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Global perspectives:

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93 Member countries

Global perspectives:

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Cover photo
HAEi Youngsters visiting the National Civil Rights Museum during the 2019 Global HAE youth advocacy workshop in Atlanta, USA.

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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 HAE INTERNATIONAL FRIENDS,

Welcome to the first 2021 edition of *Global Perspectives*. The extraordinary spirit and "can do" attitude of our global community remains evident as HAEi member organizations continue to make remarkable progress, despite the ongoing challenges posed by COVID-19 restrictions. Also, as you will read in the pages that follow, our Regional Patient Advocates (RPAs) continue to implement HAEi's vision of a decentralized yet globally connected network by establishing Regional Advisory Groups and Regional Medical Advisory Panels. These initiatives are focused on encouraging information sharing, collaboration, and dissemination of effective and practical solutions to help member organizations expedite improving diagnosis and obtaining access to modern HAE medicines.

2021 marks the 10th Anniversary of **hae day :-)** and HAEi has developed a fun and creative campaign for celebrating this important milestone. Consistent with the theme of 'Let's Take the Next Step,' HAEi will ask our friends from all over the globe to take part in and record (on haeday.org) time spent performing physical or well-being activities. All recorded activities will be converted into steps to support a virtual walk across the HAEi regions to visit with and learn about our individual member organizations.

Our contacts with member organizations revealed the need for a secure, user-friendly app that can be used to track attacks, treatments, emergency room visits and document how HAE affects quality of life. We are excited to announce the forthcoming launch of TrackR, an app for patients, designed by patients, that fulfills the requirements requested by our member organizations. Importantly, TrackR strictly protects patient privacy, is EU-GDPR compliant, and enables data sharing with a physician. We will announce the TrackR rollout on our social media platforms within the next several weeks.

Survey data we have gathered over the years reveals a critical need for significant improvement in emergency room care for people with HAE. Education is clearly the key to upgrading emergency care, and that is why HAEi has prepared a poster with important information that a doctor must know to successfully treat an HAE emergency. The posters can be brought to local emergency rooms where they can be displayed in a prominent location. See more on how to obtain posters for your country in this magazine.

Finally, we are pleased to announce the 2021 HAEi Virtual Regional Workshop for South America, Mexico, Central America and the Caribbean. The workshop has four tracks that include the international perspective, informative lectures by expert HAE physicians, youngster programs, and member organizations' updates. All videos will be offered in the presenter's local language, with subtitles in Spanish, Portuguese, and English. We look forward to a very successful event in this important part of the HAEi global network.

Wishing all in our global community the very best and look forward to meeting in person again, hopefully in the very near future.

Warmest regards and please stay safe,

Tony

Anthony J. Castaldo
President & CEO, HAEi

IN THIS ISSUE OF GLOBAL PERSPECTIVES

NEWS FROM THE HAEi REGIONAL PATIENT ADVOCATES

What a busy start to the year! There has been a lot of hard work going on behind the scenes with the Regional Patient Advocates (RPAs) and HAEi staff, and we look forward to bringing new and exciting projects and initiatives to our member organizations.

Last year HAEi held two virtual regional workshops, and now we launch a third workshop , this time for Latin America. The 2021 HAEi Virtual Regional Workshop South America & Mexico, Central America & Caribbean features presentations from local expert physicians, member organizations, HAEi, including the two RPAs for South America and Mexico, and Central America and the Caribbean. We are planning a fourth virtual workshop to take place later in the year, focusing on the Middle East, North Africa, and Sub Sahara Africa. Stay tuned for more details.

The RPAs have also been extending invitations and information to the Regional Medical Advisory Panel's nominated by our member organizations. We are planning the first meeting to take place very soon.

The **hae day :-)** campaign 'Let's Take the Next Steps' has been a significant focus for the RPAs. They have been working with their member organizations to collect country specific information that will be showcased on the haeday.org website.

Exciting, busy, and innovative times ahead.

Fiona Wardman
Chief Regional Patient Advocate

MICHAL RUTKOWSKI
CENTRAL EASTERN EUROPE, BENELUX AND MIDDLE EAST

The recent months have been busy with plenty of advocacy activities for patients in Central Eastern Europe, Benelux and the Middle East. This period was full of virtual meetings with member organizations, both individual and group, during which we discussed important projects delivered and implemented by HAEi. It is truly amazing to be part of the activities that involve patient organizations, patients, caregivers and physicians from so many countries.

An important element of the HAEi strategy, related to the decentralization of our activities, is the formation of the Regional Medical Advisory Panels in each of the regions supported and covered by the global organization. I am delighted to inform you that thanks to the intensified activities, it was possible to invite and confirm the participation of many expert HAE specialists in the Regional Medical Advisory Panel for Central Eastern Europe, Benelux and Middle East. We expect to have inaugural meetings very soon.

In addition to various virtual meetings, I am constantly working on implementing HAEi resources and projects so that each patient has access to the latest information regarding HAE. Also, we have taken the first steps related to the preparations of a website dedicated to the Middle East and North Africa regions and the organization of the 2021 HAEi Virtual Regional Workshops for the Middle East, North and Sub Sahara Africa. In these two projects, I enjoy working with my colleagues Maria Ferron and Patricia Karani.

I am happy to announce that HAE **Jordan** has joined HAEi as member number 93. Mr. Bassam Mohammad Alelimat represents the organization. Just after entering the global organization, HAE Jordan launched its website hosted by HAEi.

In a joint effort with HAE **Belarus**, the first modern therapy (plasma-derived C1-INH) for HAE patients has been registered in Belarus. Furthermore, the president of HAE Belarus, Irina Ausianik, presented the patients' perspective during a virtual conference organized by Takeda in February 2021. The conference was dedicated to health care professionals from Belarus, **Kazakhstan** and **Ukraine**.

In collaboration, HAE Kazakhstan and Takeda have set up the diagnosing program for HAE patients in the country. Also, the process of C1-INH registration is about to take place, and HAE Kazakhstan hopes it will soon have the medication registered. Also, HAE Kazakhstan has organized a successful virtual meeting for HAE patients.

HAE **Lithuania** is the first member organization from Central and Eastern Europe to implement the HAEi Emergency Room Poster. The poster was translated into Lithuanian, and HAEi covered the costs of production.

HAE **Egypt** has taken steps to support the registration of plasma-derived C1-INH, the first HAE therapy in the country for people living with HAE. Supported by HAEi, the organization has sent an official letter to the Egyptian Ministry of Health, H.E. Dr. Hala Zayed, emphasizing how important access to modern treatment options is for HAE patients.

And finally, some excellent news from HAE **United Arab Emirates**: Thanks to the involvement of the member organization, local health care professionals, the hospital, CSL Behring and myself, it was after months of shortages possible to deliver plasma-derived C1-INH to the Mediclinic City Hospital in Dubai.

MARIA FERRON
MEDITERRANEAN, NORTH AFRICA AND BRITISH ISLES

Initially, I am happy to inform you that the HAEi Emergency Room poster is now translated into Spanish, French and Arabic.

On 5 December 2020, HAE **Portugal** (ADAH) held its annual meeting, this time in a virtual format. Around 45 participants took part, and Raquel Oliveira, the President of HAE Brazil (Abranghe) and I were invited as speakers. After a word of welcome from President Ines Pessoa, there was a scientific update with Professor Branco as moderator. Here four Portuguese doctors talked about updates on new HAE forms, diagnosis and clinical manifestations, long and short terms therapies, as well as new therapies and questionnaire results on Quality of Life. Then followed a presentation from Raquel Oliveira on the current Brazilian situation while I, among other things, presented some of the HAEi resources available to the member organizations. Ines Pessoa gave some ADAH data and updates of which we can highlight these: There are an estimated 205 people with HAE in Portugal, 40 members of ADAH and 30 hospitals with HAE modern treatment. Furthermore, the annual meeting included a presentation on self-administration. Here one of the nurses dealing with HAE gave feedback on self-administration using a video to show how to do it.

HAE **France** is in the initial phase of having its website hosted under the HAEi umbrella.

HAE **Algeria** has been quite active regarding visiting the Ministry of Health to create HAE awareness and try to improve HAE patients' lives. The local authorities are now looking into the possibility of registering HAE modern treatment in the country. In February, HAE Algeria was on tv and radio and in newspapers to talk about HAE; this included some interviews with HAE patients.

Speaking of North Africa: I am still looking for some local contacts for pharmaceutical companies. Hopefully, I will have good news on this soon.

FERNANDA DE OLIVEIRA MARTINS
SOUTH AMERICA AND MEXICO

Over the past few months, I have been working with the member organizations in my region and informing them about new resources like the Emergency Room Poster and the new **HAE TrackR** app.

There has been a lot of work and communications on collecting information for the **hae day :-)** 10th anniversary campaign.

HAEi Connect is currently being rolled out in **Colombia** and **Peru.**

Most recently, I have been organizing and co-ordinating presentations and recordings for the first virtual regional meeting in Latin America. I have also been creating the scripts and timed transcripts for the videos as they will be available in Spanish, Portuguese and English. Each video needs to be checked for errors, and this process takes many hours.

Since the most recent issue of *Global Perspectives*, there have been many Instagram posts uploaded on the South American and **Mexico** Instagram page.

JØRN SCHULTZ-BOYSEN
NORDICS, GERMANY, AUSTRIA AND SWITZERLAND

It has been a pleasure starting as the Regional Patient Advocate for the Nordics and Germany, Austria and Switzerland. It is fantastic to meet – mostly online – with many of the member organizations' representatives as there are so many things to talk about. And not least for me to learn from these amazing people.

We have had some very nice and tangible successes. The emergency card has now been translated to German, covering **Germany**, **Austria** and **Switzerland**. Also, it has been translated to the national languages in **Finland, Sweden**, **Norway** and **Denmark.** Once the world will open more up again, and we can start to travel, this will undoubtedly be beneficial to HAE patients and their families. Also, the HAE Companion app holds these new translations to make it even easier to bring along the emergency cards on your trips.

The Finnish website is in the middle of the migration to the HAEi hosted environment. In Austria, the first steps have been taken to this as well.

The regional meetings in Norway, Sweden and Denmark are currently being planned as online meetings instead of physical ones.

And like last time, a callout: if you are a patient, caregiver or physician treating HAE patients in **Iceland**, the **Faroe Islands** or **Greenland** and would like to get in touch, please do not hesitate to reach out to me. It would be great to connect with you.

JAVIER SANTANA
CENTRAL AMERICA AND CARIBBEAN

I participated in an interview with Dr. Olga Barrera in **Panama** for a national newspaper to highlight HAE patients' situation in the country.

In **Puerto Rico**, I have had several communications with Dr. Rafael Zaragoza, representatives of pharmaceutical companies, lawmakers, and legislative advisers about the reconsideration of the law that would give HAE patients access to treatment through the government's public health insurance.

During the past few months, I have also been working with my member organizations and doctors in the region on the 2021 virtual conference project for Latin America, with recording videos and developing scripts and transcripts and checking videos. Furthermore, I have provided videos for the introductions for the presentations.

I wrote a letter to the Ministry of Health in **Costa Rica** in support of patients gaining access to treatments following the decision to reject drugs for HAE patients because treatments were not approved in other countries. I worked with the patients on media training and interviews to highlight the issue.

I have been in communication with a new doctor from the **Dominican Republic** who treats patients with HAE and is willing to help identify more patients in the country and ensure that treatments are registered in the future.

I am working with my member organizations on media training and have provided a list of the most important media contacts in their countries.

There have been some communications with CSL Behring Latin America, who informed me that the pharmacy is taking steps to enter its treatments for HAE in Panama and Costa Rica.

It should be noted that many countries are still in lockdown due to COVID-19, which is why it has made it difficult for the leaders of the member organizations to hold events, including being able to attend their medical appointments. Let's hope in God that these challenges end soon.

PATRICIA KARANI
SUB SAHARA AFRICA

In **Ghana**, we have been able to start discussions on HAE with the Immunology Society of Ghana (ISG). We have also been able to liaise with Rare Disease Ghana for purposes of raising awareness amongst the general public.

We have established new doctor contacts in **Tanzania**. We are in the process of holding further discussions as regards HAE awareness and how we can improve HAE knowledge amongst the health care professionals and the general public.

In **Kenya**, we are now working on spreading HAE awareness around the different major referral hospitals through doctor webinars. I have presented on HAE and started ongoing conversations with the National Council of Persons Living with Disability (NCPWD) as a way of ensuring that HAE being a debilitating condition is included in being supported as a disability. I have also presented on HAE as a speaker at the Africa Health Agenda International Conference (AHAIC) hosted in Kenya by AMREF and officially opened by the President of the Republic of Kenya as regards driving momentum to achieve Universal Health Coverage (UHC) in Africa. Rare diseases were given a platform to discuss their challenges and call for inclusivity in the UHC campaign for Africa.

