, keep the medicine with you, take part in the studies and support the HAE Center in its work because this is what gives us the privileges we have now! We often get comfortable when we get used to the support and things we got now, but it is not guaranteed. We must work to keep maintaining these conditions. You also get a group of people who understand what you are going through and how you sometimes struggle in your life – and we can support you!

ACARE NETWORK CONTINUES TO GROW IN NUMBERS

Membership in the global network of Angioedema Centers of Reference and Excellence (ACARE) – a joint venture between the Global Allergy and Asthma European Network GA2LEN and HAEi – continues to expand.

There are now 70 certified ACAREs and 17 applicant centers in the process of being certified. Professor Marcus Maurer, HAEi's Chief Medical Advisor and the GA2LEN/HAEi ACARE Coordinator expects more clinics to apply for ACARE accreditation in 2022.

"Going forward ACARE plans to: 1) create more educational programs for physicians, 2) raise awareness of the ACARE network, and 3) foster an atmosphere where the patient´s voice is front and center. This year, we continue our successful physician educational webinar programs that feature podcasts, fireside chats, journal clubs, videos, and more. We are also launching a new ACARE website hosted by HAEi."

"During 2022 we aim to work more closely with HAEi Member Organizations, explore using the HAEi Advocacy Academy platform for ACARE LevelUp, and foster a culture of collaboration between patient advocates and our ACARE centers", says Professor Maurer.

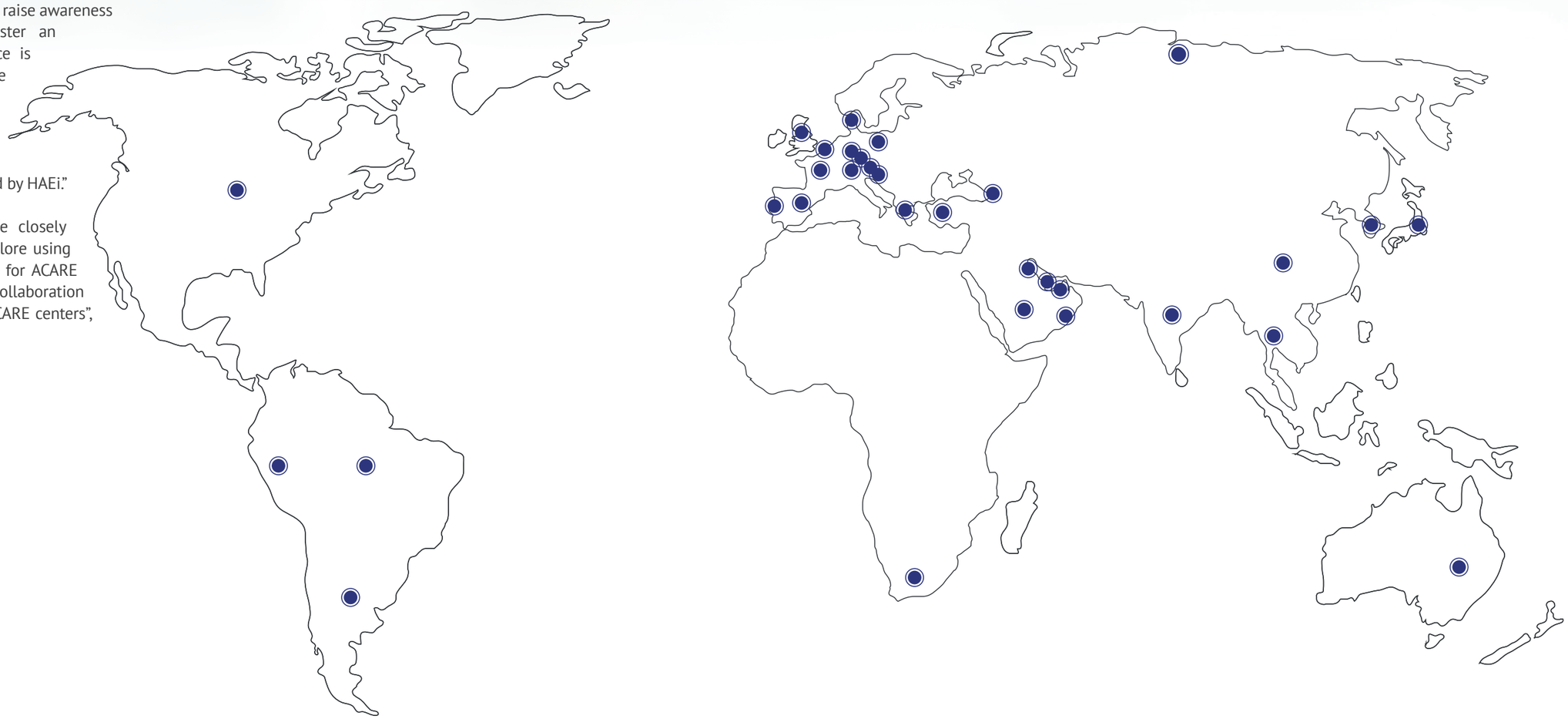
ACARE
Angioedema Centers of Reference and Excellence
A GA²LEN | HAEi NETWORK

70 ACARE CENTERS:

Argentina (4), Australia, Austria (2), Brazil (10), Bulgaria (2), China (2), Denmark, France (3), Georgia, Germany (8), Greece, Hungary, India (3), Japan (3), Kuwait, Netherlands, Oman, Peru (2), Poland (5), Portugal, Qatar, Russia (2), Saudi Arabia, Slovenia, South Africa, South Korea, Spain, Thailand, Turkey (4), United Arab Emirates, United Kingdom (2), and United States.

If you would like to become an ACARE center, please use this link for further information:

haei.org/acare



NEWS FROM MEMBER ORGANIZATIONS AROUND THE GLOBE

UKRAINE

HAEi recognizes the horrific situation in Ukraine. HAEi members stand in support and solidarity with our fellow HAE brothers and sisters in Ukraine. HAEi understands that some Ukrainians may be fleeing to neighboring countries for safety. HAEi's advice to those arriving in a country is to reach out to the HAE member organization for advice on doctors and treatment centers for HAE assistance – please see haei.org/about-haei/globally/

People with HAE in Ukraine can also reach out to an HAEi Regional Patient Advocate for further assistance – you can find contact information on our website at haei.org/about-haei/meet-the-rpas/

UNITED KINGDOM

From CEO Angela Metcalfe

Well, it's been a busy few months since I took over as the CEO of HAE UK! We have lots and lots of ideas going forward and a few exciting projects that we are hoping to get off the ground in the next few months.

One project that has just started is we asked HAE UK members to participate in a prodromes survey, we think the first of its kind in the UK. We asked members to take an online survey answering a series of simple straightforward questions about early warning signs that they may identify before an attack. We had a phenomenal response to the survey, so it will be interesting once we have collated all the information to see what indicators and signs seem to be most identifiable.

Good work has also been taking place with two different platforms recording patient information, which will be from not just a clinical perspective, but that of individual patients. It would potentially sit alongside the NHS App that 23 million people in the UK have now signed up to and will hopefully enable HAE patients to have all their treatments, breakthrough attacks, clinical and medical history sitting in one place: a huge step forward in supporting patients when they may need to present for emergency treatment.

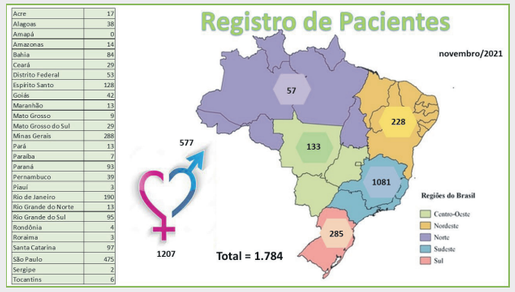
We have also been putting plans in place for our next Patient Day. This will be our first in-person patient event for three years, due to the COVID-19 pandemic, and we look forward to seeing lots of our members there. The event will likely take place in November and we will share more details once we have finalized them.

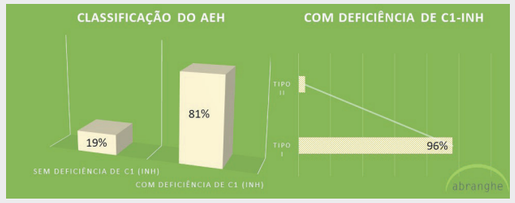
Our biggest project going forward is about raising awareness of HAE, particularly in the area of Emergency Medicine. We are looking at putting together a short presentation that can be included as part of regular training and ongoing professional development for health care professionals such as Registrars, Consultants, Immunologists, Junior Doctors, and senior nursing staff working in emergency medicine. This needs a huge amount of background work, but we hope that we can start with our first presentations by late Autumn this year.

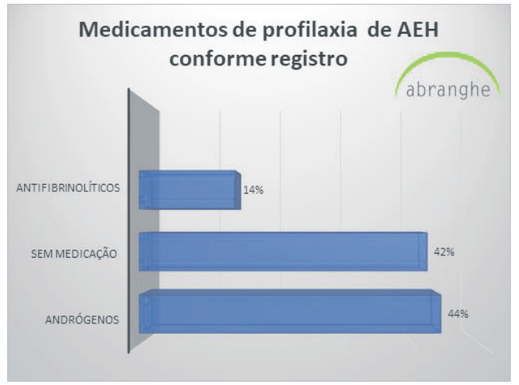
BRAZIL

From HAE Brazil (Abranghe)

We have produced some data from patients who sought out Abranghe for HAE registration and others for diagnostic guidance. The objective is to analyze data during the pandemic, from 2021 and 2020.







SWITZERLAND

From HAE Switzerland

Unfortunately, due to the corona virus, the last two patient meetings could not take place.

The Federal Council has now given the go-ahead for such events, and we are again planning with full vigor. On 30th April 2022 we will meet at Hotel Arte in Olten. The following topics are planned:

- What medicines are available to people affected by HAE in Switzerland?
- Experiences with the new HAE drug Takzhyro
- Experiences with the new HAE drug Berinert® subcutaneous 2000
- Experiences with the new HAE drug ORLADEYO™, which will soon be available in Switzerland
- Development of the Swiss HAE registry
- Stress management – What can I do for myself?
- What is mindfulness? – How can mindfulness support us in everyday life and help to promote general well-being? – lecture and practical exercises

Now we hope that the virus will not determine our lives again and that our meeting can take place.

BOSNIA & HERZEGOVINA

Find the Facebook page of HAE Bosnia & Herzegovina at facebook.com/groups/871538203660937.

USA

From Ianice Viel, HAE Advocate & Digital & Social Media Manager:

hae day :-) 2022 Awareness Campaign: The achievements of the HAE community in recent years are something to be celebrated on a national scale! Ten years ago, the HAEA recognized the need for legislative action to promote national awareness aimed at ultimately improving the lives of people affected by an ultra-rare condition called Hereditary Angioedema (HAE).

The idea was to seek a legislative initiative to establish an enduring platform for a nationwide HAE awareness and education campaign. During our travels throughout the halls of Congress, we found a champion in the senior Senator from Hawaii, Daniel K. Inouye. He enthusiastically introduced Senate Resolution 286, which affirmed 16 May as HAE Day, and received a unanimous endorsement by the United States Senate.