Furthermore, in **Lesotho**, we have established an awareness campaign through the Rare Disease Lesotho group who have shared HAE awareness materials on their platforms, which has elicited a good public response.

In **South Africa**, we have introduced the Brady Club activity book for the youngsters. This is a wonderful publication that assists kids to better understand HAE and how to manage themselves better. It also provides an opportunity to engage in fun activities and games for youngsters.

NATASA ANGJELESKA
SOUTH EASTERN EUROPE

In the course of December 2020 and January 2021, I held online meetings with patient representatives from **Montenegro**, **Greece**, **Albania** and **Bosnia and Herzegovina**. Some of the patients wanted to hear details about the vaccines for COVID-19 because they feel insecure about the safety of people with HAE. I have re-shared the link to the video of Professor Marcus Maurer, as well as explained the official advice issued from HAEi regarding vaccination.

The University Clinic of Respiratory and Allergic Diseases in Golnik has become the first ACARE Center in **Slovenia**.

In February, I used a great deal of my time in communication with member organizations in my region regarding the **hae day :-)** anniversary initiative.

I was engaged in planning an event to mark Rare Disease Day in **North Macedonia**. I gave an interview about the situation of rare disease patients' care and access to therapies for a Macedonian Information Agency that was published on 28 February. Also, I have been invited to an official event organized by the Prime Minister and the Minister of Health of the Republic of North Macedonia. We discussed the present situation and our demands and challenges as patients with rare diseases and had a chance to present our suggestions for improvement of the overall conditions and quality of life of patients, caregivers and families.

I was engaged with the HAE Macedonia team, Natasha Jovanovska Popovska and Verce Jovanovska Jankovska and initiated negotiations on getting prophylactic subcutaneous treatment in two youngsters who are dealing with frequent attacks.

On 28 February, I had a presentation entitled "Act locally, think globally" at the patient meeting organized by HAE **Serbia** on the occasion of the organization's fifth anniversary. I was asked to present different treatment options across countries in South Eastern Europe and discussed some of the challenges of HAE patients and their family members. Furthermore, I highlighted the part of the HAEi website where information and video discussions about HAE and COVID-19 (including vaccination) are posted. I also presented the HAEi Advocacy Academy opportunities via online courses and encouraged patients to start using the HAE Companion app. I also talked about the brand new **HAE TrackR** app that will hopefully replace the paper documentation that patients are using to track their attacks.

FIONA WARDMAN
ASIA PACIFIC

During the past few months, I have been working with member organizations in my region to nominate physicians for the Regional Medical Advisory Panel (RMAP) project. I am pleased with the confirmation from the nominated doctors who have accepted to be panelists. I look forward to holding the first RMAP meeting in the next few weeks.

In late December 2020, I presented 'International experience on emergency management of larynx edema caused by Hereditary Angioedema' during a webinar in **China** to help patients and physicians understand the severity of swelling of the throat and face. The Chinese Organization for Rare Disorders (CORD) and HAE China coordinated the webinar.

I have been assisting HAE **Taiwan** with the emergency department poster and emergency cards translated with Dr. Shyur and Takeda's assistance. The patients in Taiwan now have access to icatibant and have had a training session on administration.

Awareness of HAE is low in **Singapore**, and not many patients have been diagnosed or are not in touch with other patients. The head of the member organization and I have been working on her story to be shared with the Rare Disorders Singapore Society (RDSS) on their website and social media to help locate more patients in this country.

Together with HAE **India**, we have held two informal Zoom meetups with patients and doctors. These meetups are an excellent way for patients and their family members to learn more about HAE and ask questions in a supportive environment. For the February meet-up, we had a guest – Arouba, a mental health therapist and counsellor. Arouba also has a rare disease and gave practical advice and answered questions from the group. We will continue to hold virtual meetups each month.

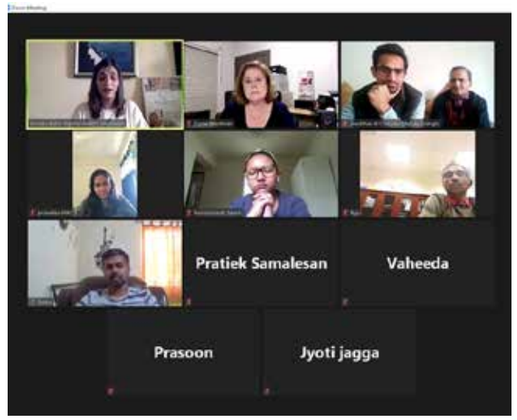
Dr. Jindal Ankur from the Post Graduate Institute of Medical Education & Research in Chandigarh, India, has created and registered a Physicians Association to assist with HAE education and awareness in India.

The Ministry of Health and Welfare in **South Korea** has expanded reimbursement for HAE patients to have two vials of icatibant. Previously patients were only allowed one prefilled syringe at a time for self-administration.

I have been working with HAE **Japan** on a webinar on HAE with Normal C1. We hope this webinar will answer a lot of questions that patients and physicians may have.

I contributed to a paper on 'Mitigating Disparity in Health-care Resources Between Countries for Management of Hereditary Angioedema'. This paper has been accepted and will be published soon.

I have been working with the member organizations on submitting their information for the 2021 **hae day :-)** campaign 'Let's Take the Next Step'.



10 YEAR ANNIVERSARY OF GLOBAL HAE AWARENESS DAY

16 May 2021 marks the 10th anniversary of the **hae day :-)** awareness day. For the last ten years, HAEi and its member organizations worldwide have used 16 May as a focus for raising awareness: not just on the day itself but in the weeks leading up to it.

Let's Take the Next Step

"We want to celebrate this anniversary with a special campaign to recognize the work of our HAE Community over the last ten years. The theme of our 10th anniversary campaign is 'Let's Take the Next Step'.

We're looking back at HAE community achievements over the past ten years and shining a light on what we want to achieve through the power of advocacy in the future. There has been lots of positive progress, but there is still a long way to go before reaching our goals of improved time to diagnosis and consistent access to lifesaving therapies for everyone with HAE around the world. Our work is far from over!", says HAEi Operations Manager Nevena Tsutsumanova.

The campaign launches on 1 April with the activity challenge of stepping around the world in time for **hae day :-)** on 16 May 2021.

Take part in physical and wellbeing activities

"We are asking HAE friends all over the globe to take part in physical or wellbeing activities and regularly record the time you spend on each activity, on our campaign website at haeday.org. Any and all activity reported here will be converted into steps. Our goal is to generate enough steps for a virtual walk that will take us to all the HAEi regions, where our member organizations will showcase their history, achievements and hopes for the future", HAEi Chief Specialist Projects and Research Deborah Corcoran explains:

"We are taking a walk around the world, and we are doing this via participation in lots of different activities both physical and wellbeing focused, not only walking. People with HAE know that stress is a trigger for attacks, which is why staying healthy both mentally and physically can help managing HAE. We're also very aware that we continue to live with restrictions to help manage the COVID-19 pandemic, so we are encouraging participation in activities that can be done both outside and inside."

Whether you are able to be out walking, running or cycling, or you have recently started following online workout classes, or you are reading, meditating or just find yourself pottering around the garden a bit more, you can enter the time for this activity.

Regularly adding activities is important

"Adding your activities to haeday.org regularly is really important as this is what will help us visit our regions and member organizations. When we get to each region, everyone will be able to read more about the HAEi member organizations in that region. For example, what are their success stories, achievements, proudest moments as a community and what are their hopes for the future of HAE – as well as some fun information about their country. This will be in both English and local language. You'll also get to hear from our Regional Patient Advocates and, hopefully, HAEi if we make it around the world in time for **hae day :-)** 2021", Deborah Corcoran explains.

Updated campaign website

The updated haeday.org website has lots of helpful information about the campaign, inspiration for activities and how you can get involved. As you add your activities to the website, you can share pictures of what you are doing on **hae day : -)** 2021. If you also share these via your social media channels, using the hashtags #active4hae and #haeday10 others will be able to find you.

"To make activity entering easier, we have introduced the option to create a profile on haeday.org. If you create a profile, you have the chance to earn our limited-edition regional badges, one for each region where you enter an activity. Your profile will show a clear overview of all your activities entered and badges earned. For those of you who don't want to create a profile but still want to enter activities and take part in the challenge, don't worry, you can still do that on haeday.org", says Nevena Tsutsumanova.

Let's Take the Next Step for HAE advocacy and see what we can achieve when we work together for people with HAE across the globe – Let's Take the Next Step together!

Prophylaxis therapies can lead to significant improvements in quality of life

According to HAEi President & CEO Anthony J. Castaldo, "A study of HAE medicines published by a group of economists who receive funding from the insurance industry concluded that new preventive HAE medicines are not cost-effective. The US HAE Association and HAEi joined forces in questioning the methods and conclusions of this analysis and responded by initiating a comprehensive study to assess both on-demand treatment and use of the new preventative medicines in the real-world. Although the focus is on the new preventative medicines, we wanted to make sure to also look at cost and quality of life impact of using on-demand–only medications."

Almost 750 people with HAE participated in the study and the results point to a high cost and quality of life burden of HAE treatment with on-demand only therapy. The real-world data also reveals that the new preventive therapies can deliver (1) remarkable decreases in attack frequency and (2) statistically significant and clinically relevant improvements in patient quality of life. After an extensive peer review, the study 'Assessing the cost and quality-of-life impact of on-demand-only medications for adults with hereditary angioedema' is now published and available in print and free online at http://bit.ly/improve_QoL.

Co-authors Anthony J. Castaldo, Deborah Corcoran, Henrik Balle Boysen from HAEi, Christian Jervelund from Copenhagen Economics, along with Bruce L. Zuraw and Sandra C. Christiansen from the Department of Medicine at the University of California San Diego, noted that, "Novel subcutaneous prophylactic therapies are transforming the treatment landscape of HAE. Although questions are being raised about their cost, little attention has been paid to the cost and quality of life impact of using on-demand-only medications. Therefore, we decided to assess the overall economic burden of on-demand-only treatment for HAE and compare patient quality of life with patients who received novel subcutaneous prophylactic therapies."

For the study, members of the US HAEA were invited to complete an anonymous online survey to profile attack frequency, treatment use, and the presence of comorbidities as well as economic and socioeconomic variables. The authors modelled on-demand treatment costs by using net pricing of medications in 2018, indirect patient and caregiver costs, and attack-related direct billed costs for emergency department admissions, physician office visits, and/or hospitalizations. Quality of life was assessed by using the Angioedema Quality of Life questionnaire.

The study shows that per patient/year, direct costs associated with modeled on-demand-only treatment totalled 363,795 USD, with additional indirect socioeconomic costs of 52,576 USD per patient/year. The most significant improvement in quality of life was seen in patients who used novel subcutaneous prophylactic therapies, as there was a 59.5 percent improvement in median impairment scores versus on-demand-only treatment. In addition, patients who used novel subcutaneous prophylactic therapies reported a 77 percent reduction in the number of attacks each year compared with those who used on-demand-only treatment.

The authors concluded that the use of novel subcutaneous prophylaxis can lead to sizeable reductions in attack frequency and statistically significant and clinically relevant improvements in quality of life. In addition, the study noted that these data could be useful to clinicians and patients as they consider therapy options.

The study 'Assessing the cost and quality-of-life impact of on-demand-only medications for adults with hereditary angioedema' is available in print and free online at http://bit.ly/improve_QoL

HAEi launches new app – by patients, for patients

Very soon HAEi will launch an app by patients, for patients. The name of the new app is **HAE TrackR** and that is just what it is: An easy way for people with HAE to track their condition, their attacks, and their treatments.

"Many HAE friends around the globe have encouraged us to introduce an app with an electronic diary to support people with HAE – no matter where they are, what medication they have access to and what kind of electronic device they are using. This has led to the design of **HAE TrackR**. While providing both patients and physicians with a better decision foundation for planning the management of the individual's HAE, the app still protects the privacy and data of the user. We believe this will be an extremely valuable help for men and women with HAE", says Henrik Balle Boysen, the HAEi Executive Vice President & Chief Operating Officer.

HAE TrackR will not only help users keep track of their HAE attacks with and without treatment. HAEi's Enterprise Technology Manager Ole Frølich explains:

"In addition, the app helps the user keep track of prophylactic treatment just as it gathers useful data that can be shared with the physician or other health care professionals. It is important to note that the data gathered by the app is the sole property of the user and only to be shared if he or she decides so. Furthermore, **HAE TrackR** has been designed by patients for patients with an emphazis on protecting the privacy of the users data.

"Both Apple's App Store and Google Play will have the app available for download. Furtermore, **HAE TrackR** can be accessed from it´s own website haetrackr.org, allowing the user to also open **HAE TrackR** from their computer."

In the words of HAEi's President & CEO Anthony J. Castaldo:

"**HAE TrackR** brings a new and very exciting tool to our global HAE community. The data stored in the app provides all the information the patient and physician needs to create an individualized HAE management plan."

Read more about the EU-GDPR compliant app at haei.org/apps

REGIONAL ADVISORY GROUPS DEFINE THEIR TOP 5 CHALLENGES

Last year the Regional Patient Advocates rolled out a new HAEi initiative called Regional Advisory Groups (RAGs) in each of the regions they represent.

The initiative followed an unanimous vote by the HAEi General Assembly during the 2018 HAE Global Conference in Vienna, Austria where it was resolved to broaden HAEi Governance participation by establishing the RAGs. This initiative is a key component of the decentralized approach to advocacy and support that HAEi has adopted.

The decentralized approach means that HAEi can focus on each country and region's specific needs more precisely.

The RAGs are made up of patients or family members from each member organization who the member organization nominated as the Advisor for their country. The appointed Advisor from each member organization meets several times a year with their Regional Patient Advocate to discuss each country and region's challenges and unmet needs. The information and outcomes from these meetings provide the HAEi Leadership with the basis for adjusting existing programs and services or establishing new projects and initiatives to best serve the needs expressed by the Advisors.

"The HAEi's global footprint has grown substantially through the work of our Regional Patient Advocates. This growth, achieved in a short amount of time highlights the importance and need for useful and meaningful tools and resources to assist our member organizations to best serve their patient community", says Fiona Wardman, HAEi Chief Regional Patient Advocate.

It is not surprising that there were five unmet needs and challenges consistently identified by all of the RAGs.

HAEi plans to hold the next Regional Advisory Group meeting in the coming months.

TOP 5 CHALLENGES

1. Lengthy time to diagnosis
2. No modern treatment access or home therapy
3. Lack of HAE awareness
4. Motivating patients and care givers
5. Lack of resources

HAEi establishes Regional Medical Advisory Panels

The HAEi Regional Medical Advisory Panel initiative is the next step in a decentralized approach to serve the global HAE community. The objective of the Regional Medical Advisory Panels (RMAP) is to obtain the physician viewpoint regarding challenges that countries (within a region) are facing in terms of diagnosis, education, awareness, and access to modern treatments. HAEi's member organizations will work with their Regional Patient Advocate (RPA) to nominate physicians to be part of RMAPs.

Each RMAP will gather physicians' perspectives on circumstances and unique needs in their country and region and share this information with the member organizations and RPAs.

"This important initiative will enable us to adapt HAEi's existing programs, activities, and services, and implement new ones to address the local and regional issues and concerns raised by the Regional Medical Advisory Panels," says Fiona Wardman, HAEi's Chief Regional Patient Advocate.

"Once a RMAP has been established, a chairperson is appointed, and every panel member is encouraged to collaborate, network, share information, and exchange ideas", Fiona Wardman explains.

Each RMAP will meet twice a year via Zoom or teleconference with the RPA to organize and take part in the call to take minutes.

"Furthermore, the RMAPs will have an opportunity to meet and interact with the HAEi Regional Advisory Groups and RPAs during our regional conferences and the HAEi Global Leadership Workshops", Fiona Wardman says.

Additionally, Advisors will have access to the HAEi's Chief Medical Advisor, and the global organization encourages each Advisor's clinic/hospital to become an accredited ACARE Center.

Launch of third virtual regional workshop

After the successful virtual regional workshops in South Eastern Europe and Central Eastern Europe and Benelux, HAEi is now focused on Latin America.

"The Latin American workshop is the first one for this region where the working language is the presenters' local language. The workshop brings together the Regional Patient Advocates Fernanda de Oliveira Martins from South America & Mexico and Javier Santana from Central America & Caribbean", says HAEi Chief Regional Patient Advocate Fiona Wardman.

The workshop features 34 videos in the presenter's local language with subtitles in Spanish, Portuguese, and English.

The workshop is divided into four tracks: HAEi, Experts, Youngsters, and updates from the member organizations.

The workshop begins with brief introductions from HAEi Leadership and the two Regional Patient Advocates. The first part of workshop covers 'Building foundations for a better future' (President & CEO Anthony J. Castaldo and Executive Vice President & Chief Operating Officer Henrik Balle Boysen), 'Decentralized Approach in Practice' (Fiona Wardman), 'ACARE' (Anthony J. Castaldo and Professor Marcus Maurer) as well as a presentation of HAEi services such as emergency card, hosted websites and HAEi Connect.

The expert presentations are delivered by Dr. Olivera, Panama (Diagnosis), Dr. Olivares, Colombia (Symptoms), Dr. Grumach, Brazil (Treatment), and Dr. Calderón, Peru (ACARE), while the Youngsters are represented by Nathan Galarza and Isabel Brunkan.

All 17 member organizations in Latin America – that is Argentina, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Guatemala, Ecuador, El Salvador, Mexico, Panama, Paraguay, Peru, Puerto Rico, Uruguay, and Venezuela – are presented through short videos on the present situation in each country.

The workshop's final part is a Q&A video with the two Regional Patient Advocates teaming up with Dr. Olivera, Dr. Olivares, Dr. Grumach, and Dr. Calderón.

VIDEOS IN SPANISH, PORTUGUESE AND ENGLISH

You have access to all the videos of the Latin American workshop at **haei.org/2021-haei-virtual-regional-workshop-latam**

Meeting old and new friends via HAEi Youngsters' online meetups

By Hana Faulds

Hey Youngsters!

What a crazy year 2020 was, right! And to that note we send our love to all of you around the globe.

2020 was the year of changes and for many that meant finding different ways to connect. Meeting online has a whole new and different meaning, hasn't it?

We are very sad we didn't get the chance to see everyone at the 2020 HAE Global Conference, however that pushed us to think outside the box and find a new way to stay in touch.

Chatting with our international friends is what we miss the most and that is why the HAEi Youngsters Advocacy Group launched the HAEi Youngsters online meetups in November 2020, and it was a huge success! Our hope is that through those meetups we get the chance to catch up, have fun, talk about HAE and support each other. We are happy we found a way to do this with the help of HAEi.

The idea is simple. At the end of each month, we invite you to join us on a Zoom call and say hello. On our Instagram you can always find more information about the theme of the meetup, the date and time as well as a registration link. (Psst.. If you're not already doing so, make sure to follow our Instagram account @ haeiyoungsters so you never miss out on any updates from us)

We want to make sure that everyone on the call gets a chance to share their story and that is why we have a limited space of 15 people per call. If you are new to the community and have never joined a youngsters meeting, don't worry! We always start the meetups with a (virtual) roundtable introduction to break the ice.

Our first two meetups in November and December 2020 and were a lot of fun! In November we introduced the theme 'Meet around the world' and we were overjoyed to say it was fully booked. We had youngsters joining us from six different countries! Some had never met young people with HAE before, and some had never been to a global conference, but they were all excited to chat with HAE friends and share their stories. And in December we were all about the holiday spirit and what people were most excited about this holiday season.

It was wonderful to meet new people and reconnect with old friends and it was definitely the highlight of our 2020! We are so grateful for this global community and we look forward to many more meetups to come in 2021!

If you want to say hello, keep a look out on our Instagram for more meetups that you could join!

IMMEDIATE CARE REQUIRED

Emergency room posters help raise awareness

HAEi friends in many countries cite the need for significant improvement in emergency room care for people with HAE. Because education is the key to better emergency care, HAEi has prepared a poster with important information on recognizing HAE and successfully treating an emergency.

To ensure the most widespread use of the poster, it is to be translated into as many languages as possible. At this point, it exists in for instance English, Spanish and Arabic – and over the coming months, it will turn up around the world in many local languages.

There are three versions of the poster. The first is a standard poster with HAEi contact information and logo, while the second has the same information with space to include the national member organization's logo and website or other contact details. Thirdly there is a fully customizable poster. This version is without the HAEi watermark and logo and can thus be customized by the member organization.

Over the last few months, member organizations have been in contact with hospitals and clinics in their country to present the poster and encourage them to use the poster within the emergency rooms.

Production of the poster takes place locally as HAEi emails a print-ready file for the poster to the member organization, who then sources a local company to print the poster. Distribution is managed either as hand-delivered or by mail, in both cases via the member organization.

Established member organizations with funding sources are requested to fund printing, postage or delivery. In contrast, patient groups without a funding source can have their print expenses covered by HAEi. However, if version three of the poster is chosen, the member organization will be covering all costs for customization, printing and distribution.

The emergency room poster files are available in three sizes:

- A2 (420mm x 594mm)
- B1 (500mm x 700mm)
- Poster Size Large 609.6mm x 914.4mm

Option 1: The original standard poster with HAEi contact information and logo.

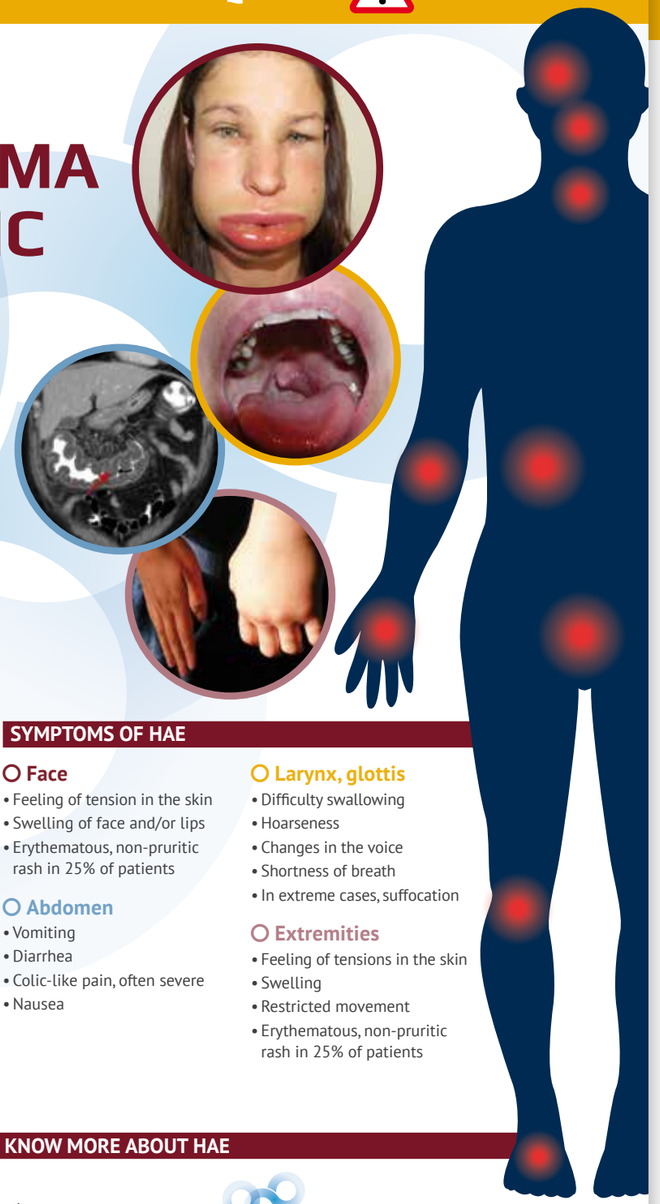
Option 2: The original standard poster with space to include the member organization's logo and website or contact details. The example is with the HAE Scandinavia logo and information.

Option 3: A fully customizable poster without the HAEi and logo. The poster can be fully customized by the member organization.

2

IMMEDIATE CARE REQUIRED

NOT ALL ANGIOEDEMA IS ALLERGIC



Hereditary Angioedema (HAE) presents with recurrent cutaneous swelling, abdominal pain, and/or airway obstruction due to angioedema.

HAE is often misdiagnosed as allergic or histamine-mediated angioedema.

HAE SWELLING IS CAUSED BY EXCESSIVE BRADYKININ PRODUCTION TYPICALLY DUE TO LOW C1-INH PROTEIN FUNCTION.

Allergy medications (antihistamines, corticosteroids, epinephrine) are ineffective in treating angioedema due to HAE.

Swelling of the airway is dangerous and can lead to death by asphyxiation.

TREATMENT OF HAE

- Drugs approved for treating acute HAE attacks (where available)
- Fresh Frozen Plasma (FFP) (when no approved HAE treatments are available)

Airway swelling is particularly dangerous and can lead to death if not treated immediately.