On 16 May 2012 and every year since, the HAEA community including people with HAE, caregivers, families, healthcare practitioners, scientists, and the pharmaceutical industry commemorates HAE Day by organizing events that promote HAE awareness and educational activities.

The approval of Senate Resolution 286 also led to developing a variety of HAEA events that include HAE IN-MOTION®, Meet & Greet, Youth Advocacy Programs, giving campaigns, and our annual Capitol Hill Day, among many others. We are also proud to report that HAE Day is now celebrated by thousands of people around the globe, from the edge of Patagonia in Argentina to the islands of Japan.

HAE Day also challenged us to advocate for better therapies and an improved quality of life. Today, we enjoy an unprecedented number of effective therapies, with eight FDA-approved products and thirteen more in development. We count on the momentum and the galvanizing force of HAE Day to continue motivating the quest for new and better HAE treatments.

The US HAEA is proud to announce the launch of our annual **hae day :-)** Awareness Campaign. This year's storytelling campaign invites members of the HAE community to share their personal HAE stories to raise awareness for HAE! To assist community members in developing memorable and powerful stories, the US HAEA is providing those who participate with a storytelling toolkit along with unique resources that will guide them through the storytelling process, whether it be a written or video testimonial.

Our goal for this campaign is to flood our social media platforms with community stories and amplify our rare voices to raise awareness for HAE. This campaign allows us to reflect back on the group of committed and passionate advocates who came together to make this historic anniversary possible, as well as the great strides we have made as an HAE community!

Advances in HAE Research: The US HAEA continues its robust research program and is embarking on timely and relevant projects that will focus on the unique needs of the HAE community. Our ongoing projects include:

- ***An HAE-Specific Instrument to Measure Quality of Life:*** The US HAEA is wrapping up a unique, ground-breaking research study that seeks to accurately show how HAE affects overall quality of life (QoL). The aim of the study is to develop and validate a broad-based HAE QoL instrument that more accurately depicts disease burden. This research will help us publish a QoL questionnaire that (1) truly captures the way HAE affects the everyday life of individuals and families, and (2) demonstrates to health insurers – and others – the value of life-changing improvements in health and QoL that result from modern HAE medicines. Based on concepts derived from behavioral economics, this tool will be more sensitive than any that are currently being utilized. We believe that this cutting edge project could revolutionize QoL measurement of HAE and other chronic conditions.
- ***Shared Decision-Making Tool:*** We are currently developing a Shared Decision-Making tool that will enable physicians and people with HAE to work together when making healthcare decisions. This tool works to ensure that both the physician and the person with HAE have a voice in their treatment plan.
- ***HAE and Aging Study:*** The US HAEA study on HAE and Aging will help us to better understand the demographic and clinical characteristics, HAE treatment patterns, HAE impact and burden, and perceived health-related quality of life of the aging HAE population. This study is being designed with a comparator population of people without HAE, and we plan to have these results published in a manuscript when complete in early 2022. This research project is uniquely important to the HAEA community, as current data on HAE and Aging does not exist.
- ***HAEA Study on the Number of People with HAE in the US:*** The US HAEA is dedicated to offering its unique programs, services, and activities to everyone in the US that has HAE. We believe that past estimates underestimate the true prevalence of HAE. Estimates regarding the number of people with the condition in the United States have an extremely large range, which means we have no idea if we are reaching the entire population. We have initiated a study using sophisticated data mining techniques and expert HAE physician input to calculate the number of people with HAE in the United States. The results of this study will help the US HAEA to target its outreach efforts to continue building the HAEA community.

Clinical Trials: The US HAEA assists in clinical trial recruitment for individuals with HAE Type I, Type II, or HAE with Normal C1-Inhibitor and is currently assisting with recruitment efforts for an unprecedented seven HAE clinical trials. Clinical trial participation is crucial in medication development, as well as a critical part of expanding our knowledge of this rare disease.

Using our broad and curated database, we are able to identify and target community members based on location and screening criteria. We reach out via email and phone to provide general information and participation requirements for each study and connect interested and pre-screened individuals with the site coordinator at the trial location to answer any additional questions or to begin the registration and screening process.

The HAEA has a proven and successful track record in clinical trial recruitment and continues to recruit for open trials whenever possible. To view a list of active clinical trials please visit https://www.haea.org/pages/p/clinical_trials.

HAEA Round Table: Because HAE is so rare, it can feel isolating to deal with the everyday challenges of learning how to manage living with this rare chronic illness. However, when we come together as a community to talk about our struggles, it is easier to see that we are not alone in our efforts to live a normal life with HAE.

We also realize that at different life stages, HAE can affect individuals in various ways. That is why we have developed the HAE Round Table as a platform for members of our community to connect with their peers about the issues that currently affect them.

Through the HAEA Round Table we will discuss questions such as:

- How do you explain your HAE diagnosis when dating?
- Is your HAE affected by drinking alcohol?
- How do you overcome a fear of needles?
- How did you go about obtaining insurance with your HAE diagnosis?

The HAEA Round Table will premiere every other month on the US HAEA official Facebook page Live. Save the calendar of events below to make sure you tune in for every event that is relevant to you and your loved ones with HAE:

- 12 April: For Youth with HAE Ages 12-15 – Anxiety, Stress, and Growth with HAE
- 14 June: For Youth with HAE Ages 16-20 – How Do You Talk to Others About Your HAE?
- 9 August: For Young Adults with HAE – Growing Into Adulthood with HAE
- 11 October: For Baby Boomers with HAE – How Does HAE Affect Aging?
- 1 November: For Caregivers and Parents – What is the Best Way to Support Someone with HAE?

NEW episodes of the HAE Speaks and #BeyondHAE podcasts!

PODCAST HAEA Speaks #BeyondHAE Youth Podcast

Listen today on Spotify, Apple Podcasts, or anywhere podcasts are available!

US HAEA Podcasts: The US HAEA is continuing to present community stories on both of our podcast platforms. These podcasts include:

- ***HAE Speaks Podcast*** features adults with HAE or their caregivers who speak about various topics that affect the everyday lives of our community members. These topics include learning to come to terms with your diagnosis, mastering travel with HAE, how HAE can affect pregnancy, and gaining a sense of purpose through advocating for HAE. There are twenty-two informative episodes of the HAE Speaks podcast.
- ***#BeyondHAE Podcast*** presents stories from the youngest members of our community. Young people with HAE can face a series of unique challenges when it comes to their diagnosis, so the HAEA has created the #BeyondHAE podcast to unite the youth community through shared experiences. Featured topics include understanding anxiety and how it relates to HAE, facing fear of needles, speaking to significant others or classmates about HAE, and creating a strong support system. There are thirty-six illuminating episodes of the #BeyondHAE podcast.

These podcasts are available on Spotify and Apple Podcasts!

RUSSIA

From HAE Russia

During the fall and winter season, HAE Russia experienced many important events. We won a prestigious award, held several webinars for our members, and conducted spectacular art meetings for children diagnosed with HAE within the "Call a Friend" program.

- In late October 2021, under the "Call a Friend" cycle, HAE Russia organized an art therapy online meeting timed to coincide with the Halloween holiday. The hosts discussed with juvenile patients with HAE how Halloween can relieve negative feelings. On New Year's Eve, young children with HAE attended the meeting "New Year's Wonders", and teenagers participated in the New Year psychological game "Wonderful New Year". In February, we held an online meeting regarded managing emotions. Such skills are especially valuable for young patients with HAE, since strong emotional experiences can cause a sudden attack.
- On 6 November 2021, an online school for patients with HAE "Step by step" addressed issues of drug supply in the regions of the country. The doctors focused on premedication during surgical interventions and other medical manipulations.
- In late December 2021, HAE Russia presented a webinar introducing the results of the annual survey based on the fall 2021 survey of the Society members. This is a sample of that data:
  - *About 90% of Russian patients receive effective emergency medications*
  - *81.5% of patients with HAE save the rapid-relief medication for the most extreme case*
  - *63.7% feel unprotected from HAE attacks in everyday life*
  - *34.7% of survey participants admitted that angioedema affected significantly their quality of life in the past few months, 46% considered their situation as "satisfactory," and only 19.3% noted a slight impact.*
- On 17 February 2022, the annual Andrew Ado Award ceremony rewarded HAE Russia in the category "Public activity aimed at improving the health of the population as a whole and patients with allergic diseases specifically".
- On 12 February 2022, HAE Russia hosted a webinar for HAE patients from the North Caucasus Federal District of Russia. On 1 January 2022, new clinical guidelines came into force in Russia. Ilya Ushankov, lawyer, introduced participants to the key provisions of the guidelines and presented a step-by-step procedure required to obtain effective rapid-relief medications.
- On 19 February 2022, HAE Russia invited HAE patients to a webinar on "Law and Criteria". The event gathered experts in the field of law and immunology. Ilya Ushankov, lawyer, reported on international experience in the treatment of angioedema. Irina Manto, allergist-immunologist and researcher of the Federal State Research Center Institute of Immunology of the Federal Medical and Biological Agency of Russia, shared her views on changes in approaches to treatment with the appearance of the Federal Clinical Guidelines.
- In February, we launched a virtual exhibition "HAE Family" on our website. The expo, honoring the International Rare Disease Day, introduces the life of families with children diagnosed with HAE.

Visit our exhibition! Visit HAE Russia's website at https://op-nao.ru/hae-family. You can also log in through the QR-code. In the options you can choose the preferred language – Russian or English.

EL SALVADOR

In El Salvador two HAE knowledgeable physicians have been added to the HAEi world map – please see https://haei.org/hae-member-countries/el-salvador for contact information.

DENMARK, NORWAY, AND SWEDEN

From HAE Scandinavia

We are pleased to inform you about new treatment options in Scandinavia. In Norway, ORLADEYO™ (capsule) was approved on 1 December 2021 for the preventive treatment of HAE in adults and adolescents/children from 12 years of age. In Sweden, both ORLADEYO™ (capsule) and TAKHZYRO™ (injection under the skin) were approved on 1 January 2022 for the preventive treatment of HAE in adults and adolescents/children from 12 years of age.

The Danish Medicines Council has just recommended ORLADEYO™ (capsule) as a preventive treatment for HAE in adults and adolescents/children from 12 years.

SOUTH AFRICA

From HAE South Africa

On 11 January 2022 HAE South Africa embarked on a new social media campaign. As of 28 February, our Facebook reach was up by 955% compared to the previous period, with our Instagram reach growing 330%. Our new website will be launched in the next couple of weeks.

We received several enquiries from people who had recognized the symptoms and pictures shared on our social media sites and they were referred to our HAE physicians for testing. We have added another four patients to our database and are awaiting the test results for a few others.

For Rare Disease Day on 28 February, we created a video detailing our achievements since our inception in 2016 – and on 5 March, some of our patients took part in the Rare Diseases South Africa family day along with other rare disease patients and organizations.

HAE South Africa chairman Janice Strydom was invited to do a presentation at the Takeda conference in Johannesburg on 3 March to talk about her experience as an HAE patient and discuss the role of patient organization within the healthcare context.

Our early access/pre-authorization program for icatibant is working well and has simplified the process for our patients to access this acute medication.

COSTA RICA

Diana Madrigal has taken over from Angie Leitón as President of HAE Costa Rica. You can contact the new President via dianamadrigal61@gmail.com.