Mortality rate:
30 %

SYMPTOMS OF HAE

Face
- Feeling of tension in the skin
- Swelling of face and/or lips
- Erythematous, non-pruritic rash in 25% of patients

Abdomen
- Vomiting
- Diarrhea
- Colic-like pain, often severe
- Nausea

Larynx, glottis
- Difficulty swallowing
- Hoarseness
- Changes in the voice
- Shortness of breath
- In extreme cases, suffocation

Extremities
- Feeling of tensions in the skin
- Swelling
- Restricted movement
- Erythematous, non-pruritic rash in 25% of patients

KNOW MORE ABOUT HAE

HAE Scandinavia

www.haescan.org

HAE Scandinavia is the national patient organization for HAE patients in Denmark, Norway and Sweden.

HAEi
HAE International

www.haei.org

HAE International is the global umbrella organization for HAE patient groups around the world.

SUPPORTED BY HAE INTERNATIONAL · HAEI.ORG

ACARE IN ACTION

Professor Marcus Maurer
HAEi's Chief Medical Advisor
and GA²LEN/HAEi ACARE Coordinator

The network of ACARE centers continues to grow despite the many challenges created by COVID-19.

ACARE is a joint venture with GA²LEN and HAEi that fulfills HAEi's longstanding goal of establishing a worldwide network of accredited angioedema care centers.

In 2020 and 2021, the ACARE Network launched, hosted and aired two webinar series.

The first was 'Hereditary Angioedema in Times of COVID-19', two webinars on the pandemic and its effects in dermatology and allergy, with a particular focus on the impact of the pandemic on patients with recurrent angioedema, including HAE. Faculty were Professor Maurer, Dr. Melba Munoz-Roldan and Professor Markus Magerl, all from the Angioedema Center of Reference and Excellence at Charité Universitätsmedizin, Berlin, Germany. Both webinars were well attended and received with more than 100 participants, each representing over 30 countries.

The second webinar with the title 'The power of prophylaxis' was a three episodes webinar series on the burden of HAE, the aims of treatment, and the role and relevance of prophylaxis. This series' objective was to review the impact of HAE on patients and their families, discuss the aims of HAE management and guideline recommendations, talk about strategies for assessing treatment needs and responses, and the tools to help with this. Furthermore, the webinars reviewed the efficacy and safety of prophylactic treatment options and shared real-life experience. For these webinars, the faculty was Chief of Service Margarida Goncalo from the University of Coimbra in Portugal, Associate Professor Maria Staevska from Sofia Medical University in Bulgaria, Consultant Clinical Immunology Sorena Kiani from Royal London Hospital in the United Kingdom, Dr. Hilary Longhurst from Auckland District Health Board, New Zealand, Dr. Anna Sala-Cunill from Universitat Ramon Llull in Barcelona, Spain, as well as Professor Magerl and Professor Maurer from Charité Universitätsmedizin, Berlin, Germany. Furthermore, featured guests were President & CEO Anthony J. Castaldo and Executive Vice President & COO Henrik Balle Boysen, HAEi. Here the reach was between 116 and 172 attendees representing almost 40 countries.

In 2019, live ACARE preceptorships on recurrent angioedema were held in Beijing, China and Muscat, Oman. More live ACARE preceptorships will happen once this is possible again, the next one in Hiroshima, Japan.

ACARE is currently working on two scientific projects:

- IMAGINE – with the pilot phase ongoing – is focused on the identification of mutations in genes of patients with recurrent idiopathic and hereditary angioedema. The aim is to identify known and novel mutations in patients with bradykinin-mediated recurrent angioedema using dried blood spot analysis. Project leads are Markus Magerl, Thomas Buttgereit and Marcus Maurer.

- SHAERPA – a project in development – focuses on stopping androgen treatment in HAE patients with characterization of reasons and protocols and development of advice for patients and physicians. Here the aim is to develop guidance on how to discontinue androgen treatment based on patient data. Project leads are Carolina Vera, Marcus Maurer and Markus Magerl.

Furthermore, the network is currently working on the INTERACT preceptorship, and the 'Make a Difference' webinar series.

With the INTERACT preceptorship series, to be held during the second, third and fourth quarters of 2021, ACARE is reaching out to physicians who treat patients with recurrent angioedema with a series of region-specific, web-based educational training programs, focusing on the differential diagnosis, diagnostic work-up and treatment of recurrent angioedema.

"The four-hours-long INTERACT preceptorships will not only focus on the clinical spectrum, burden, differential diagnosis, and the diagnostic work-up in patients with recurrent angioedema but also the management of recurrent angioedema, with a special focus on new insights and treatment options that have recently become available. Each preceptorship will include interactive elements, case discussions, and lectures, with additional material provided online for download", HAEi's Chief Medical Advisor and GA²LEN/HAEi ACARE Coordinator Marcus Maurer explains.

As for 'Make a Difference', it is a direct continuation of the 'The Power of Prophylaxis' series of webinars. Planned to be held during the two last quarters of 2021 and the first quarter of next year, this series of five webinars will explore how physicians can best aim to provide the optimal diagnostic work-up and therapy to all HAE patients as early as possible. The webinars will cover the strategy of an earlier and broader diagnostic strategy that reduces delay in diagnosis and of a close-meshed therapy control that allows optimizing therapy methods continuously.

Regarding future projects, Professor Maurer says that ACARE is currently working to implement a platform and program for physician education and information on recurrent angioedema under the name 'ACARE LevelUp':

"ACARE LevelUp will be a comprehensive and long-term educational platform and program for healthcare professionals to learn, network, and share best clinical practices in recurrent angioedema, worldwide. ACARE LevelUp will be interactive, virtual and aim to update physicians on recent developments in angioedema and establish a platform for interaction among physicians who treat patients with recurrent angioedema. Furthermore, the aim is to help health care professionals involved in the management of angioedema to network on a regional, national and global level and to improve the interaction of general practitioners and specialists, including ACAREs, to streamline the patient journey to disease control. ACARE LevelUp will feature several formats and activities, including webinars, informational websites, podcasts, poster sessions and more."

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

EXPANDING GLOBAL NETWORK OF ACARE CENTERS

Today the global network of ACARE centers consists of more than 50 members spread over most of the globe. Please see **acare-network.com** for contact details of all ACARE centers. Presently the centers are:

Argentina:
- Hospital Italiano de Buenos Aires, Buenos Aires
- Instituto de Alergia e Inmunologia del Sur, Hospital Italiano Regional del Sur, Buenos Aires

Brazil:
- Alergoalpha/CPAlpha Allergy Clinic and Clinical Research Center, Barueri
- Clementino Fraga Filho University Hospital Federal University of Rio de Janeiro, Internal Medicine Department, Immunology Service, Rio de Janeiro
- Clinical Hospital of Ribeirão Preto Medical School, Division of Allergy and Immunology, University of São Paulo, Ribeirão Preto
- Division of Clinical Immunology and Allergy, São Paulo University, São Paulo
- Federal University of São Paulo, São Paulo
- Servico de Alergia e Imunologia, Complexo Hospital de Clinicas Universidade, Curitiba
- Serviço de Referência em Angioedema do Hospital Santa Casa de Misericórdia de Vitória, Vitória
- University Center Health ABC, Medical School, São Paulo

Bulgaria:
- Clinic of Allergology, University Hospital„ Alexandrovska“, Medical University of Sofia, Sofia
- Medical Center Excelsior, Sofia

China:
- First Hospital, Peking University, Beijing
- Sun Yat-sen Memorial Hospital, Guangzhou

Denmark:
- Bispebjerg Hospital, Department of Dermatology, Copenhagen

France:
- CREAK: National french reference center for angioedema, Grenoble
- Montpellier University Hospital, Montpellier
- Service de dermatologie et allergologie, Hôpital Tenon, APHP, Paris

Georgia:
- Center of Allergy and Immunology Tbilisi, Tbilisi

Germany:
- Department of Dermatology, Venereology and Allergology, Universität Leipzig, Leipzig
- Elbeklinikum Buxtehude, Klinik für Dermatologie, Buxtehude
- Hautklinik und Poliklinik Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Mainz
- Klinik für Dermatologie, Venerologie und Allergologie, Charité – Universitätsmedizin Berlin, Berlin
- Occupational Dermatology Department of Dermatology, Universitiy Hospital Carl Gustav Carus, Technical University Dresden, Dresden
- Universitätsmedizin Götting, Göttingen

Greece:
- Referral Center of Occupational Dermatological Diseases, Athens

Hungary:
- Hungarian Angioedema Reference Center, Budapest

India:
- Allergy Immunology Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh
- Department of Dermatology at Postgraduate Institute of Medical Education and Research, Chandigarh
- Dr. D.Y. Patil Medical College & Hospital, Mumbai

Japan:
- Department of Dermatology, Graduate School of Biomedical and Health Sciences, and Hiroshima University Hospital, Hiroshima
- Division of Dermatology, Kobe University Graduate School of Medicine, Kobe
- Yokohama City University Hospital, Yokohama

Kuwait:
- Al-Rashed Allergy Center Kuwait, Kuwait City

Netherlands:
- Amsterdam UMC, location AMC, Amsterdam

Oman:
- Immunology and Allergy Unit, Royal Hospital Muscat, Muscat

Peru:
- Allergy Unit at Clinica San Felipe, Lima
- SANNA / Clínica el Golf, Lima

Poland:
- Centralny Ośrodek Wrodzonego Obrzęku Naczynioruchowgo, Centrum Alergologii Klinicznej, Szpital Uniwersytecki w Krakowie, Krakow
- Department of Dermatology, Venerology and Pediatric Dermatology, Samodzielny Publiczny Szpital Kliniczny Nr.1, Lublin
- European Center for Diagnosis and Treatment of Urticaria, Zabrze

Portugal:
- Clínica de Dermatologia Centro Hospitalar e Universitário de Coimbra, Coimbra

Qatar:
- Allergy and Immunology Section, Hamad General Hospital, Doha

Russia:
- Moscow Center of Allergy and Immunology, City Clinical Hospital № 52, Moscow
- NRC Institute of Immunology FMBA Russia, Moscow

Saudi Arabia:
- King Faisal Specialist Hospital & Research Centre, Riyadh

Slovenia:
- University Clinic of Respiratory and Allergic Diseases Golnik, Golnik

South Africa:
- UCT Lung Institute, Cape Town

Spain:
- Department of Dermatology Hospital del Mar, Barcelona

Thailand:
- Siriraj Urticaria and Angioedema Center, Bangkok

Turkey:
- Division of Immunology and Allergic Diseases, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul
- Hacettepe University Faculty of Medicine, Ankara
- Kayseri City Education and Research Hospital, Kayseri

United Arab Emirates:
- Immunology & Allergy Clinic, Cleveland Clinic, Abu Dhabi

United Kingdom:
- Barts Health NHS Trust, London
- The London Allergy & Immunology Center, London

If you would like to become an ACARE center, please use this link for further information:
acare-network.com/index.php/become-an-acare-center

PATIENT STORY

Patient story: Emily Wheeler, Australia

ONCE I WAS DIAGNOSED WITH HAE, I FELT VERY RELIEVED THAT I HAD ANSWERS – AND TREATMENT

I experienced the first HAE attack in 2018 – I was 19 at that time. I had just moved to Perth to start my nursing studies at the university, and I was in my first semester of study.

The first symptom I had was swelling of my left foot. It was a slow and gradual swelling that happened over 24 hours. I thought I had an allergic reaction to something, so I went to the doctors and was told I had gout and given some mysterious medication. They never told me what it was. Three pills were placed in an envelope and given to me, and they told me to come back in the morning for a follow-up appointment. I had two of the pills as instructed. About an hour later, I started vomiting uncontrollably and had excruciating pain in my abdomen. I went to the hospital, where they stopped the vomiting and gave me pain relief. My feet swelling started to go down, and the vomiting and pain stopped after several hours.

There was no HAE diagnosis at that point?

No, the swelling in my feet was ruled as an allergic reaction and undiagnosed. The vomiting and pain were diagnosed as a result of the pills I was given. The next morning, I was sent home feeling much better and my feet swelling almost gone. The following night I was in the shower, and I noticed my abdomen beginning to swell. I went from having a flat stomach to looking six months pregnant within about half an hour. Alongside this, I had pain, so I went back to the hospital. It was St Patrick's day, and as it was extremely busy, I was told they wouldn't see me for hours. I decided to leave and go to Bunbury, my hometown and see my GP, who rushed me in for a CT and ultrasound. Both were showing abdominal ascites. This is where my journey with HAE begun.

I was diagnosed with HAE in 2020, at the age of 21. Between 2018 and 2020, I had swelling in my stomach. On the 4th and 20th of every month when I ovulated, and I menstruated. Every month I would go for scans and ultrasound showing nothing at all as by the time I went for a scan, the swelling would go down, and I would urinate the fluid out. No one could explain why or what was happening. I was sent to multiple doctors and surgeons. I was told I was making it up, and that it was bloating or bad PMS. I had two exploratory laparoscopes, both finding a fibroma – that is a benign tumor – on my ovaries. This was removed. Following that, I was retrospectively diagnosed with Meigs Syndrome and told it would never come back, and I would be fine.

But you weren't?

Well, for five months, I was. I then started to have abdominal swellings again. I was sent to more doctors where I was told I was not their problem, and it was gynecology related. Some doctors would even refuse to have appointments with me as they said it was not

their area. Emergency doctors told me I would never find a diagnosis and that I should just learn to live with it and gave me a script for opioids to take daily to help cope with the pain.

In January 2020, I was in Bunbury when I experienced excruciating pain at 9 pm on a Saturday. I was unable to move. I was vomiting and never had pain this intense, this time very localized to my right side. I thought my appendix had burst. However, I was so sick and tired of being sent away that I ended up refusing to go to the hospital as I knew they would take a blood test and send me home once again with no answers. Most of the time, it eased after a few hours when the swelling would start to go.

But in fact, you did go back this time?

I did. At 7 am Sunday, when there was no improvement, I went to the Emergency Department where I was wheeled into Emergency as I was unable to walk. I was rushed through where I saw a doctor who had seen me for this swelling before and remembered me. He sent me for an ultrasound. This came back, showing that I was filled with a large amount of fluid, and he had never seen this much fluid before. I remember being told this and crying as someone finally believed me and didn't think I was just bloated or making it up. He assured me he would find an answer and got the surgical team involved. They then sent me for a CT scan to see why there was this fluid. The scan showed a bowel intussusception, which only ever happened in babies; therefore, the doctors were shocked, and I was rushed into surgery. After surgery, I was told that my bowel had undone itself, and it did not need to be removed. However, they had drain just under two liters of fluid from my abdomen. The surgeon reassured me he was going to find an answer as to what was causing this. I was then referred to a gastroenterologist in Perth to discuss why this might have happened.

I was convinced another fibroma had caused this, and when it was removed the year earlier, I felt better. I made an appointment with my gynecologist where we discussed shutting my ovaries off and essentially going through menopause for three months to test whether all this pain and swelling was due to my ovaries. If it was, I was to have them removed. I was confident this was what was needed. After this appointment, I had another one with the gastroenterologist, where I told him the whole story. He said I might have an enzyme deficiency that he has only seen once in a patient due to being on blood medication for a long time. However, he said it was worth a shot. I left that appointment thinking there's no way I have an enzyme deficiency and was convinced I would need my ovaries removed.

But this was really the breakthrough, right?

A week later, the doctor rang me personally and told me to sit down as he had a diagnosis. He told me I had Hereditary Angioedema. I was in such shock that I kept saying, "are you sure?" and "is this definite?". I said thank you and hung up. I then googled it, and everything for the first time in two years matched up every symptom, every pain. I rang the doctor back once I had processed this information and thanked him and told him how much he changed my life by diagnosing me. He told me I was his miracle patient and was so happy he could help. I then continued to see an immunologist to get treatment.

What was your most severe HAE attack?

That was my bowel intussusception caused by the swelling in my abdomen. After being diagnosed, my attacks worsened after trying to control my estrogen. I got an etonogestrel birth control implant put in, and it made my attacks go from twice a month to every day. I was in Emergency every second day at one point for about a month, with a total of 20 visits to Emergency and hospital admissions. However, having a diagnosis and receiving C1 Inhibitor Esterase intravenously helped a lot as it made my admission a lot quicker. My initial monthly attacks were severe, always resulting in vomiting from the pain. Whereas my current everyday attacks don't hurt, I just swell in my abdomen.

No doubt it must have been hard to keep up the good spirit during this ordeal.

During the two years that I was having symptoms without being diagnosed, I found it challenging. As mentioned, I began to believe the doctors thought I was making my symptoms up, and that perhaps it was just bloating. I felt as though no healthcare professional, other than my GP, gynecologist, cared that I was going through this and did not want to help me at all, especially when doctors refused to take a look at my case. I also became very anxious around the 4th or the 20th of the month because I knew I would swell up and be in pain. I did not know when it would happen, and it would then prevent me from going to events or wearing clothes that I wanted and really became self-conscious of the way I looked when I was swollen. I was anxious about going into Emergency every month, knowing I would be told there was nothing wrong and be sent home again. Alongside this, I started to lose hope of ever finding a diagnosis, and I would just have to live with this. I felt as though they put me in the 'too hard' basket' and it angered me how much I had to fight for doctors to even consider an appointment with me and that it took a bowel intussusception for them to take my symptoms seriously.

But that changed when you were diagnosed?

Once I was diagnosed with HAE, I felt very relieved that I had answers – and treatment. I also felt relieved because I had confirmation that I was not making my symptoms up or just having bad PMS, that this it was all very real. However, I became quite anxious when I had attacks as I had learnt I could get swelling in my throat. I was also scared because I knew this would be a lifelong condition, and I didn't know if I would get back my old life, which I still battle with today. I was very supported by my family and partner, making the journey a whole lot easier.

Speaking of family – how would you describe your childhood growing up with HAE?

As a child, I never had any HAE symptoms. When I was 19, I had the birth control implant but had breakthrough bleeding and went on the estrogen/progesterone contraceptive pill to regulate the contraceptive implant. From that, my symptoms started and triggered my HAE.

No one in my family has HAE. They have all been tested, so we know that I am the only one. Today my family, as well as my partner, is very aware of what it is like as they are around me all the time when I have the attacks and are the ones who take me to hospital. Unless you see an attack, it is a tough concept to grasp the complexity of what happens and that not only my stomach swells, but that strains my back and my organs causing a lot of pain.

I think people around me, in general, know what my condition is called and that my stomach swells, and it can be dangerous if it was to happen in my throat. However, I don't think they understand the complexity of HAE or its impact on a person's life when unstable.

Has your HAE prevented you from your everyday activities?

Yes, I had to withdraw from the university in the early part of 2020 because my HAE was so uncontrolled. My social life came to a standstill, and I would often not go to things because of the fear of an attack. I couldn't exercise like I used to, and also work became a real struggle.

I would say that HAE has affected my life dramatically as I had to defer a university semester to focus on getting well. I have been too unwell to work or exercise as everything has been causing attacks. My fatigue from being medicated continuously and from my body being under stress from dealing with attacks constantly has left me living most of 2020 in bed. My body has had limited energy to undergo everyday activities. It has put a considerable pause on my life, and I am looking forward to getting back some normality. I know now that even though my stomach swells, it is not painful, and it doesn't stop me from exercising. I just have to be aware of how far to push myself and how my body is feeling.

In Australia, you have access to modern HAE medication in the form of plasma-derived C1-inhibitor as well as a bradykinin receptor antagonist. Do you use any of these medications for your attacks?

Yes. I am currently on intravenous plasma-derived C1-inhibitor twice a week as subcutaneous injections have

not worked for me. My stomach was too sensitive to the needle and recognized it as trauma, and it would result in an attack. I also use an additional intravenous unit when I have an attack which works really well as it works almost instantly and prevents me from going to the hospital. I also use a bradykinin receptor antagonist for acute attacks. However, sometimes it does not work because my stomach recognizes it as trauma, effectively making me worse during an attack. I also have pain relief to try and stop the pain as that can make the attack worse. Some work best for me when I am in the hospital while others help calm me and my body as stress can make my attacks worse.

Do you have access to preventative treatment?

I am on intravenously administered plasma-derived C1-inhibitor twice a week, which works the majority of the time. I currently have an intrauterine device that releases the hormone levonorgestrel into the uterus. It helps control my estrogen as the plasma-derived C1-inhibitor just doesn't hold me, especially during these times where my estrogen is peaking. I am hoping that these two treatments together will continue to stop my daily attacks as it is still early days that I have been on both these treatments together. Even with my intravenous medication, my attacks are varying from weekly to daily and I am seeing a slow improvement, however, they are not painful all of the time. This way I can get a bit of normality back in my life, such as exercise and finishing my university studies and start my nursing career.

Overall, having access to treatment has been life-changing: As soon as I feel any pain or sign of swelling, I can treat it and go on with my day rather than end up in the hospital.

What message would you like to convey to people regarding HAE and having such a rare disease?

I want people to be aware of HAE and that it does exist – and that it may be more common than you think but just left undiagnosed. I urge people to advocate for themselves. As much as we should trust doctors to do that for us, they don't always, especially when it's something uncommon. Moreover, you don't need to feel embarrassed about asking for help and wanting to be treated.

Have you made any use of the offers provided by HAE Australasia?

Yes, I have had contact with the association's HAE community on Facebook where people post question and queries. That is a really nice forum to have as it makes me feel as though I'm not alone with this condition or symptom.

EMILY'S STORY IN BRIEF

- Born 1998 in Perth, Western Australia.
- Bachelor of Nursing at the University of Norte Dame, Australia – becoming a Registered Nurse July 2021. Will be undertaking a Graduate Nursing Program at Sir Charles Gardner Hospital, Nedlands, Western Australia in August 2021.
- HAE symptoms registered at 19. Diagnosed age 21.
- Other HAE patients in her family: None.

HAEi staff news

Rachel Annals has been appointed as Assistant to the Chief Regional Patient Advocate. This action allows HAEi to accommodate the phenomenal growth of the Regional Patient Advocacy program.

Rachel will support the Chief Regional Patient Advocate, Fiona Wardman, and the Regional Patient Advocates, as they implement the programs and services that fuel the global HAEi patient advocacy movement.

Rachel also serves as the Executive Officer of HAE UK. She is focused on patient advocacy and one-to-one support as well as organizing patient events and projects.

Rachel, who is an HAE patient herself, lives with her daughter in Bridgwater, United Kingdom.

In January 2020, **Steen Bjerre** left HAEi to pursue other opportunities. However, he has missed his many good HAE contacts, so he has returned to the role of Communications Manager. Among other things, Steen is responsible for content for *Global Perspectives* and other HAEi media, maintenance of websites and databases as well as general communication tasks including the creation of reports. He is also involved in planning and conducting global activities.

Based on a BA in Journalism, Steen was with the first wave of independent television and radio stations in Denmark. After years with advertising agencies, he established a communications company in 1992. Steen worked for HAEi 2012 to 2020 and returned 1 February 2021.

The HAEi media

In addition to producing four *Global Perspectives* issues with contributions from a growing number of the member organizations, HAEi is active on several media outlets.

"A cornerstone in our communication is the website at haei.org. In 2019 it underwent a major update, including a graphical facelift as well as enhanced user experience", says HAEi Communications Manager Steen Bjerre.

Most recently, HAEi has worked on a massive update of the campaign website at haeday.org.

HAEi continues to raise HAE awareness via several social media channels:

Facebook – group: This group was launched in 2009 and is aimed at not least patients and caregivers. Typically, there are a handful of new members each week and often the Regional Patient Advocates can use their contact information when creating new national contacts. Presently the group more than to 2,900 members.
>> facebook.com/groups/HAEinternational

Facebook – page: The page was launched in January 2019 aiming to reach anyone interested in HAE related information. At the moment there are 1,050 followers. **>> facebook.com/haeinternational**

LinkedIn: This social media outlet is open to anyone interested in HAE related information. Presently there are 900+ followers.
>> linkedin.com/company/haeinternational

Twitter: This communication channel is also open to anyone interested in HAE related information. Here we have 900+ followers.
>> twitter.com/HAEDAY

Instagram: Furthermore, there is an Instagram profile with presently around 375 followers.
>> instagram.com/hae_international

There are a few other social media outlets – either run by HAEi or marketed under the organization's name. These are:

An Instagram profile run solely by the HAEi Youngsters Community, today with around 450 followers.
>> instagram.com/haeiyoungsters

A Facebook group solely administrated by the HAEi Youngsters Community, presently with close to 200 members.
>> facebook.com/groups/470967886612519

A Facebook group for participants in the Camino/Jakobsweg Walk events with 130+ members.
>> facebook.com/groups/1704846256399874

A YouTube channel run by HAEi
>> youtube.com/user/haedaychannel

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
- Different member types available
- Many custom fields available

WANT TO KNOW MORE?

VISIT HAEI.ORG FOR INFORMATION ON THESE AND OTHER FREE RESOURCES

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

NEWS FROM MEMBER ORGANIZATIONS AROUND THE GLOBE

JORDAN

During the first weeks of 2021 HAEi could welcome member organization number 93: HAE Jordan. The national contact is Bassam Mohammad Alelimat – please see haei.org/hae-member-countries/jordan for contact information.