Two more HAE knowledgeable hospitals have been added to the HAEi world map. Please see contact information at https://haei.org/hae-member-countries/costa-rica.

DOMINICAN REPUBLIC

The HAEi world map has been updated with both HAE knowledgeable physicians and HAE knowledgeable hospitals in the Dominican Republic. Please see https://haei.org/hae-member-countries/dominican-republic for contact information.

PANAMA

In Panama, there are additions to both HAE knowledgeable physicians and HAE knowledgeable hospitals on the HAEi world map – please see contact information at https://haei.org/hae-member-countries/panama.

CANADA

From HAE Canada

Our first big piece of news to share is that the HAE Canada team has blossomed to eight Board of Director members. At the 2021 Annual General Meeting on 7 December, we thanked our outgoing Board members, and welcomed our new Board members who will bring their own expertise to the Board:

- Kerstyn Lane (Regional Director: Pacific)
- Martine Paquette (Regional Director: Quebec)
- Dwayne Semple (Regional Director: Atlantic)
- Kim Speiss (Regional Director: Central)

For the past year, Kerstyn has been a member of our Governance Committee and we are thrilled she has agreed to continue in this role and will work towards accreditation with Imagine Canada. Martine is a returning Board member from Quebec, and we are grateful she will bring her knowledge and experience (& energy!) back to the table. Dwayne, an experienced paramedic, will assist with our ongoing project to have HAE added to the ACLS/PALS course. Kim, a member of our Advocacy Committee for the past four years, will focus on our HAE Canada Café.

We are grateful our experienced Board members remain on the team:

- Jacquie Badiou (President)
- Michelle Cooper (VP & Regional Director: Ontario)
- Carmen Craciun (Treasurer & Secretary)
- Tina McGrath (Director at Large)

We are lucky to have new, fantastic people join us at HAE Canada. Daphne Dumbrille, our COO, is excited and looking forward to working on upcoming projects with the new team.

HAE Canada President, Jacquie Badiou, was presenting our poster titled "HAE with normal C1-INH: Treatment and attack frequency based on data from the Canadian 2020 national survey", at the 2022 American Academy of Asthma & Immunology (AAAAI)'s Annual Meeting in February in Phoenix, Arizona, USA. This was her first in-person event representing HAE Canada since the start of COVID-19 and her packed agenda shows how excited everyone was to finally meet in person once again.

Over the past few months, HAE Canada has been collaborating on a few projects with Canadian Blood Services (CBS), the national organization that provides blood-derived HAE treatments to Canadian patients. One project is regarding CBS's procurement process for their plasma-derived products to be listed on the CBS formulary. We are proud to report that an HAE Canada Board member is part of the Request for Proposals (RFP) committee. This Board member will represent the concerns of HAE patients while providing support and advice to CBS throughout the process. We trust CBS is in good hands and look forward to learning the outcome of this very thorough and extensive process.

Also, CBS invited Jacquie to be one of the founding members of the CBS Patient Engagement Forum, a new initiative to improve how CBS connects, listens to, and collaborates with patient organizations. This is an amazing accomplishment. We are both privileged and proud to be part of these important projects with CBS and would like to thank Daphne and past Board members who were instrumental in making this happen.

Helping HAE patients gain access to new treatments is always a top priority for HAE Canada. To illustrate how effective new treatments are, patients and clinicians need to have the ability to share their experiences. That is why we have hired a health policy consultant to complete the patient and clinician submissions for the Common Drug Review (CDR) for the Canadian Agency for Drugs and Technology and Health (CADTH) in support of the new oral treatment, ORLADEYO™ (berotralstat). Our aim in completing these submissions is to bring Canadian patients one step closer to accessing ORLADEYO™. We want to thank our Advocacy Committee, HAE Canada members and the physicians who contributed to these submissions by sharing their real-life experiences and knowledge.

To ensure our members remain engaged and connected, HAE Canada hosts Patient Information Updates throughout the year. Our next update will be from Saskatchewan; however, it will be virtual and open to our entire membership. Dates and details will be shared with our membership very soon. We look forward to hosting this event "from" beautiful Saskatchewan.

AUSTRALIA & NEW ZEALAND

From HAE Australasia

HAE Australasia has held two in-person patient and carers meetings in February. The first meeting was held in Sydney, Australia, on 5 February, the main venue with presenters in Sydney. Brisbane and Melbourne were linked via Zoom. Other patients and carers around Australia and New Zealand could dial in to watch presentations from Dr. Connie Katelaris (Australia), Dr. Marc Riedl (USA), a genetic counsellor, clinical psychologist, gynecologist and obstetrician, and HAEi, and a patient story. HAE Australasia's CEO presented on the achievements of our member organization over the last 10 years and the importance of advocacy and the resources available to patients.

On 26 February, it was New Zealand's turn for an in-person meeting in Auckland where patients and carers heard from local and international speakers Dr. Hilary Longhurst, Dr. Anthony Jordan, Dr. Karen Lindsay, a patient story and a fascinating talk on stress and lifestyle.

HAE Australasia is busy working on the next round of the "Living Well with HAE" video series for our website www.haeaustralasia.org.au. We are looking forward to posting the new videos on HAE with information from a gynecologist and genetic counsellor.

We are excited by the launch of the Elizabeth Macarthur Virtual Angioedema Centre (EMVAC). This virtual center is a pilot project with Dr. Connie Katelaris and HAEi. EMVAC is available to patients, healthcare professionals and others who want to make an appointment for HAE information and care. EMVAC services provided are one-on-one appointments with Dr. Katelaris, HAE nurses, clinical psychologists, and coming soon more access to more specialists to answer questions on HAE and support.

GERMANY

Also in Germany there are a number of additions to the HAEi world map of physicians, hospitals and ACARE centers. You will find the updated contact information at https://haei.org/hae-member-countries/germany.

GREECE

Yet another country to register the first HAE knowledgeable physician is Greece. His name is Psarros Fotios, he is located in Athens – and you will find his contact information at https://haei.org/hae-member-countries/greece.

TURKEY

Three more HAE knowledgeable physicians – located in Ankara, Izmir, and Gaziantep – have been added to the HAEi world map. Please see contact information at https://haei.org/hae-member-countries/turkey.

NORTH MACEDONIA

HAE Macedonia now also has an official Youtube channel – please have a look at www.youtube.com/channel/UCcM-y4N44zD85aMexhSYyUA.

PORTUGAL

From HAE Portugal (ADAH)

This past December 2021, ADAH held the second online event of its annual conference, under the theme of the advantages and challenges towards the autonomy process of patients with HAE. The occasion was meant to promote the share of up-to-date scientific knowledge on the disease, while providing an opportunity for doctors, patients, and association representatives to meet, interact and debate under the same roof.

The conference was divided into three panels:

- The scientific panel, coordinated by Professor Manuel Branco Ferreira, was comprised of four presentations by specialists in HAE from Portugal and Brazil, who addressed topics such as genetics and Angioedema; the life quality of those affected by HAE; the real experience of a patient in a peripheral hospital; as well as the Portuguese legislation on HAE and its importance for patients.
- This was followed by a panel constituted by Patient Associations, highlighting their contribution towards the process of empowering HAE patients. The debate versed around the main difficulties faced by these entities, and the obstacles presented by both the Ministry of Health and some hospitals against the widespread practice of home treatment for patients with HAE, allegedly the high cost of medication, and the risk of medicine wastage, due to expiration dates. On this panel, ADAH was joined by HAEi, represented by Executive Vice President & COO Henrik Balle Boysen and Regional Patient Advocate Maria Ferron.
- Lastly, a panel of patients reunited several testimonies focused on the impact of HAE in their personal and family trajectories, before and after accessing home treatment. There was a consensual reference to the significant improvement in the patients' life quality through home therapy, emphasizing the practical and rapid resolution of acute crises. Also mentioned were the decrease in the numbers of hospital visits, and in school and professional absenteeism levels.

An important Q&A session followed, resulting in a widespread exchange of experiences between the attending patients, association representatives and doctors. Notwithstanding the difficulties still faced by those affected by HAE towards acquiring treatment autonomy, we acknowledge its undeniable progress in Portugal. It's time to consolidate it and, more importantly, make it available to all of those who will benefit from it.

SLOVENIA

The first HAE knowledgeable physician has been added to HAEi's world map of important contact points. The location is Golnik – and you will find the contact information here: https://haei.org/hae-member-countries/slovenia.

CROATIA

From President Michaela Sogoric, HAE Croatia

In collaboration with psychologist Maja Batista, MD and clinical immunologist Višnja Prus, MD, PhD, HAE Croatia has designed a brochure for parents, children's guardians and adolescents. The brochure named "Psychosocial aspects of HAE" is made in the form of an educational book that will be distributed at the annual meeting of HAE Croatia.

The HAE Croatia annual meeting will take place in Šibenik on 14-15 May 2022. At this event doctors from clinical hospital centers will present lectures. After the lectures there will be an open-air concert on the occasion of **hae day :-)** 2022. Members of HAE Croatia will distribute the educational brochures to all people during the concert. Through these events, HAE Croatia endeavors to raise people's awareness of the existence of this rare disease.

SPAIN

From President Sarah Smith, HAE Spain (AEDAF):

General Assembly & Annual Meeting: The 24th General Assembly and Annual Meeting of AEDAF took place 26 March 2022 in La Paz Hospital in Madrid. After two years of pandemic, we are very, very happy to again be able to have an in-person meeting and to see each face to face in real life. We had a very interesting program with news about activities, innovations, and new initiatives for HAE patients.

Survey: The project submitted by AEDAF to the call for proposals for the 2021 CSL Behring EU LEAD Grants was a survey (one for patients and one for physicians) on the availability of and access to modern HAE treatments in Spain based on place of residence. After receiving the grant and dealing with some delays, the survey was launched during the autumn and closed in mid-December 2021. AEDAF now has the draft of the Final Report on data analysis and interpretation (also containing an updated list of hospitals in Spain with a knowledge of HAE and availability of modern treatments). It reveals interesting data that confirm our suspicions of major differences in access to and availability of these modern treatments in Spain, as well as in approval for patients to keep these treatments at home and learn self-administration, depending on the Autonomous Region where they live.

The last phase of our project will be to disseminate and publish the survey results and submit them to the national Ministry of Health and the Regional Ministries of Health in Spain to underline these differences and to advocate for equality in healthcare and access for patients all over Spain, regardless of treatment price.

Workshop: The 1st National Scientific Angioedema Workshop, organized by the HAE and Dermo-Allergy CSURs (Reference Centers, Services and Units of the Spanish National Health System) of La Paz University Hospital, as well as CIBERER U754, CIBERER U761 and IdiPaz groups 21 and 44, and coordinated by Dr. Teresa Caballero Molino, took place on 17-18 February 2022 in La Paz Hospital in Madrid.

The idea is to hold this course, which is very important for improving knowledge and raising awareness of HAE, every two years. On behalf of AEDAF, we congratulate Dr. Caballero, the Scientific Committee and all the speakers for this excellent Workshop.

Patient Support Program: In an online press conference on 17 February 2022, CSL Behring announced its new innovative HAE patient support program in long-term prophylaxis. The program has been designed to lower the burden of disease and improve the patient's quality of life, with individual attention and training in the subcutaneous self-administration of the C1-INH protein.

The program, developed in collaboration with the GEAB (Spanish Study Group on Bradykinin-Induced Angioedema) and now available throughout Spain, responds to the need to adopt individualized therapeutic strategies due to the heterogeneity of the disease.

ROMANIA

The the city Targu Murres you will find the first HAE knowledgeable physician registered in Romania. Contact information can be found at https://haei.org/hae-member-countries/romania.

ALGERIA

From Vice-President Salah Alioui, HAE Algeria

HAE Algeria organized its first national HAE awareness day on 25 December 2021 at Lamaraz Hotel in Algiers. The day was under the patronage of the Minister of Health and the Minister of the Pharmaceutical Industry. The slogan "Speaking out, gives hope! Taking actions, saves lives!" was chosen for this first edition.

The awareness day was aimed to raise awareness on HAE and how to improve the difficult situation of Algerian patients. The event was the first of its kind and saw significant media coverage.

A range of national and international experts animated the conferences. Two workshops were held during the evening session, one for patient advocacy and the other for health professionals to debate how to improve the care and diagnosis for patients struggling to get the proper care and diagnosis. A list of recommendations on improving the diagnosis and care was later handed to the relevant authorities.

The conference and workshops were a unique occasion for the patients and the media present to know more about this severe disease, its impact on the patients' lives, and how modern and innovative treatments are improving the life quality of patients worldwide.

The patients present at the conference gave both caregivers and authorities moving testimony of their daily suffering and permanent fear for their lives. Officials from the two ministries made public and official commitments for patients to support them and improve their situations.

This awareness day was very important for HAE Algeria to uncover the suffering of our patients to the public and the authorities. However, the ultimate purpose would be to ensure access to modern therapies that exist worldwide but are still not available for Algerian patients.

Despite its young age (created in 2019), the HAE Algeria has made significant progress on all fronts. Our first feat since its foundation was to bring together the patients for the first time and allow them to speak out about their illnesses and to be listened to and supported.

After a large awareness campaign on the various media and newspapers, the list of diagnosed or undiagnosed Algerian patients has not stopped growing, same for the number of distress calls from patients. Patients call us for different reasons, asking for help dealing with doctors who are often totally unaware of HAE, asking for medicines, or seeking help with socio-professional issues due to the absence of official recognition of the disease.

PUERTO RICO

The first two HAE knowledgeable physicians in Puerto Rico have been added to the HAEi world map, one in San Juan and one in Humacao. Please see contact information at https://haei.org/hae-member-countries/puerto-rico.

GUATEMALA

In Guatemala the first couple of HAE knowledgeable physicians have been added to the HAEi world map. Their contact information is ready for you at https://haei.org/hae-member-countries/guatemala.

CUBA

Another two HAE knowledgeable physicians have been located in Cuba. They are both in La Habana – and you will find their contact information at https://haei.org/hae-member-countries/cuba.

NEW INTERNATIONAL GUIDELINE FOR HAE MANAGEMENT

Earlier this year, the European Journal of Allergy and Clinical Immunology published the 2021 revision and update of the international WAO/EAACI guideline for the management of HAE.

The updated guideline reflect consensus among an international panel of 60 HAE experts, and includes 28 recommendations that provide physicians and patients with guidance on important clinical issues, such as: (1) How should HAE be diagnosed? (2) When should HAE patients receive prophylactic on top of on-demand treatment, and what treatments should be used? (3) What are the goals of treatment? (4) Should HAE management be different for special HAE patient groups such as children or pregnant/breastfeeding women? and (5) How should HAE patients monitor their disease activity, impact, and control?

These are the 28 recommendations:

1. We recommend that all patients suspected to have HAE are assessed for blood levels of C1-INH function, C1-INH protein, and C4

2. We suggest that testing for C1-INH function, C1-INH protein, and C4 is repeated in patients who test positive, to confirm the diagnosis of HAE-1/2

3. We recommend that patients who are suspected to have HAE and have normal C1-INH levels and function are assessed for known mutations underlying HAE-nC1-INH

4. We recommend that all attacks are considered for on-demand treatment

5. We recommend that any attack affecting or potentially affecting the upper airway is treated

6. We recommend that attacks are treated as early as possible

7. We recommend that attacks are treated with either intravenous C1 inhibitor, ecallantide or icatibant

8. We recommend that intubation or surgical airway intervention is considered early in progressive upper airway edema

9. We recommend that all patients have sufficient medication for on-demand treatment of at least two attacks and carry on-demand medication at all times

10. We recommend considering short-term prophylaxis before medical, surgical or dental procedures as well as exposure to other angioedema attack-inducing events

11. We recommend the use of intravenous plasma-derived C1 inhibitor as first-line short-term prophylaxis

12. We suggest considering prophylaxis prior to exposure to patient-specific angioedema-inducing situations

13. We recommend that the goals of treatment are to achieve total control of the disease and to normalize patients' lives

14. We recommend that patients are evaluated for long-term prophylaxis at every visit, taking disease activity, burden, and control as well as patient preference into consideration

15. We recommend the use of plasma-derived C1 inhibitor as first-line long-term prophylaxis

WORLD ALLERGY ORGANIZATION

EAACI
EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY

16. We recommend the use of lanadelumab as first-line long-term prophylaxis

17. We recommend the use of berotralstat as first-line long-term prophylaxis

18. We recommend the use of androgens only as second-line long-term prophylaxis

19. We suggest all patients who are using long-term prophylaxis be routinely monitored for disease activity, impact, and control to inform optimization of treatment dosages and outcomes

20. We recommend testing children from HAE-affected families be carried out as soon as possible and all offspring of an affected parent be tested

21. We recommend C1 inhibitor or icatibant be used for the treatment of attacks in children under the age of 12

22. We recommend plasma-derived C1 inhibitor as the preferred therapy during pregnancy and lactation

23. We recommend that all patients have an action plan

24. We recommend that HAE-specific comprehensive, integrated care is available for all patients

25. We recommend that patients are treated by a specialist with specific expertise in managing HAE

26. We recommend that all patients who are provided with on-demand treatment licensed for self-administration should be taught to self-administer

27. We recommend that all patients should be educated about triggers that may induce attacks

28. We recommend screening family members of patients for HAE

HAEi President & CEO Anthony J. Castaldo and EVP & COO Henrik Balle Boysen represented the global patient community as authors of the guidelines.

The guideline can be accessed online at **onlinelibrary.wiley.com/doi/10.1111/all.15214**

MEDICAL PAPERS

Here are summaries of some of the recently published HAE related scientific papers:

Why does it take so long for rare dis ease patients to get an accurate diagnosis? – A qualitative investigation of patient experiences of HAE – *by Moeko Isono, Osaka University, Japan, et al.:*

One of the most important factors related to the prolonged undiagnosed period is the lack of suspicion of a rare disease by patients and their medical professionals. While current policies tend to focus on the period from suspecting rare diseases to the time of a clear diagnosis, our results strongly suggest that measures are needed to facilitate patients and clinicians to become aware of rare diseases.

PLoS One, March 2022

Inhibition of Prekallikrein for HAE – *by Lauré M. Fijen, University of Amsterdam, the Netherlands, et al.:*

In this phase 2 trial, we randomly assigned patients with HAE with C1 inhibitor deficiency to receive four subcutaneous doses of either donidalorsen (80 mg) or placebo, with one dose administered every four weeks. Among patients with HAE, donidalorsen treatment resulted in a significantly lower rate of angioedema attacks than placebo.

N Engl J Med, March 2022

Pharmacological suppression of the kallikrein kinin system with KVD900: An orally available plasma kallikrein inhibitor for the on-demand treatment of HAE – *by Edward J. Duckworth, KalVista Pharmaceuticals, et al.:*

Oral administration of KVD900 in a first-in-human clinical trial achieved rapid and near complete inhibition of dextran sulphate-stimulated plasma kallikrein enzyme activity and high molecular weight kininogen cleavage and reduced plasma prekallikrein and Factor XII activation in plasma. On-demand administration of KVD900 may provide an opportunity to halt the generation of bradykinin and reverse HAE attacks.

Clin Exp Allergy, March 2022

Long-term prevention of HAE attacks with lanadelumab: The HELP OLE Study – *by Aleena Banerji, Harvard Medical School, the United States, et al.:*

Lanadelumab demonstrated sustained efficacy and acceptable tolerability with long-term use in HAE patients.

Allergy, March 2022

Prophylactic use of an anti-activated factor XII monoclonal antibody, garadacimab, for patients with C1-esterase inhibitor-deficient HAE: a randomized, double-blind, placebo-controlled, phase 2 trial – *by Timothy Craig, Penn State University, the United States, et al.:*

In this double-blind, placebo-controlled, phase 2 study, patients with HAE-C1-INH were recruited from 12 research centers in Canada, Germany, Israel, and the United States. Garadacimab 200 mg and 600 mg every four weeks significantly reduced the number of monthly attacks versus placebo and was well tolerated during the study. Garadacimab is an efficacious, subcutaneous prophylaxis in patients with HAE-C1-INH and warrants phase 3 evaluation.

Lancet, March 2022

Population pharmacokinetic modeling and simulations of berotralstat for prophylactic treatment of attacks of HAE – *by Amanda Mathis, BioCryst Pharmaceuticals, et al.:*

Despite the covariate effect of weight, simulations in adolescents and adults who were underweight, low weight, and overweight demonstrated similar predicted exposures to those observed at therapeutic doses in a clinical trial. Therefore, no dose adjustment is required in these HAE patient subpopulations.

Clin Transl Sci, February 2022

A review of oral kallikrein inhibitor berotralstat for HAE – *by YingYu Gao, Penn State Health Milton S. Hershey Medical Center, the United States, et al.:*

The ongoing phase III APeX-2 trial showed a 67% reduction in HAE attacks at the standard 150-mg dosing. Mild to moderate gastrointestinal side effects are most commonly seen and minimal serious adverse effects have been reported. Other first-line therapies for HAE prophylaxis rely on burdensome subcutaneous or intravenous routes. Thus far berotralstat has shown to be effective and well tolerated for HAE prophylaxis with the convenience of once-daily oral dosing.

Drugs Today (Barc), February 2022

KVD900, an oral on-demand treatment for HAE: Phase 1 study results – *by Andreas Maetzel, KalVista Pharmaceuticals, et al.:*

KVD900 was administered in two clinical studies. Both of these phase 1 studies evaluated the pharmacokinetics/pharmacodynamics profile of KVD900, showing that KVD900 rapidly achieves near-complete plasma kallikrein inhibition and is generally safe and well tolerated.

J Allergy Clin Immunol, January 2022

In vitro pharmacological profile of PHA-022121, a small molecule bradykinin B2 receptor antagonist in clinical development – *by Anne Lesage, Pharvaris GmbH., et al.:*

PHA-022121 is a novel, low-molecular weight, competitive antagonist of the human bradykinin B2 receptor with high affinity, high antagonist potency, and high selectivity. It is about 20-fold more potent than icatibant at the human bradykinin B2 receptor as assessed using recombinant or endogenously expressed receptors.