BULGARIA

From Chairman Danail Dimov, HAE Bulgaria

The next important goal HAE Bulgaria wants to achieve is to improve the access of HAE patients to plasma protein therapies and in particular to HAE prophylaxis. Our goal is to collaborate more closely with patients' community, Bulgarian authorities and health care professionals in order to improve the access to treatment with C1 Esterase Inhibitor (Human) and especially in terms of prophylaxis with the subcutaneous form. We deeply believe that this therapy new to Bulgaria will significantly improve patient compliance and will lead to positive lifestyle changes. We started this campaign at the end of 2019 and almost managed to persuade the Ministry of Health to propose the requested changes to Parliament, but unfortunately the COVID-19 crisis shifted the agenda and delayed things. Now we are starting the campaign again and we also submitted our application for Behring Local Empowerment for Advocacy Development (LEAD) Grant to support this campaign.

Main objectives: Access to prophylaxis – Changes in the legislation ensuring the access of the patients with HAE to prophylaxis for improving the quality of life by providing prophylactic treatment. Current legislation covers only on-demand treatment.

The pandemic has significantly changed the living and treatment conditions for HAE patients in Bulgaria. The ongoing pandemic has as a direct and immediate result the difficulty and restriction of access of patients with HAE to timely diagnosis and treatment of their disease, which in turn leads to a direct and immediate danger to the lives of the patients. This is especially true for those who have very frequent and acute attacks and for whom the need for prophylactic treatment is on the agenda in order to preserve their life and health and significantly improve their quality of life. Insofar as the Bulgarian legislation does not provide for the possibility of prophylactic treatment of patients with HAE, we consider it our duty and priority to ensure that patients have access to such treatment. The difficult access of HAE patients to specialized medical care in the conditions of the COVID-19 pandemic makes prevention even more important for them.

Expected direct results: Significant improvement of the quality of life of patients with HAE, protection of their life and health in extremely difficult pandemic conditions and difficult access to specialized medical care in hospitals.

Indirect results: Improvement of the awareness among the Bulgarian legislators, the executive power and the society in general about HAE and the problems of HAE patients; providing faster and better access to timely diagnosis and treatment of patients with HAE; raising awareness among patients about the disease as well as their ability to apply the prescribed therapies at home as the fastest way to obtain the necessary treatment and to overcome and prevent attacks of the disease; acquiring the necessary publicity of the need for treatment and prevention for these patients in order to thwart future legislative attempts to limit or prevent patients' access to timely and adequate treatment of their disease.

We have a good history in our attempts to change the legislation for the benefit of the patients. We have done it twice over the last three years and this gives us the confidence that we will succeed again.

COLOMBIA

HAE Colombia is now also present on Facebook – pay the organization a visit and leave a 'like' at facebook.com/acolaeh.

LEBANON

Nour El Chami has taken over the role as national contact for HAE Lebanon – for contact information please see haei.org/hae-member-countries/lebanon.

UNITED KINGDOM

From CEO Laura Szutowicz, HAE UK

Groundhog Day! For those of you not familiar with the expression, the day is 2 February, when the groundhog is said to come out of its hole at the end of hibernation. If the animal sees its shadow – for instance if the weather is sunny – it goes back into its hole, which portends six weeks more of winter weather. It has now come to mean a situation in which a series of unwelcome or tedious events appear to be recurring in exactly the same way and gave the name to a film in which the same day gets repeated over and over.

I had thought that the UK was moving on out of the whole COVID-19 lockdown situation, until the Government put us all back into it after Christmas. The UK is still better off than many countries as at least we are allowed and encouraged to take exercise every day, but the strain is beginning to tell on many people.

That was one reason why we were very grateful to Dr. Mari Campbell for giving us her time and expertise in some **Zoom meetings**. Mari is a consultant psychologist specializing in rare diseases and particularly Primary Immune deficiency at the Royal Free Hospital in London. She has worked with some HAE patients in the past and we are hoping to help her and her team set up a similar service in the Royal London.

Mari gave us an interesting insight into how stress happens, and that it actually is entirely natural, one of the 'fight or flight' responses that kept us safe from sabre-tooth tigers and nowadays helps us to do that impressive presentation for our boss! It is when it runs away that it becomes a problem, and the COVID-19 pandemic has become the modern day sabre-tooth tiger of which we are nervous.

Mari provided us with us many strategies for coping with and managing stress, and was extremely generous with her time and advice, also giving us resources such as this advice:

This and many other resources Mari have provided can be found here: haeuk.org/advice-support/stress-anxiety

One of our members and HAE UK volunteers, June Cole, has not let the pandemic prevent her carrying on with her beloved singing. She writes:

"Hello, my name is June Cole, and I am a patient with type 1 HAE. I would like to share with you some of my positive experiences during this historic pandemic and lockdown.

I sing with many other people but overnight that stopped because of lockdown. The Rock Choir came up with the brilliant idea of organizing daily singing sessions live via Facebook and weekly sessions, tutorials and virtual gigs via Zoom, which hundreds of people joined during the pandemic. We also made recordings and a video which were used in aid of the Mental Health Foundation Charity to raise awareness and funds. We did this by recording from home individually using our phones to make a recording. Over 4,500 of us recorded the song 'Keeping the Dream Alive' in this way and then submitted our recordings to Rock Choir for all our voices to be included on a download single. This was released in December 2020 and went straight in at number 1 on both of the iTunes and Amazon download charts. This made everyone involved feel really uplifted!

These daily sessions and the recordings were great fun and a wonderfully joyous experience, keeping everyone's spirits up and helping their wellbeing while in lockdown, in addition raising awareness and funds for the Mental Health Foundation Charity.

I also phoned my elderly relatives virtually every day to make sure they were okay and whether they needed anything. This was a great way to keep in touch with each other and help prevent loneliness."

Many thanks to June for this inspirational piece. For anyone who wants to see the Rock Choir in action have a look and listen at youtube.com/watch?v=rJKMV1WPO2o&feature=youtu.be. And I defy anyone not to spend the day singing 'My dog can do the cancan better than my cat can'!

Furkhanda Haxton, our volunteer for Scotland, is again taking part in **the Kiltwalk** which is being run as virtual event 23-25 April 2021. She will be raising money for HAE UK again and we are very grateful to her for this and all the great work she does for us. Please see more at thekiltwalk.co.uk/charity. The Kiltwalk is extraordinary in that not only does 100 percent of money go to charity, but every amount raised in increased by 50 percent donated by the Hunter Foundation.

This is from when June organized a Rock Choir 'FlashMob' in aid of HAE UK.

We have also heard that our Iron Man, Paul Carroll (see his story on our Patient Day website youtu.be/2OoQ7DdTuKE) is going to do a 'Double Ironman' Event, **'The Brutal'** later in the year.

Keeping the best news to last: The UK is rolling out the **coronavirus vaccination** program and many of our members have already had their first vaccination. Most people have had no side effects, and one or two have reported mild reactions but in line with what has been previously stated.

It has taken a very long time, but at last our **HAE UK Expert Nurse Training Program** is ready for nurses to access and complete. This is an on-line resource for registered nurses working with HAE patients. There are modules covering testing, genetics, treatment, home therapy etc. and each module finishes with a test. Once all completed and passed the nurse then receives a certificate of completion. This came out of conversation with Theo Grosse-Kreul, who is the Senior Specialist Nurse at Kings College, who suggested it and it has been thoroughly edited by our nurse advisors Christine Symons, Fran Ashworth, Emily Carne and John Dempster. The development of the course has been kindly sponsored by Pharming.

So, all good news and I am even starting to get a little hopeful that we may be able to once again think about having a **'real' Patient Day**. For anyone that has not yet seen our presentations from November 2020, they are absolutely excellent and full of information – please have a look at www.haeuk.org/pd2020/.

KENYA

In February, HAE Kenya President Patricia Karani appeared on NTV Kenya, the country's number one urban station owned by East Africa's largest media house the Nation Media Group. The program focused on plasma, critical for treating many serious health problems and how a pint of blood saves more than a life. You can see the program at facebook.com/NTVKenya/videos/1690712067804908.

LATVIA

HAE Latvia is yet another national organization to have a website hosted with HAEi. You will find the new website at haelatvia.haei.org.

VENEZUELA

HAE Venezuela is now also present on Instagram: instagram.com/fundacionaehve.

RUSSIA

From HAE Russia

Pandemic spreading affected the plans of HAE Russia. Many events had to be switched to online. However, even remotely, we actively helped patients with HAE to deal with legal issues, organizing online meetings with doctors, psychologists and lawyers. Representatives of HAE Russia participated in major international events – and during the winter 2020-21, we launched several new significant projects, including one aimed at young patients with HAE.

On 11-12 December 2020, representatives of HAE Russia attended the open scientific and practical forum **'Innovative Genetics. Modern knowledge about human diseases, advanced approaches to health care organization based on orphan diseases'**. The forum was held online. Among the speakers were scientists, medical practitioners, representatives of pharmaceutical companies and patient organizations. The forum focused on developing a comprehensive approach to the detection and treatment of genetic and orphan diseases and the development of new methods of organizing pharmaceutical care. In the 'Special Report' section, HAE Russia's Chairman Elena Bezbozhnaya presented the directions of our activities, while patients (including HAE patients) described the difficulties they face in everyday life and the real situation with pharmaceutical provision in the Russian regions.

The 2020 HAEi Virtual Regional Workshop Central Eastern Europe & Benelux was held on 12 December 2020. The discussion covered the diagnosis, methods of patient care following the international HAE treatment standards, including new pathogenic medicines, and the issues of planning pregnancy and childbirth for patients with HAE. Representatives of patient associations shared information on their activities, and the situation in their countries with regard to the diagnosis and treatment of HAE patients. Elena Bezbozhnaya and Ilya Ushankov, lawyer of HAE Russia, participated in the seminar and introduced the audience to our activities.

On 25 December 2020, we held a **webinar for HAE patients from St Petersburg and the Leningrad region**. Elena Bezbozhnaya addressed the meeting and commented on the overall satisfactory situation with drug provision in Russia: "For the third year in a row, the provision with effective drugs has been at 87 percent of the total need. We help the remaining 13 percent in all possible ways, providing consulting, organizational and legal support."

Elena Bezbozhnaya also reported on the pilot program for early access to a long-term preventive drug. The program now involves several members of HAE Russia. The drug has not yet been registered in Russia due to clinical trials – most likely, this will happen in 2021. Ilya Ushankov provided a presentation on legal support for patients diagnosed with HAE. The lawyer gave examples from his practice of providing legal assistance to patients regarding preferential drug provision.

On 26-27 December 2020, we organized **a series of New Year's Eve meetings for underage patients with HAE** within the project 'Call a Friend'. Three online

meetings were held for HAE patients of different age groups: from 5 to 8 years, from 9 to 12 years and from 13 to 18 years. Julia Faikova, psychologist and HAE patient, conducted the sessions and gathered children from many regions of Russia. Sixteen-year-old Dasha Bezbozhnaya acted as co-host and administrator of the meetings. The children had the opportunity to meet each other, chat and participate in creative activities, intellectual games and online journeys.

On 28 December 2020, HAE Russia held **an online teleconference titled 'Routing and Beyond'** with our lawyer. Participants in the meeting from different cities and regions of the country shared personal patient stories and described the problems they encountered while receiving their medications. Yulia Faikova, head of Moscow Regional Department of HAE Russia, presented typical situations and described the algorithm of patient's actions in cases of obstacles on the part of regional health authorities. Lawyer Ilya Ushankov reviewed the situation with medical provision in the regions and outlined the major problems with drug supply.

On 28 January 2021, we held **the first webinar within the new series of 'HAE from A to Z' meetings for patients**. This series will include theory and practice sessions to help HAE patients increase their knowledge of the disease, its prevention and treatment methods, rights and benefits. The first webinar focused on commonalities and differences between primary immunodeficiencies and HAE from medical and legal perspectives. The main speakers were our lawyer Ilya Ushankov and the allergologist-immunologist Ekaterina Viktorova. The doctor spoke about the nature of the development of this group of diseases and noted the problems of detection of rare diseases. Today, the Russian Register of Persons with Primary Immunodeficiencies includes 3,500 patients. However, considering the global rate of detection, it should be around 14,000 people.

On the same day we held **a workshop on the new Russian Clinical Guidelines**, which came into force in January this year with HAE Russia as a contributor. Lawyers Ilya Ushankov and Olesya Manankova presented changes in diagnostics, prevention and therapy of HAE. At the meeting, the patients were also presented with the Angioedema Activity Diary developed by the Russian Association of Allergists and Immunologists. Based on these diaries, the doctor will be able to assess the disease severity, the treatment effectiveness and adjust the drug requirement. The second part of the meeting was interactive. The speakers answered patients' questions, simulated various situations that may arise in the process of prescribing treatment, choosing a doctor, and carrying out diagnostics.

On 30-31 January 2021, we organized **the second series of 'Call a Friend' meetings for young HAE patients** of different age groups. As for the first time, the meetings were held online. The presenter was the psychologist Yulia Faykova, the co-host was Dasha Bezbozhnaya. Younger children were engaged in a relaxation session introducing them to sand drawing. The children in the middle age group attended a cinema therapy session, watching cartoons and searching for answers to the questions concerning what brings joy to heroes and how you can find reasons for joy in everyday life. The facilitator played a 'Support' game with the older group where the teenagers discussed situations in which a person needs the support of others. Dasha conducted exciting interactive games of varying degrees of difficulty for the participants, depending on the age range of the participants in each of the three groups.

EGYPT

Mohamed Osman is additional national contact for HAE Egypt. Please see contact information at haei.org/hae-member-countries/egypt.

USA

From Digital & Social Media Manager Ianice Viel, US HAEA

hae day :-) 2021: The US HAEA is excited to announce our plans for the celebration of **hae day :-)** 2021. We are thrilled to be a part of the HAEi campaign for the 10th anniversary of the global HAE awareness day and all of our activities will be converted into steps in support of the global virtual walk.

The theme for our **hae day :-)** activities will be "Take Action for HAE" which involves HAEA members delivering ER toolkits to local hospitals, firehouses, and first responders in an effort to educate the public about HAE. Our ER Toolkit is an educational resource for medical professionals that contains a Pocket Guide with disease state information, a poster for a quick reference regarding symptoms and treatments, and information on our free, accredited CME course, among other items. Along with the ER Toolkits, we have produced an EMS educational video to quickly and comprehensively explain the symptoms and treatment of HAE to the public.

hae day :-) 2021 will engage members of our community in high impact activities to ensure that medical professionals, particularly emergency care teams, have sufficient information to successfully deal with critical, potentially life-threatening symptoms often faced by people with HAE.

US HAEA Meet and Greet Events: We are proud to host a series of virtual Meet & Greet events for HAEA youth and adults that offer an opportunity to connect with peers while learning about what the HAEA has planned for them in 2021. People affected by HAE have found the HAEA Virtual Meet & Greet events to be incredibly educational and enjoyable. The HAEA Virtual Meet & Greet Events are a perfect way to reach out and meet others affected by HAE.

"I always love the meet and greets. I get new information from them each time. Please go to gain knowledge, ask questions, meet others just like you!" – Aysha B.

Advances in HAE Research: We are working hard on many fronts to sponsor research to improve the quality of life of people with HAE. We are pleased to share with you an overview of current research initiatives:

HAEA/HAEi Health Economics Study Demonstrates the Value of New HAE Preventive Medicines

A study of HAE medicines published by a group of economists who receive funding from the insurance industry concluded that new preventive HAE medicines are not cost effective. The HAEA questioned the methods and conclusions of this study and responded by initiating a comprehensive analysis to determine the financial and quality of life impact of the new preventive medicines. Almost 800 people with HAE participated in the study, and the results point to a drastically different reality from the economists' study. The data reveals that the new preventive therapies yield (1) substantial economic value in light of remarkable decreases in attack frequency, and (2) statistically significant improvements in patient quality of life. After an extensive peer review, the paper is now published, and available in print and free online at ingentaconnect.com/content/ocean/aap/pre-prints/content-200127

Hereditary Angioedema Primer

The HAEA joined forces with the prestigious medical journal Allergy and Asthma Proceedings and expert HAE physicians to develop a special supplemental edition on HAE diagnosis and management. The supplement was published in the journal's 1 November 2020 edition. It contains 14 peer reviewed articles on vitally important HAE topics and has been mailed to over 40,000 health care providers, including a targeted list of allergy-immunology fellows and specialists in training. HAEA members have free access to the supplement here: ingentaconnect.com/content/ocean/aap/2020/00000041/a00106s1

US HAEA Medical Advisory Board 2020 Guidelines

The US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema have been published and are downloadable from the Journal of Allergy and Clinical Immunology – In Practice, at jaci-inpractice.org/action/showPdf?pii=S2213-2198%2820%2930878-3

The guidelines provide the US medical community with a comprehensive scientific overview of HAE in all its forms (type 1, type 2, and HAE with Normal C1-Inhibitor) and offer best practices that emphasize the importance of the patient voice in determining an optimal treatment approach. The document embodies a consensus of prominent HAE physician scientists in the US and will be used as an authoritative source for treatment related questions raised by health insurers.

US HAEA and Angioedema Center at UCSD Study of COVID-19

The US HAEA and the US HAEA Angioedema Center at University of California at San Diego have conducted a survey with 1,400 respondents that included people with HAE and members of their household. The study is designed to 1) help determine if people with HAE are at greater risk of contracting COVID-19 or, if infected by the virus, manifest symptoms different from those seen in the general population, and 2) provide data regarding the impact, if any, of HAE medicines on the susceptibility to, or course of, a COVID-19 infection. The ultimate goal of the study is to safeguard our community's well-being by understanding the interaction between HAE and the virus. The results of this survey, which have been submitted to a peer reviewed medical journal, will help medical professionals develop the best treatment options and protocols for people with HAE who are afflicted with the virus.

HAEA Study of Insurance Reimbursement Challenges Faced by People with HAE

The HAEA has completed a major research initiative designed to help people with HAE and their prescribing physicians obtain insurance reimbursement for HAE medicines. To understand all aspects of the issue, we conducted detailed surveys of people with HAE and reimbursement specialists in the offices of prescribing physicians. We also conducted structured interviews with a representative sample of health insurers to gather their perspectives on HAE medicines. Based on this data, we have prepared guidebooks to help navigate the complex and often frustrating process for obtaining reimbursement for HAE medicines in the US. Separate guidebooks will soon be available for people with HAE and physicians who prescribe HAE medicines.

Continued HAEA Investment into Research for HAE with Normal C1-Inhibitor

The HAEA is dedicated to supporting the important members of our community who suffer from swelling that is not caused by a deficiency in C1-Inhibitor. We recognize that a sharpened scientific understanding of HAE biology and genetics is the first step in developing new and more effective treatments. That is why we support the search for genetic causes and biomarkers that define HAE with Normal C1-Inhibitor. Scientists at the US HAEA Angioedema Center at UCSD now have in-house genetic testing for several genes that are believed to be implicated. Physician scientists at the Center are committed to expanding the knowledge of this condition and working tirelessly to the development of suitable treatments.

Therapies in the Horizon: We have good news to report as we start the new year. The FDA has approved BioCryst's Orladeyo in the US – the first oral treatment for preventing HAE attacks that is not an anabolic steroid. In addition, the FDA approved Haegarda (C1 Esterase Inhibitor Subcutaneous [Human]) in preventing HAE attacks in pediatric patients six years of age and older. Takeda is still recruiting for its clinical trial testing the effectiveness of Takhzyro for HAE with normal C1-Inhibitor, and as many as three other companies will start clinical trials for new HAE therapies at some point during the year.

Despite being faced with a lifetime of daunting challenges, people with HAE have always found a way to overcome obstacles and achieve a positive outcome. This "can do" approach to life will undoubtedly be on display in our community throughout 2021. The global HAE community continues to attract significant interest in developing new therapies. Interest in HAE clinical research continues to be strong.

Nine companies are in the process of developing new HAE treatments. These include:

- Four oral pill therapies
- A new monoclonal antibody treatment
- Three prospective gene therapies
- A treatment based on an antisense technology

You can learn more about these developing treatments by listening to Episode 3 of the HAE Speaks Podcast: Ongoing Research for New HAE Treatments of the HAE Speaks Podcast, hosted by HAEA President and CEO, Tony Castaldo. Listen on Spotify or Apple Podcasts or go to anchor.fm/haespeaks

2021 US HAEA Virtual Summit Series: We are pleased to announce the 2021 US HAEA Virtual Summit Series, which will take place May-August 2021. Although we cannot meet in person, the Virtual Summit will offer a comprehensive program that will cover:

- challenges faced by our HAE community,
- exciting ongoing HAE research,
- special youth programs, and
- information that will help you evaluate your personal situation and explore alternatives to improve your quality of life.

The 2021 US HAEA Virtual Summit Series will be presented in one-day events throughout the Summer, beginning on **hae day :-)** 2021, and will offer engaging live and on-demand events.

2021 Virtual Summit Series Calendar of Events:

Sunday 16 May 2021: 7:00 PM EST – **hae day : -)** Take Action for HAE

Wednesday 16 June 2021: 7:00 PM EST – Ask the Experts – US HAEA Medical Advisory Board

Wednesday 14 July 2021: 7:00 PM EST – Currently available HAE therapies and those on the horizon

Wednesday 18 August 2021: 7:00 PM EST – Navigating Insurance Coverage for HAE Medicines

To register for the 2021 US HAEA Virtual Summit Series please visit haea.org.

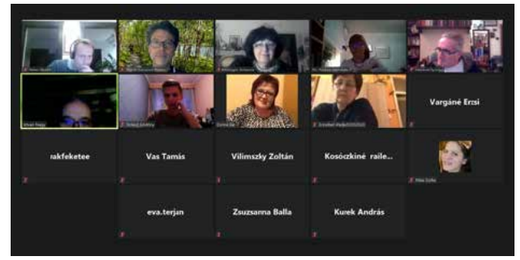
CUBA

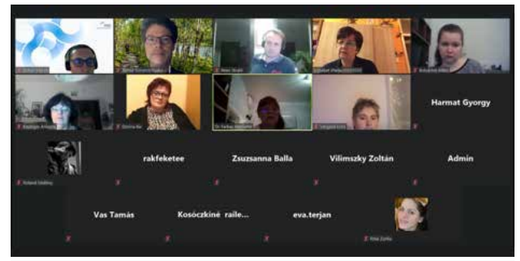
The second HAE knowledgeable physician in Cuba has been added to the HAEi global map. Please see haei.org/location/physician-camaguey-cuba for further information on Dr. Ana Claudia Bover Campall in Camaguey.

HUNGARY

From HAE Hungary

HAE Hungary held the first-ever online event on 30 November 2020 with about 20 participants including patients, physicians, and representatives of the pharmaceutical companies Takeda and ExCEEd Orphan representing Pharming. It was a great two-and-a-half-hour meeting.





At the first part of the meeting, Zoltan Maros, the Secretary of HAE Hungary talked about the events of 2020 where the association took part. The first one was the Rare Disease Day on 29 February which was just before the pandemic lockdown in Budapest. Raising

the attention of the public and decision-makers was accompanied by colorful, scientifically valuable programs and, last but not least, programs organized with great devotion for those involved, including children.

The Hungarian rare disease umbrella organization (RIROSZ) held its **preparatory on-line conference** just three days before our patient meeting. The ambitious goal of this meeting was to urge the government's public health arm to rev up the planning process of Europlan 2020, dealing with the rare disease patients' issues.

Our online meeting attendees got some insight from it both from Istvan Nagy, President of HAE Hungary, and from the representatives of the pharmaceutical companies.

After that Zoltan Maros talked about the HAE Virtual Global Conference and also about the program for the upcoming 2020 HAEi Virtual Regional Workshop Central Eastern Europe & Benelux. Zoltan and Istvan summarized the 2019 CEE workshop which was held in Warsaw, Poland. After discussing these events, Professor Henriette Farkas, the co-chair for professional affairs of the organization, and Zoltan Maros reported about the Takeda workshop about the journey of the HAE patients. It was a really interesting one-day workshop in the Hungarian Takeda office.

Then Professor Farkas talked about the current state of the HAE Center of Reference and Excellence, because the center moved to a new department of the Semmelweis University in Budapest. She mentioned that the center has introduced telemedicine for the yearly visits to avoid COVID-19 exposure of the HAE patents. Also, we heard some good news about Beata Visy, MD, who defended her PhD thesis about the "Evaluation of factors influencing the onset of HAE attacks" with excellent results. Last, but not least Professor Farkas told good news about the 12th C1-Inhibitor Deficiency and Angioedema Workshop to be held 3-6 June 2021.

Before the participants started the free chat, Istvan Nagy explained the patient organization's financial year and the organization held its yearly meeting, too. All participants chatted about their pandemic experiences and how they deal with it in their everyday life. The first online meeting was a great success, and everybody agreed that in 2021, HAE Hungary has to organize these kinds of meetings regularly.

From Henriette Farkas, Chairperson of the 12th C1-inhibitor Deficiency & Angioedema Workshop

It is our great pleasure to invite you to the 12th C1-inhibitor Deficiency & Angioedema Workshop, which will take place 3-6 June 2021, for the first time in cyberspace.

Since health and safety is extremely important for us, we decided not to organize a conventional Workshop in 2021, so in order to keep our community together, we will step into the virtual world with our meeting this year. However, the aim is the original: To provide you with presentations and discussions of the latest scientific findings related to bradykinin-mediated angioedemas.