Int Immunopharmacol, April 2022

Reviewing clinical considerations and guideline recommendations of C1 inhibitor prophylaxis for HAE – *by John Anderson et al., AllerVie Health Birmingham Alabama, the United States:*

Assessing the need for long-term prophylaxis is vital in the ongoing dialogue between clinicians and patients, as both disease-related factors and patient preferences may change over time. Among available options for long-term prophylaxis, plasma-derived C1INH is the broadly recommended first-line option for long-term prophylaxis in patients with HAE, including pregnant/lactating women and pediatric patients (≥6 years).

Clin Transl Allergy, January 2022

Attenuated androgen discontinuation in patients with HAE: a commented case series – *by Marcus Maurer, Charité-Universitätsmedizin Berlin, Germany, et al.:*

Healthcare teams need to undertake careful planning and monitoring after attenuated androgens discontinuation and modify treatment strategies if HAE control is destabilized with an increased number of attacks. Discontinuation of attenuated androgens is definitively an option in an evolving HAE treatment landscape, and outcomes can be favorable with additional patient support and education.

Allergy Asthma Clin Immunol, January 2022

Management of pregnancy in HAE in a resource constrained setting: Our experience at Chandigarh, North India – *by Ankur Kumar Jindal, Postgraduate Institute of Medical Education and Research, Chandigarh, India, et al.:*

Our results suggest that frequency of attacks may increase during pregnancy especially during second trimester and post-delivery (during breastfeeding). However, HAE attacks are rare at the time of delivery. In resource limited settings, treatment with fresh-frozen plasma/tranexamic acid needs to be individualized.

Immunobiology, March 2022

PubMed

Global perceptions of the current and future impacts of COVID-19 on HAE management – *by Vesna Grivcheva-Panovska, University Saints Cyril and Methodius, North Macedonia, et al.:*
Two online surveys show that both patients and healthcare professionals globally reported that the pandemic has limited the availability of HAE medical care, and they expect the restrictions to continue far beyond the pandemic. In addition, the results suggested that telehealth use has increased across the globe but has been more successfully implemented in high-income countries. Patients and healthcare professionals expect that HAE-related care will be negatively impacted by the pandemic for many years. Disparities in medical care and technologic infrastructure may exacerbate these challenges in non-high-income countries. Supportive tools and global infrastructure should be established to provide aid to non-high-income countries throughout the pandemic and several years after.

Allergy Asthma Proc, January 2022

Small molecule drugs for atopic dermatitis, rheumatoid arthritis, and HAE – *by Bob Geng, University of California San Diego, the United States, et al.:*

Scientific advances have led to an increase in the development of targeted small molecule drugs for the treatment of chronic immunologic disorders, which may revolutionize the management of these diseases. Head-to-head studies and real-world evidence are needed to fully compare treatment attributes between biologics and small molecule drugs, including safety, efficacy, adherence, impact on quality of life, and cost-effectiveness.

Ann Allergy Asthma Immunol, March 2022

Time Trade-Off Utilities for HAE Health and Caregiver States – *by Siu Hing Lo, Acaster Lloyd Consulting Ltd., the United Kingdom, et al.:*
Time trade-off utility values demonstrate that HAE places a significant burden on patients, which is influenced by attack location, and on caregivers. These utility weights can provide important information on quality of life for future economic evaluations of treatments.

Pharmacoecon Open, March 2022

Identification of novel biomarkers to distinguish bradykinin-mediated angioedema from mast cell-/histamine-mediated angioedema – *by Gesa Bindke, Hannover Medical School, Germany, et al.:*

This study is the first to compare HAE, ACE-inhibitor induced angioedema, and chronic spontaneous urticaria angioedema. Although significance is limited by small sample size, Tie-2 was identified as a new promising biomarker candidate for HAE. FAP-a and tPA might serve as a marker for angioedema in general, whereas sE-selectin and Ang-2 were increased in bradykinin-mediated angioedema only. Our results add information to the role of endothelial dysfunction and serine proteases in different angioedema subtypes.

Allergy, March 2022

ORLADEYO™ (Berotralstat): A Novel Oral Therapy for the Prevention of HAE – *by Jason Powell, University of Florida, the United States, et al.:*

Berotralstat 150 mg daily has been proven safe and effective in clinical studies and appears to be a viable oral alternative to parenteral medications currently used in HAE prophylaxis.

Ann Pharmacother, April 2022

PubMed

CLINICAL TRIALS

According to clinicaltrials.gov under the U.S. National Institutes of Health, the EU Clinical Trials Register, and the International Clinical Trials Registry Platform under World Health Organization (WHO) the following trials should be recruiting at this moment:

A Gene Therapy Study of BMN 331 in Subjects with HAE

– recruiting in the United States

A Phase 3, Multicenter, Randomized, Single-Blind, Dose-Ranging, Crossover Study to Evaluate the Safety and Efficacy of Intravenous Administration of Cinryze™ (C1 Esterase Inhibitor [Human]) for the Prevention of Angioedema Attacks in Children 6 to 11 Years of Age with HAE

– recruiting in Argentina, Germany, Italy, Mexico, Romania, the United Kingdom, and the United States

Assessment of the State of Health, Quality of Life and Expectations of Patients with HAE

– recruiting in France

A Study of Lanadelumab in Persons with HAE Type I or II

– recruiting in Austria, Germany, Israel, Italy, Kuwait, Portugal, Spain, and Switzerland

A Study of Lanadelumab in Teenagers and Adults with HAE in Argentina

– recruiting in Argentina

A Study in Teenagers and Adults with HAE Type I or Type II who use Lanadelumab as Long-Term Prophylaxis

– recruiting in Austria, France, Germany, and Greece

A Trial to Evaluate the Efficacy and Safety of Different Doses of KVD824 for Prophylactic Treatment of HAE Type I or II

– recruiting in Australia, Canada, Czech Republic, France, Germany, Hungary, Italy, New Zealand, Puerto Rico, the United Kingdom, and the United States

Biomarker for HAE Disease

– recruiting in Armenia, Georgia, India, Peru, Poland, Romania, and Turkey

CLOUD-R HAE REGISTRY

– recruiting in France

C1 Inhibitor Registry in the Treatment of HAE Attacks

– recruiting in Bulgaria, Croatia, Czech Republic, France, Germany, Hungary, Italy, North Macedonia, Norway, Poland, Slovakia, Slovenia, and Sweden

Contrast-Enhanced Ultrasound for the Evaluation of Changes in Tumor Blood Flow Surrounding HAE

– recruiting in the United States

Dose-ranging Study of Oral PHA-022121 for Acute Treatment of Angioedema Attacks in Patients with HAE

– recruiting in Bulgaria, Canada, Czech Republic, France, Germany, Hungary, Israel, Italy, the Netherlands, Poland, Spain, the United Kingdom, and the United States

CLINICAL TRIALS

Dose-ranging Study of Oral PHA-022121 for Prophylaxis Against Angioedema Attacks in Patients with HAE Type I or Type II

– recruiting in Canada, the United Kingdom, and the United States

Efficacy and Safety of Lanadelumab (SHP643) in Japanese Subjects with HAE

– recruiting in Japan

Epidemiological Analysis for HAE Disease

– recruiting in Germany, Italy, Japan, Poland, Turkey, and the United Kingdom

Expanded Access Program with Lanadelumab for Japanese People with HAE

– recruiting in Japan

Firazyr® General Drug Use-Results Survey (Japan)

– recruiting in Japan

Firazyr® Patient Registry (Icatibant Outcome Survey - IOS)

– recruiting in Australia, Austria, Brazil, Czech Republic, Denmark, France, Germany, Greece, Ireland, Israel, Italy, Spain, Sweden, and the United Kingdom

Global Registry to Gather Data on Natural History of Patients with HAE Type I and II

– recruiting in Italy

HAE Kininogen Assay

– recruiting in Germany

Involvement of Monocytic B1 and B2 Receptors in Inflammation and Chronic Vascular Disease in Patients with Hereditary Bradykinetic Angioedema

– recruiting in France

Long-term Safety and Efficacy of CSL312 (Garadacimab) in the Prophylactic Treatment of HAE Attacks

– recruiting in Australia, Canada, Czech Republic, Germany, Hong Kong, Hungary, Israel, Japan, the Netherlands, New Zealand, Russia, Spain, Taiwan, and the United States

NTLA-2002 in Adults with HAE

– recruiting in New Zealand

OASIS-HAE: A Study to Evaluate the Safety and Efficacy of Donidalorsen (ISIS 721744 or IONIS-PKK-LRx) in Participants with HAE

– recruiting in the United States

Pathophysiological study for autoimmune dysregulation of HAE

– recruiting in Japan

Patient Registry to Evaluate the Real-world Safety of Ruconest®

– recruiting in the United States

Study to Assess the Tolerability and Safety of Ecallantide in Children and Adolescents With HAE

– recruiting in the United States

Study to Evaluate the Real-World Long-Term Effectiveness of Lanadelumab in Participants With HAE

– recruiting in Austria, Germany, Israel, Switzerland, and the United Kingdom

The Role of the Coagulation Pathways in Recurrent Angioedema

– recruiting in France

A Study of the Burden of Illness and Treatment Patterns in Teenagers and Adults with HAE

– will be recruiting

A Phase III, Crossover Trial Evaluating the Efficacy and Safety of KVD900 for On-Demand Treatment of Angioedema Attacks in Adolescent and Adult Patients with HAE

– will be recruiting

A Study with Lanadelumab in Persons with HAE in Poland

– will be recruiting in Poland

Read more about these and other clinical trials at:

- clinicaltrials.gov
- clinicaltrialsregister.eu
- apps.who.int/trialsearch

NEWS FROM THE INDUSTRY

7 January 2022

Intellia Therapeutics, Inc. outlines its expected HAE milestones and strategic priorities for 2022:

"Unequivocally, 2021 was a landmark year for Intellia. We demonstrated that our proprietary CRISPR-based platform and LNP technology can turn revolutionary science into potentially transformational medicines. Our platform enables us to advance genome editing approaches, which maximizes our ability to target a multitude of life-threatening diseases," says Intellia President and CEO John Leonard, M.D. "As we begin 2022 with great momentum, we are poised to significantly expand our full-spectrum pipeline of potentially curative therapies with the nomination of new in vivo candidates and our first allogeneic development candidate during the year. Importantly, we look forward to sharing interim results from the Phase 1/2 study of NTLA-2002, which we expect will further demonstrate the modularity of our genome editing platform."

NTLA-2002 leverages Intellia's proprietary in vivo LNP delivery technology to knock out the KLKB1 gene in the liver with the potential to permanently reduce total plasma kallikrein protein and activity, a key mediator of HAE. This investigational approach aims to prevent attacks for people living with HAE by providing continuous suppression of plasma kallikrein activity following a single dose and to eliminate the significant treatment burden associated with currently available HAE therapies. In December 2021, Intellia dosed the first patient in its second clinical study of a CRISPR-based therapeutic candidate evaluating NTLA-2002 for HAE. The first-in-human Phase 1/2 trial is expected to evaluate the safety, tolerability and activity of NTLA-2002 in adults with Type I or Type II HAE.

The Company expects to present interim data from the Phase 1/2 study in the second half of 2022. These results are expected to characterize the emerging safety and activity profile of NTLA-2002 and demonstrate preliminary proof-of-concept.
(Source: Intellia)

10 January 2022

"Following 12 months of a successful launch through a global pandemic, we have a clear picture of the continued commercial trajectory for ORLADEYO™ based on a very attractive product profile, leading to strong patient demand to switch from injectable therapies to our oral, once-daily medicine, with 70 percent patient retention through the first year," says Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc.**

Fourth Quarter 2021 ORLADEYO™ Launch Dynamics:

- New patient demand for ORLADEYO™ remains strong and consistent, with a similar number of new patients added in Q4 2021 as in each of the previous three quarters of the year. Patients switching from other prophylactic therapies and acute-only therapy continue to drive the launch. More than half of patients new to ORLADEYO™ since launch had a previous prophylactic medicine prior to ORLADEYO™ and most of the remainder were from acute-only treatment.
- Most patients are well-controlled on ORLADEYO™ and remain on therapy. Approximately 70 percent of patients starting ORLADEYO™, including those switching from injectable prophylaxis, remain on ORLADEYO™ in the first year.
- ORLADEYO™ is now covered by all major payors and national and regional pharmacy benefit managers, which will lead to more patients being reimbursed quickly.
- The ORLADEYO™ prescriber base continues to grow significantly. The number of new physicians prescribing ORLADEYO™ in Q4 2021 was similar to the number added in Q3 2021. In market research, 60 U.S. physicians, who treat an average of seven HAE patients each, reported that they expect to double their use of ORLADEYO™, and that ORLADEYO™ will become their most prescribed prophylactic treatment in the next 12 months.

"We expect ORLADEYO™ revenues in 2022 to more than double in our second year of launch as we benefit from a full year of reimbursement and continued strong demand from patients and physicians. ORLADEYO™ is transforming the lives of HAE patients, which is why ORLADEYO™ is on a trajectory to become the market leader in HAE prophylaxis," says Charlie Gayer, Chief Commercial Officer of BioCryst.
(Source: BioCryst)

14 January 2022

Takeda Canada Inc. launches the Takeda Canada Innovation Challenge, an initiative that aims to discover new and breakthrough digital technologies and artificial intelligence (AI) solutions that support enhanced patient care. Takeda Canada is looking for innovative solutions within the fields of early diagnosis or integrated and personalized care, applicable to the therapeutic areas of inflammatory bowel disease or rare genetic diseases such as HAE.

The selected winner(s) of the challenge will be eligible to receive a direct response about collaboration at the end of the Challenge, the opportunity to benefit from Takeda's internal expertise and international network of partners and suppliers, and funding from Takeda to build a proof-of-concept project with a relevant Takeda team.

"We are incredibly excited about this initiative that directly supports two of our commitments, improving patient care and investing in homegrown innovation and talent," says Rute Fernandes, General Manager, Takeda Canada. "Canada is an innovation hub of excellence and has exceptional talent and expertise, recognized globally. We know we can accomplish more by partnering with experts. Our objective with this campaign is to open doors for new innovation with entrepreneurial minds who may not have the resources to move their ideation into practice."

"Healthcare innovation is a critical component to enhancing and improving patient outcomes across our incredible health system," says Dr. Jefferson Tea, Vice President, Medical and Scientific Affairs, Takeda Canada. "This initiative allows us to literally look outside the box and identify new ideas and make the next big innovation in patient care a near-future reality."
(Source: Takeda)

25 January 2022

KalVista Pharmaceuticals, Inc. announces data from the Phase 1 clinical trials of oral, on-demand treatment KVD900 in patients with HAE, published online by the Journal of Allergy and Clinical Immunology (JACI).

The objective of the Phase 1 studies was to evaluate the safety, tolerability, pharmacokinetics, and clinical pharmacology of KVD900, an orally administered inhibitor of plasma kallikrein in healthy adults. KVD900 was administered to 98 participants in total, and the data showed that KVD900 achieves near-complete plasma kallikrein inhibition within 30 minutes and was generally safe and well tolerated.

"We are pleased to see these data published in JACI to further describe our ongoing work to bring a safe, oral on-demand treatment option to the market for HAE patients," says Andrew Crockett, CEO of KalVista. "These data show that KVD900 rapidly suppresses plasma kallikrein activity, a key mediator of HAE attacks, and may provide the early relief from HAE attack progression that represents a currently unmet need in orally administered management of the disease. These findings have since been further validated by the results of our Phase 2 clinical trial for KVD900."
(Source: KalVista)

15 February 2022

The U.S. Food and Drug Administration (FDA) has approved the TAKHZYRO™ (lanadelumab-flyo) injection single-dose prefilled syringe (PFS) to prevent attacks of HAE in adult and pediatric patients 12 years of age and older. The PFS is ready to use and requires fewer preparation steps than the current TAKHZYRO™ vial injection, while also reducing supplies and waste.

"The announcement is an important innovation for TAKHZYRO™, offering people living with HAE and their caregivers an enhanced treatment administration experience with proven sustained reduction of attacks. This product delivery enhancement is intended to improve the overall patient experience and reflects Takeda's continued commitment to the HAE community; we look forward to introducing this new option to patients later this year", says Cheryl Schwartz, Senior Vice President, Rare Disease Business Unit at **Takeda Pharmaceutical Company Limited.**

TAKHZYRO™ is supported by a robust clinical development program, which includes one of the largest prevention studies in HAE with the longest active treatment duration. TAKHZYRO™ is currently approved and available in more than 30 countries around the world.
(Source: Takeda)

21 February 2022

Newbury Pharmaceuticals AB has successfully entered the Swedish and Norwegian market by making its first product available to patients and prescribers. It is the first launch and thereby an important milestone in validating the business model.

"Making Icatibant Newbury available in Sweden and Norway is an important milestone to Newbury as we see the fruits of the seeds sown. We expect to see more products being launched this year and to harvest some of these fruits during the second half of 2022 and 2023 with an ambition of growing the business continuously", says Lars Minor, CEO of Newbury.

Icatibant Newbury is indicated for the treatment of acute attacks of HAE in adults. The product is a portable acute therapy option that can go wherever patients go, so patients are always prepared to treat an attack if needed. Icatibant Newbury is supplied as a 3-ml, pre-filled syringe and is administered by patients in the abdomen or stomach.
(Source: Newbury)

23 February 2022

At the presentation of the **BioCryst Pharmaceuticals, Inc.** financial results for the fourth quarter and full year ended 31 December 2021, President and CEO Jon Stonehouse says:

"The successful launch of ORLADEYO™, the rapid advancement of our pipeline and the additional capital we acquired last year have transformed BioCryst. We are focused on compounding the value of the company by allocating capital to grow ORLADEYO™ and advancing our complement program to get our oral drugs to patients suffering from many different rare diseases."

Program Updates and Key Milestones
U.S. launch of ORLADEYO™: New patient demand for ORLADEYO™ remains strong and consistent, with a similar number of new patients added in Q4 2021 as in each of the previous three quarters of the year. Patients switching from other prophylactic therapies and acute-only therapy continue to drive the launch. More than half of patients new to ORLADEYO™ since launch had a previous prophylactic medicine prior to ORLADEYO™ and most of the remainder were from acute-only treatment.

Most patients are well-controlled on ORLADEYO™ and remain on therapy. Approximately 70 percent of patients starting ORLADEYO™, including those switching from injectable prophylaxis, remain on ORLADEYO™ in the first year.

The ORLADEYO™ prescriber base continues to grow significantly as physicians gain real-world experience. In market research, 60 U.S. physicians, who treat an average of seven HAE patients each, reported that they expect to double their use of ORLADEYO™, and that ORLADEYO™ will become their most prescribed prophylactic treatment in the next 12 months.

ORLADEYO™ is now covered by all major payors and pharmacy benefit managers, which will lead to more patients moving quickly to paid product.

"We are excited by the strong start to the ORLADEYO™ launch and the favorable experience most HAE patients are having controlling their HAE attacks with an oral, once-daily capsule. With a sizeable base of patients already on therapy, reimbursement in place for the full year in 2022, and more face-to-face opportunities for our commercial team to engage directly with patients and physicians, we are looking forward to more than doubling our revenue this year as we continue on our trajectory to become the market leader in HAE prophylaxis," said Charlie Gayer, CCO of BioCryst.

ORLADEYO™ Global Updates: ORLADEYO™ has been launched in France, Germany, Japan, Norway, Sweden, the United Arab Emirates, and the United Kingdom. The company expects launches in additional countries throughout the year.
(Source: BioCryst)

24 February 2022

Long-term prophylactic treatment of HAE is becoming a reachable goal thanks to pharmacological therapies that target the bradykinin-producing cascade.

A study funded by **CSL Behring** provides the first clinical evidence and a proof of concept for FXIIa inhibition as a novel strategy for HAE prophylaxis. Garadacimab, a first-in-class recombinant monoclonal antibody targeting Factor XIIa, proved to be efficacious and well tolerated when subcutaneously administered every four weeks over a period of 12 weeks.

HAE is associated with dysregulation of the kallikrein–kinin system. Factor XII (FXII)

is a key initiator of the kallikrein–kinin system, which produces bradykinin, a central mediator of angioedema.

The study aimed to investigate garadacimab as a treatment every four weeks for patients with HAE-C1-INH. In a double-blind, placebo-controlled, phase 2 study, patients were recruited from 12 research centers in Canada, Germany, Israel, and the United States. Eligible patients were aged 18–65 years and must have had at least four attacks of any severity over a consecutive two-month period during the three months before screening or initiation of previous HAE prophylaxis. After a run-in period of four to eight weeks, patients were randomly assigned. They were then given an initial intravenous loading dose, and on day six and every four weeks for 12 weeks, they were given a subcutaneous dose of their allocated treatment. The primary endpoint was the number of monthly attacks in the intention-to-treat the population (defined as all patients who underwent screening, provided consent, and were assigned to treatment) during the 12-week subcutaneous administration period assessed in the 200 mg and 600 mg garadacimab groups versus placebo.

Garadacimab 200 mg and 600 mg every four weeks significantly reduced the number of monthly attacks versus placebo and was well tolerated during the study. Garadacimab is an efficacious, subcutaneous prophylaxis in patients with HAE-C1-INH and warrants phase 3 evaluation.
(Source: CSL Behring)

27 February 2022

BioCryst Pharmaceuticals, Inc. announces new long-term efficacy and safety data from the APeX-2 clinical trial evaluating oral, once-daily ORLADEYO™ (berotralstat) for the prophylactic treatment of HAE showing sustained reductions in attack rates and improvement in quality of life (QoL) among patients living with HAE, regardless of their baseline attack rates and initial responses to ORLADEYO™.

The data are being presented at the 2022 American Academy of Allergy, Asthma & Immunology (AAAAI) annual meeting.

"The long-term data from APeX-2 show that HAE patients in our clinical program had an experience consistent with what we are seeing commercially in the real world; that ORLADEYO™ provides noteworthy, sustained, consistent reductions in HAE attack rates that persist and maintain over time, resulting in meaningful quality of life improvements," says Dr. William Sheridan, chief medical officer of BioCryst.

"The 96-week data from APeX-2 showcase the durable, long-term efficacy of ORLADEYO™ and build on the strong reductions in attack rates that have previously been reported, with all patients experiencing an average of 94 percent attack-free days at Week 96. ORLADEYO™ can be an effective prophylactic therapy for HAE patients regardless of their baseline attack rate," says Dr. Emel Aygören-Pürsün, specialist in internal medicine at the division of oncology, hematology and hemostaseology at the department for children and adolescents of the University Hospital Frankfurt.

BioCryst AAAAI 2022 Presentation Highlights:
APeX-2 included 121 HAE patients who were randomized 1:1:1 to ORLADEYO™ 110 mg or 150 mg, or placebo, once daily for 24 weeks (part 1 of the study). At Week 24, patients on ORLADEYO™ continued on the same dose and placebo patients were re-randomized to ORLADEYO™ 110 mg or 150 mg for another 24 weeks (part 2 of the study). At Week 48 and thereafter, all patients continued on ORLADEYO™ 150 mg (open-label phase).

The 96-week safety and efficacy data were previously reported in July 2021. These additional analyses from APeX-2, as reported in the posters at AAAAI, evaluated the long-term efficacy of ORLADEYO™ 150 mg in patients who completed 96 weeks of treatment (n=21).

In APeX-2, ORLADEYO™ was safe and generally well tolerated, with no drug-related serious adverse events reported.

Sustained Reductions in HAE Attack Rates Observed over 96 Weeks of Oral Berotralstat Treatment Regardless of Initial Response:
This analysis stratified all 21 patients by their initial reduction in HAE attack rate from baseline to Week 24 in three groups: Group A (<50 percent attack rate reduction; n=4), Group B (≥50 percent attack rate reduction; n=17) and Group C (≥70 percent attack rate reduction; n=14). To note, Group C was a subset of Group B.

A sustained reduction in HAE attack rates was observed from baseline to Week 96 across all three groups of patients. Group A had a mean decrease of 2.3 attacks/month, Group B had a mean decrease of 2.5 attacks/month and Group C had a mean decrease of 2.6 attacks/month.

The percentage of attack-free days across all patients for the entire study duration (96 weeks) was 94 percent (88 percent, 96 percent and 96 percent in Groups A, B and C, respectively), demonstrating ORLADEYO™ is an effective oral HAE prophylactic treatment even in patients who may have a lower initial response.

Oral Berotralstat Treatment for 96 Weeks Consistently Reduces HAE Attack Rates Regardless of Baseline Attack Rate:
This analysis stratified all 21 patients based on baseline attack rate: Group 1 (<2 attacks/month; n=7), Group 2 (≥2 to <3 attacks/month; n=7) and Group 3 (≥3 attacks/month; n=7). A >80 percent reduction in mean attack rates was observed at Week 96 of treatment regardless of the patients' baseline attack rates (100 percent for Group 1, 90 percent for Group 2 and 82 percent for Group 3). At Week 96, median attack rates were 0.0 regardless of baseline attack rate. These data demonstrate ORLADEYO™ is an effective prophylactic therapy for patients with HAE regardless of baseline attack rate.

Sustained Improvement Observed in Patient-Reported Quality of Life (QoL) with 96 Weeks of Oral Berotralstat Treatment:
This analysis assessed the QoL of all 21 patients using the Angioedema Quality of Life Questionnaire (AE-QoL), a validated tool to measure QoL impairment in patients with recurrent angioedema. The minimal clinically important difference (MCID) was defined as a change of six points in total score. A mean of 77 percent of patients reported clinically meaningful improvements using the AE-QoL total scores (ranging from a high of 91 percent to a low of 62 percent over time), including improvements observed as early as Week 4, and at each time point through 96 weeks of treatment (improvement of 19.8, 18.3 and 23.0 points at Weeks 24, 48 and 96, respectively). The largest improvement was observed in the functioning domain with a mean improvement (SEM) of 33.4 (6.08) points at Week 96, suggesting patients reported less impairment in their day-to-day activities while on ORLADEYO™ 150 mg. The improvement in total AE-QoL scores and the percentage with an MCID in these long-term results show that patients continue to experience QoL improvements compared to baseline over time with ORLADEYO™.
(Source: BioCryst)

27 February 2022

In its fourth-quarter and full-year 2021 financial results **Intellia Therapeutics** states:

NTLA-2002 for HAE: NTLA-2002 leverages Intellia's proprietary in vivo LNP delivery technology to knock out the KLKB1 gene in the liver with the potential to permanently reduce total plasma kallikrein protein and activity, a key mediator of HAE. This investigational approach aims to prevent attacks for people living with HAE by providing continuous suppression of plasma kallikrein activity following a single dose and to eliminate the significant treatment burden associated with currently available HAE therapies.

- In December 2021, Intellia announced the first patient was dosed with NTLA-2002. The first-in-human study is expected to evaluate the safety, tolerability and activity of NTLA-2002 in adults with Type I or Type II HAE.
- The Company anticipates presenting interim data from the Phase 1/2 study in the second half of 2022. The data are expected to characterize the emerging safety and activity profile of NTLA-2002, and to potentially demonstrate preliminary proof of concept.

(Source: Intellia)

28 February 2022

At the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Scientific Meeting, **KalVista Pharmaceuticals, Inc.** presents data for its lead oral drug candidate, KVD900, in development for on-demand treatment of HAE. Data presentations included new data from the Phase 2 trial highlighting rapid suppression of plasma kallikrein activity after KVD900 administration and its relationship with symptomatic relief.

"These data from our phase 2 trial in on-demand use for HAE attacks show that oral KVD900 is quickly absorbed, leading to rapid, near-complete suppression of plasma kallikrein activity, a key mediator of HAE attacks," says Andrew Crockett, CEO of KalVista. "We believe that this rapid absorption followed by rapid suppression of plasma kallikrein activity is the basis for the early symptom relief we observed in the trial."

Poster #1: Rapid Plasma Kallikrein Inhibition Following Oral KVD900 is Associated with Early Symptom Relief in Patients with Hereditary Angioedema
- KVD900 was rapidly absorbed, reaching maximum plasma concentrations within 1 hour
- Plasma kallikrein activity was >80% inhibited within 15 minutes with near-complete inhibition (>95%) observed within 1 hour
- A significantly shorter median time (1.6 hrs.) to symptom relief was observed in patients receiving KDV900 compared with placebo (9 hrs.)

Poster #2: Agreement of Patient Global Impression of Change (PGI-C) with Attack Resolution or Use of Rescue Mediation in Patients with Hereditary Angioedema
- 113 HAE attacks were treated in a blinded manner with either KVD900 or placebo
- Symptom relief, as captured by improvement on the PGI-C, occurred in 72% of attacks within 24 hours, and among those only 16% of HAE attacks were associated with use of rescue medication, while approximately 60% achieved complete attack resolution without use of rescue
- Conversely, for the 28% of attacks where symptom relief was not achieved, 66% were associated with use of rescue medication and less than 4% achieved complete attack resolution without use of rescue
- PGI-C is an effective tool to monitor attack symptoms may be an early predictor of attack resolution in patients with HAE

(Source: KalVista)

2 March 2022

At the American Academy of Allergy, Asthma and Immunology (AAAAI) 78th Annual Meeting **Takeda** presents four abstracts including interim real-world data from the observational Phase 4 EMPOWER study of TAKHZYRO™ (lanadelumab) as a treatment for people with HAE Type I or II in North America, as well as findings from a post-hoc analysis of the HELP Open Label Extension study of long-term safety and efficacy of TAKHZYRO™ in HAE patients 12 years of age and older.

"A big challenge for HAE patients is the unpredictability of attacks and the impact that the attacks have on quality of life. We are encouraged by the initial results of the EMPOWER study, along with the additional evidence presented in the HELP Open Label Extension," says Associate Professor Paula Busse, MD, Division of Allergy and Clinical Immunology, Icahn School of Medicine at Mount Sinai in New York, NY, USA. "Data from both studies show that lanadelumab had marked reduction in attack rates, and that angioedema control was sustained for 12 months."

Key findings from the data presentations include:
- Improvements among new users and sustained outcomes in established users were reported in scores of the Angioedema Quality of Life Questionnaire (AE-QOL), Angioedema Control Test (AECT), and the Treatment Satisfaction Questionnaire for Medication (TSQM-9) when collected every three months, as presented in the EMPOWER IA2 Patient-Reported Outcomes interim data presentation.
- An average of 1 in 5 established TAKHZYRO™ users were able to extend treatment from every 2 weeks to 4 weeks as shown in interim data shared in the EMPOWER IA2 Treatment Patterns and Subgroups
- Interim real-world data showed marked attack rate reduction of 83% and no new safety signals based on patient self-reporting reduced attack rates in the EMPOWER IA2 Effectiveness and Safety
- A post-hoc analysis of HELP and HELP OLE showed that reduction of attack rates with TAKHZYRO™ were similar for patients previously on androgen treatments as they were for the wider treatment population in these studies in the Switch from Androgens to TAKHZYRO™ in HELP 03 and HELP 04.

"We are pleased to see the real-world data from EMPOWER show improvements in angioedema control and treatment satisfaction. These interim results provide a better understanding of the overall patient experience with TAKHZYRO™," says Neil Inhaber, MD,

Head, Rare Genetics and Hematology, Global Medical Affairs, Takeda. "With more than a decade of experience and innovation for patients with this devastating condition, Takeda remains committed to continuing our unwavering support for the HAE community."

The observational Phase 4 EMPOWER study, evaluating real-world HAE attack rates before and after treatment with TAKHZYRO™ in patients with HAE types I and II, is ongoing. Full results of the EMPOWER study are expected to be published in 2024. HELP OLE is a completed Phase 3 study of the safety and efficacy of TAKHZYRO™ in patients previously treated with androgens and other therapies for long-term prophylaxis prior to transitioning to TAKHZYRO™.
(Source: Takeda)

7 March 2022

KalVista Pharmaceuticals, Inc. announces the initiation of the Phase 3 KONFIDENT clinical trial evaluating the efficacy and safety of KVD900 as the first potential oral, on-demand therapy for HAE attacks. This worldwide, double-blind, placebo-controlled crossover trial will evaluate the efficacy of two dose levels of KVD900 compared to placebo in adolescents and adults experiencing acute HAE attacks. KVD900 is the most advanced potential oral on-demand therapy for HAE in clinical development and is intended to provide a substantial improvement over the current on-demand therapies for HAE attacks, which are all delivered by injection.

"Beginning the KONFIDENT trial represents a major milestone for us", says Andrew Crockett, CEO of KalVista. "We believe that KVD900 has the potential to transform the treatment paradigm for HAE patients experiencing acute attacks, whether they primarily treat with on-demand medications or use long-term prophylaxis. Based upon the results of our Phase 2 study released last year, we expect that KVD900 can provide patients with symptom relief as rapidly as existing therapies, but with an oral tablet that will allow earlier treatment of all patient-recognized HAE attacks. Our goal is to provide patients with the confidence that their attacks will be controlled in the earliest stages and without the associated treatment pain and other challenges of injectable therapies."

The Phase 3 KONFIDENT trial is a worldwide clinical study being conducted at approximately 60 sites in 20 countries. The trial is intended to enroll a minimum of 84 HAE adolescent and adult patients who will complete treatment of three attacks: one each with 300 mg KVD900, 600 mg KVD900 and placebo in a double-blinded, randomized sequence. The primary endpoint of the trial is time to the beginning of symptom relief, evaluated on a Patient Global Impression of Change (PGI-C) scale, and additional endpoints will evaluate other measures of patient response and attack progression, as well as safety. Patients will dose upon first recognition of an attack, and all attack types including laryngeal attacks will be eligible for treatment. Patients will be permitted to take an additional dose of investigational drug, if symptoms warrant, and will always have access to their conventional injectable therapy. Study participants also will be allowed to maintain their prophylaxis regimen if they were receiving one at study enrollment.

KalVista anticipates that data from KONFIDENT will be available in the second half of 2023.
(Source: KalVista)

11 March 2022

In a corporate update following the financial results for the fourth quarter and full-year ended 31 December 2021, **Astria Therapeutics, Inc.** CEO Jill C. Milne, Ph.D. says:

"We are excited to advance STAR-0215 to the clinic this year with the planned initiation of our Phase 1a study. STAR-0215 was created with a clear vision aimed at reducing the treatment burden for HAE patients with dosing once every three months or longer. Our goals for the Phase 1a trial are to evaluate safety and tolerability, demonstrate inhibition of plasma kallikrein activity, and establish the prolonged half-life of STAR-0215. We expect initial results from this trial by the end of this year."

Astria is on track to file an Investigational New Drug application for STAR-0215 in the middle of this year and plans to initiate a Phase 1a clinical trial shortly thereafter with initial results anticipated by year-end. The Phase 1a clinical trial is planned to be conducted in healthy volunteers and evaluate several single ascending dose cohorts with subcutaneous administration. The goals of this initial proof of concept trial are to demonstrate safety and tolerability, establish a prolonged half-life of STAR-0215, and demonstrate inhibition of plasma kallikrein activity. Astria plans to initiate a Phase 1b/2 trial in patients with HAE in 2023.
(Source: Astria)

16 March 2022

An agreement between **Takeda Global**, SingHealth in Singapore, Western Australia's King Edward Memorial Hospital, Curtin University, and FrontierSI will advance diagnosis and treatment monitoring for rare diseases, which globally impact more than 300 million people.

The study, funded by Takeda Pharmaceutical Asia-Pacific Medical Affairs in Rare Diseases, will enable researchers to analyze the facial features of HAE across Singapore and Western Australia.

It will ensure clinicians at SingHealth, Singapore's largest group of healthcare institutions, are trained to capture and analyze 3D facial images using Curtin University's Cliniface software platform. As a specialist hospital under SingHealth, KK Women's and Children's Hospital (KKH) will be adopting the technology to provide more targeted therapies and improve management outcomes among children diagnosed with HAE.

Currently, only subjective clinical descriptions of the nature of facial swelling in people with HAE exist. Giving clinicians an objective understanding of the facial swelling will help assess the onset of an attack, its severity, recovery, and treatment, potentially assisting with the initial diagnoses.

FrontierSI CEO Dr. Graeme Kernich welcomed the exciting development: "We have been working diligently with our partners Curtin University and WA's North Metropolitan Health Service (NMHS) to develop the Cliniface platform to deliver an equitable and accessible digital health solution and this ground-breaking research will ensure translation into clinical practice. Congratulations to the Cliniface team at Curtin University and NMHS, and the visionaries at Takeda and SingHealth for their collaboration and belief in this innovative global body of work."

Dr. Saumya Jamuar, Senior Consultant, Genetics Service at KKH and Head of SingHealth Duke-NUS Genomic Medicine Center, says: "As the first hospital in Singapore to adopt this, we are extending the vision KKH has set out 30 years ago to improve diagnostics with therapeutic options and outcomes for patients who have very rare conditions. If we can achieve these earlier in a patient's childhood, they and their family can enjoy a far better quality of life."

Cliniface and study clinical lead Professor Gareth Baynam, the Head of the Western Australian Register of Developmental Anomalies at King Edward Memorial Hospital, NMHS, says: "The agreement is exciting news. After years of trials using our Cliniface technology to demonstrate that we can produce reference statistics of 3D facial norms, we will expand this to include the Singapore population to support more advanced, accessible, and equitable diagnosis and monitoring of rare diseases in our Asia Pacific region. We look forward to collaborating with Takeda, SingHealth, and FrontierSI as we expand further internationally and for a broad range of rare diseases".

Dr. Dae Wook Lee, Head of medical portfolio management in APAC from Takeda, says: "It was our great pleasure and excitement for our first implementation of innovative digital 3D facial analytics in the Asia-Pacific region. The advancement of technology enables us to identify the distinctive features of a multi-ethnic population, which seeks to envision our patients and community of rare and complex genetic disorders with our core principle of patient-centricity. The agreement clearly displays a strong foundational and remarkable cross-border multi-national partnership between FrontierSI and SingHealth, which is only the beginning to undoubtedly larger accessibility to medical professionals treating rare and complex diseases with emerging trends of digitalization in healthcare."

Computer scientist Dr. Richard Palmer, from Curtin University's School of Earth and Planetary Sciences, who developed the Cliniface technology, said the 3D facial images of 900 people would be processed through the Cliniface platform, extracting more than 50 facial measurements from each image: "The resulting de-identified data will be transmitted from SingHealth to the Cliniface team at Curtin University for analysis, allowing us to generate modeling that outlines facial features specific to the Singapore population. By working together, we will expand our understanding of the facial features of this rare genetic disorder with the ultimate aim of potentially making it easier for

clinicians to treat patients and ultimately improve the lives of people living with HAE."
(Source: Curtin University/Takeda)

17 March 2022

At the presentation of the **Pharming Group N.V.** preliminary (unaudited) financial report for the full year ended 31 December 2021, CEO Sijmen de Vries says:

"2021 marked the beginning of an important period in Pharming's development. The strength of our commercial business, which we continued to build on during the year through the reimbursement of Ruconest® in new markets and expanding the reach of the product through new licensing agreements, has enabled us to increase our investment in long-term growth to achieve a number of additional strategic goals. Also, we were able to make an upfront payment for an investigational gene therapy for the potentially curative treatment of HAE, OTL-105. This product leverages our significant in-house expertise in HAE as we remain focused on driving research and development of specialist products through our existing business and through further in-licensing and acquisition opportunities."

Operational highlights - Ruconest®

- Reimbursement of Ruconest® (recombinant human C1 esterase inhibitor, or "rhC1INH") agreed with the Spanish Ministry of Health for the treatment of acute HAE attacks in Spain.
- Exclusive license agreement signed with NewBridge Pharmaceuticals for the distribution of Ruconest® in the Middle East and North Africa.
- Renewed strategic manufacturing partnership with Sanofi. Extended five-year contract, with options for extension, ensures the continuation of the downstream processing in the production of Ruconest®.

Earlier stage pipeline - OTL-105

- Strategic collaboration with Orchard Therapeutics, a global gene therapy leader, to research, develop, manufacture, and commercialize OTL-105, an investigational ex-vivo autologous hematopoietic stem cell (HSC) gene therapy for the treatment of HAE.

(Source: Pharming)

17 March 2022

Ionis Pharmaceuticals, Inc. announces the publication of positive Phase 2 data for donidalorsen (formerly IONIS-PKK-LRx) in the New England Journal of Medicine. Donidalorsen is an investigational antisense medicine Ionis is evaluating for treating patients with HAE. In the Phase 2 study, donidalorsen demonstrated a 90% reduction in angioedema attacks compared with placebo at the 80 mg monthly dose. There was significant improvement in quality of life as assessed by the Angioedema Quality of Life Questionnaire (AE-QoL) in the patients treated with donidalorsen.

Donidalorsen is designed to reduce the production of prekallikrein, which plays a key role in the activation of inflammatory mediators associated with acute attacks of HAE. Donidalorsen uses Ionis' advanced LIgand-Conjugated Antisense (LICA) technology platform.

"Positive Phase 2 data demonstrate that treatment with donidalorsen reduced attack frequency and disease burden of HAE," says Kenneth Newman, M.D., M.B.A., Ionis' Vice-President of Clinical Development: "The promising findings from this study are particularly encouraging as we continue to advance the Phase 3 clinical study for donidalorsen and underscore our commitment to deliver transformative treatments for patients with unmet therapeutic needs."

Patients reported higher overall health-related quality of life (HRQoL) over 17 weeks with donidalorsen. There were improvements observed across all individual domains of the AE-QoL compared with placebo.

The majority of adverse events during the study were mild with a frequency that was similar between patients receiving donidalorsen and placebo groups.
(Source: Ionis)

22 March 2022

KalVista Pharmaceuticals, Inc. announces the publication of new data in Clinical & Experimental Allergy characterizing KVD900, a novel, potent and selective oral inhibitor of plasma kallikrein, a critical mediator of attacks in patients with HAE. In this new publication, orally administered KVD900 was shown to be quickly absorbed and provided rapid and near-complete inhibition of plasma kallikrein and strong suppression of kallikrein-kinin system activation in patients with HAE.

"Based on these results, on-demand administration of KVD900 is further demonstrated to block the generation of plasma kallikrein and bradykinin in HAE patient plasma and thereby may provide an opportunity to halt and reverse HAE attacks," says Andrew Crockett, CEO of KalVista. "These data provide the underlying basis for the clinical results we reported for our phase 2 trial of KVD900 in on-demand treatment of HAE attacks, and further support our ongoing phase 3 KONFIDENT trial for KVD900 in the same indication."
(Source: KalVista)

23 March 2022

Pharvaris publishes pharmacological data for the novel small molecule bradykinin B2-receptor antagonist PHA121 and its active metabolite PHA-022484, in *International Immunopharmacology*.

The preclinical data demonstrate PHA121 specificity and potency for both recombinant and endogenous B2 receptor, including 20-fold higher potency than icatibant, an approved injectable B2-receptor antagonist. Relative to icatibant, PHA121 exhibited improved intrinsic clearance, which predicted the improved in vivo half-life and oral bioavailability seen in clinical studies to date. This novel small molecule bradykinin B2 receptor antagonist is in clinical development for the treatment and prevention of hereditary angioedema attacks. Early clinical data in healthy participants indicate that PHA121 is orally bioavailable, with rapid absorption, favorable pharmacokinetics, and good tolerance.

"To our knowledge, PHA121 is the most potent, and the only oral, small-molecule human bradykinin B2 receptor antagonist that has ever been reported," says Anne Lesage, Ph.D., Chief Early Development Officer of Pharvaris and lead author on the publication. "PHA121 acts as a selective and competitive antagonist of the bradykinin B2 receptor, blocking the effect of elevated bradykinin levels that lead to angioedema. This specificity is shown through large margins of inhibition at other targets. Its high potency allows for oral administration with a small dose and supports Pharvaris' development of this compound for on-demand and prophylactic treatment of HAE."

The dataset demonstrates the in vitro pharmacological characteristics of PHA121 and its active metabolite, PHA-022484. Both compounds show high affinity for the recombinant human bradykinin B2 receptor. In contractility assays, both PHA121 and PHA-022484 demonstrate potent and reversible B2 antagonist activity. The data support a high degree of selectivity over a wide range of molecular targets, including the bradykinin B1 receptor.
(Source: Pharvaris)

HAEi AROUND THE WORLD

Currently there are HAE member organizations in **93** countries. You will find a great deal of vital information on the HAE representations around the globe at **haei.org** – and the world map will provide you with contact information for the member organizations as well as ACARE centers, hospitals, physicians, and available medication.

The information on **haei.org** is being updated as soon as HAEi receives fresh data from the national member organizations.