Our main objective is to maintain the high level of professional and scientific content in the cyberspace, too, or even raise the Workshop's quality by taking the advantages of virtual event. In addition to this, we will provide you with a lot of fun and surprises which aim to compensate you for the lack of the physical presence. We hope to be able to show you in a brand-new way how great an online event can be. We encourage you to join.

To read further information on the Workshop, please visit 2021.haenetworkshop.hu. Please note that the site is still under construction – the online registration and abstract submission are coming soon.

PARAGUAY

Now you can also find HAE Paraguay on Facebook – have a look at facebook.com/Angioedema-Hereditario-Paraguay-2444926349068677.

CANADA

From HAE Canada

We made it through 2020 and excited to welcome 2021! Despite dealing with COVID-19 and all that it throws at us, thankfully we have some great achievements to share.

Earlier we mentioned that we launched our **2020 National Report Card** survey to our membership; we are thrilled to report we had a fantastic participation rate. We want to thank our tireless Board members and volunteers, Lorraine Coumont, Michelle Cooper, Suzanna LeVatte-MacDonald, Tina McGrath, Anne Rowe, Tamara Phillips, and Kim Speiss, who got on their phones and computers to contact our members to ask they fill out this important survey. Their huge efforts were greatly appreciated. We also need to thank our engaged and dedicated members who took the time to carefully fill out this survey to provide the important data that will ultimately be used to understand patient product use, symptoms and needs so we may continue to advocate for improved access to treatments for Canadians living with HAE.

In November 2020, we were proud to learn that our abstract titled **'Real World Data of Canadian Adults living with Angioedema – Health Economic Burden'** was accepted as a poster presentation to the 2021 AAAAI Virtual Annual Meeting in February 2021. We are very fortunate to have a talented team to help develop our abstracts. Once again, Dr. Suzanne Kelly of Red Maple Trials was key in developing this abstract and poster, and our Advocacy Committee and Board members provided helpful assistance.

Also, in November 2020, we held our **Annual General Meeting** when we successfully passed our updated Bylaws and welcomed three new Board members: Carmen Craciun (Director at Large), Michelle Cooper (Regional Director: Ontario) and Suzanna LeVatte-MacDonald (Regional Director: Atlantic). We are excited to work with our new Board members who will bring enthusiasm and their own expertise to the Board. We also said goodbye and thank you to three outgoing Board members: Richard Badiou, Anne Rowe, and Kari Feere whose contributions over these past years have been greatly appreciated. Richard spent many years as Treasurer, ensuring HAE Canada's finances are properly kept in order in accordance with all rules and regulations. We are grateful Richard will remain on our Finance Committee. Anne Rowe is also leaving our Board; however, thankfully she will remain on our Governance Committee. Anne has been with HAE Canada from the start and has spent many years ensuring we adhere to all proper governance rules, while sharing her nursing knowledge with the rest of the Board. Her years devoted to HAE Canada are truly appreciated. Kari has provided support to the Atlantic members for the past few years and her kindness was appreciated. We are thankful that three Board members have agreed to remain with HAE Canada for another year: Jacquie Badiou (President), Tina McGrath (VP) and Lorraine Coumont (Pacific Regional Director).

For the past few years, staff at Takeda Canada have been diligently working towards providing HAE patients in Canada with lanadelumab (Takhzyro). We are thrilled to report that this hard work and dedication is paying off because **eligible HAE patients in Alberta, British Colombia, Manitoba, New Brunswick, and Ontario now have access to lanadelumab** through their provincial drug plans. It has been a long journey to arrive where we are today, and we are proud we helped advocate to get at this point in the road.

In February, Jacquie Badiou, HAE Canada's President, participated in Health Canada's virtual meeting titled: **'National Strategy on High-Cost Drugs for Rare '"** to help provide input into how best to create a national strategy on high-cost drugs for rare diseases. HAE Canada is encouraged and excited that long awaited attention is going towards learning how to provide patients with rare diseases access to important treatments in Canada.

We continue to hope people are staying safe and coping to make it through what hopefully is the final stretch of this COVID-19 pandemic.

ARMENIA

HAEi welcomes the national organization in Armenia as a new user of the global web hosting service.

Please see www.hae.am for the HAE Armenia website.

FRANCE

In February, HAE France (AMSAO) presented a video conference meeting with the adult and pediatric team from the angioedema reference center CREAK in Grenoble. The event was intended for children or adolescents and their parents as it enabled the sharing of information and experiences between caregivers and patients.

Dr. Boccon-Gibod talked about the 130 children currently followed by CREAK, while the pediatric psychologists Karine Guichardet and Gaëlle Buisson-Papet discussed with participants the feelings experienced by children or their parents during HAE attacks. The program also included a talk by Dr. Kevorkian-Verguet on clinical trials in children, while

President Michel Raguet of HAE France briefly recounted the history of the patient association founded 24 years ago. He highlighted the move towards better diagnostics, the arrival of emergency treatments (Berinert and Firazyr) and more recently the arrival of two new prophylactic treatments with monoclonal antibodies which restrict the production of kallikrein (lanadelumab and berotralstat).

The French National Agency for Medicines and Health Products Safety has granted a temporary authorization for use for Orladeyo (berotralstat) to prevent HAE attacks in patients aged 12 and older. This allows people with HAE in France to receive treatment with berotralstat before the drug is granted marketing authorization by the European Commission. The final approval decision from the Commission on the marketing authorization application for Orladeyo – a brand of plasma kallikrein inhibitor delivered through oral administration and is approved for self-administration – is expected in the second quarter of 2021.

UNITED ARAB EMIRATES

The national organization in the United Arab Emirates has changed its national contact. The new person in charge in Shradha Singhania – please see contact information at haei.org/hae-member-countries/united-arab-emirates.

THAILAND

HAEi welcomes the new national contact for HAE Thailand: Suchitta Kengtanyagarn. Please see details at https://haei.org/location/hae-in-thailand.

SERBIA

From Ivana Golubović, HAE Serbia

2020 has been a challenging year for our HAE community. Delays in the supply of our medicines, limited access to hospital care, etc. However, it also gave me the impression that rare disease patients mentally handled the COVID-19 situation much better than the rest of our otherwise healthy community. Some would say that, due to the nature of our illness, we are more used to being locked inside and that the concept of mortality is somehow closer to us. We surely do meditate on death more often than a regular person. An average HAE patient twice a month.

So, what is our cure for anxiety? Live your life. Even during the pandemic, adjust and make the most of each day. It may seem counterintuitive not to put your plans on hold, but it is important to make plans. Yes – make plans. Remember, the lesser you live your life, the greater anxiety you will suffer, as Yalom put it. Also – prepare. Prepare in whatever way makes you feel prepared for the future, the readiness is all. Last year, on rare disease day, two weeks prior to the lockdown we organized a training in self-administration of our medicines. It helped us fell more ready for what will follow.

And on a final note – the only thing constant is change & this too shall pass!

SPAIN

From President Sarah Smith, HAE Spain (AEDAF)

Activities: We do not plan to hold any face-to-face events in 2021 due to the ongoing pandemic. We are involved in various activities, including a documentary for **hae day :-)** 2021, informative online training courses and programs, a burden of illness survey, etc. We also plan to begin very soon a survey to understand the differences in patient access to treatment and modern HAE therapies depending on place of residence, as there are still obvious and glaring differences in patient care across Spain's 17 autonomous regions.

Commercialization of Takhzyro: Takeda has announced the commercialization in Spain of Takhzyro (lanadelumab), a subcutaneously administered drug approved in Europe for the routine prevention of recurring attacks of HAE in patients over 12 years of age. It is very good news for the Spanish HAE patient community to have this medicine added to the other currently available HAE therapies.

UKRAINE

In March 2020, Cinryze was registered and for some months now the medication has been physically available to HAE patients in Ukraine.

AUSTRALIA & NEW ZEALAND

From CEO Fiona Wardman, HAE Australasia

HAE Australasia held a strategy meeting to talk about current and new projects for the year ahead. We have some exciting and useful ideas for projects and initiatives, and we look forward to bringing them to fruition.

HAE Australasia is very proud of the videos and downloadable documents for new resources on our website called 'Living Well with HAE'. HAE Australasia engaged one of our very supportive Clinical Psychologists who has worked with our Australasian patients over the years. Dr. Chris Basten gives helpful tips to managing stress and anxiety and coping with empathy gaps and emotions related to HAE. The 'Living Well with HAE' videos series is available to view via haeaustralasia.org.au/resources/video-resources/.

HAE Australasia has written a formal letter to the National Blood Authority on behalf of patients who no longer have access to Danazol as this medication is discontinued and ineligible to receive long-term prophylaxis access due to the current strict criteria of eight attacks or more a month.

Plans are underway for our 10th birthday celebrations later in the year, which will coincide with the HAE Australasia Patient & Carers Conference – more details soon!

HAE Australasia is looking forward to both New Zealand and Australian patients and their family and their friends taking in the HAEi **hae day :-)** campaign.

MEDICAL PAPERS

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

Assessing the cost and quality-of-life impact of on-demand- only medications for adults with HAE – *by Anthony J. Castaldo, US HAEA, the United States of America, et al.:*

Novel subcutaneous prophylactic therapies are transforming the treatment landscape of HAE. Although questions are being raised about their cost, little attention has been paid to the cost and quality of life impact of using on-demand-only medications. This study shows the cost and quality of life burden of HAE treatment with on-demand-only therapy. Use of novel subcutaneous prophylaxis can lead to sizeable reductions in attack frequency and statistically significant and clinically relevant improvements in quality of life.

(Allergy Asthma Proc, Mar 2021)

A case of HAE due to C1-inhibitor deficiency with recurrent abdominal pain diagnosed 40 years after the occurrence of the initial symptom – *by Daisuke Honda, Juntendo University, Japan, et al.:*

A 56-year-old patient with HAE-C1-INH underwent numerous abdominal operations and frequently needed hospitalization with the administration of opioid due to severe abdominal pain. After diagnosis with HAE-C1-INH at 55, he started self-administration for acute attacks with icatibant and didn't need hospitalizing for ten months after the beginning of the treatment, thus improving his quality of life.

(Clin J Gastroenterol, Feb 2021)

Biomarkers in HAE – *by Grzegorz Porebski, Jagiellonian University Medical College, Poland, et al.:*

Although biomarkers have been extensively investigated and validated in many diseases and pathologies, very few are currently useful for the diagnosis, evaluation of disease activity, and treatment of HAE. Pathophysiologic pathways involved in HAE reveal a plethora of molecules from the complement, coagulation, and fibrinolysis systems or from the vascular endothelium, which may serve as biomarkers. The most promising candidates should be evaluated with regard to their analytical and clinical validity and utility. Such biomarkers should be linked to the pathomechanisms of HAE, particularly the bradykinin-generating cascade. Additionally, major advances in high-throughput omics-based technologies may facilitate the discovery of new candidate biomarkers.

(Clin Rev Allergy Immunol, Feb 2021)

Current and Prospective Targets of Pharmacologic Treatment of HAE Types 1 and 2 – *by Lauré M Fijen, University of Amsterdam, the Netherlands, et al.:*

The emergence of improved treatment options will presumably change HAE guidelines, but adherence to these recommendations may become restricted by high treatment costs. It is therefore essential to determine the indications and identify the patients that will benefit most from the newest treatment generations. Ultimately, current preclinical research into gene therapies may lead towards curative treatment options. An increasing shift towards the use of highly effective long-term prophylaxis is anticipated, drastically abating the burden on HAE patients.

(Clin Rev Allergy Immunol, Jan 2021)

Current medical management of HAE: Follow-up survey of US physicians – *by Marc A. Riedl, University of California San Diego School of Medicine, the United States of America, et al.:*

US physician survey data reflect improvements in the HAE management in recent years. Therapeutic advances in HAE have led to reported higher rates of home treatment of attacks, reduced concern for adverse treatment effects, and high levels of patient satisfaction.

(Ann Allergy Asthma Immunol, Oct 2020)

HAE: a disease seldom diagnosed by pediatricians – *by Régis de Albuquerque Campos, Universidade Federal da Bahia, Brazil, et al.:*

HAE is little known by pediatricians due to delay in diagnosis. The presence of recurrent angioedema that does not respond to treatment with antihistamines, corticosteroids and adrenaline should increase the diagnostic suspicion.

(J Pediatr (Rio J), Nov 2020)

HAE Attack in Utero and Treatment of the Mother and Fetus – *by Vesna Grivcheva-Panovska, University Saints Cyril and Methodius, North Macedonia, and Bruno Giannetti, Pharming Group NV, the Netherlands:*

A 23-year-old woman with type I HAE had abdominal, facial, and peripheral attacks throughout her first pregnancy. Two hours after treatment of her HAE attack, she spontaneously delivered a healthy male infant. Photographs taken within two minutes of delivery revealed resolution of the infant's facial edema, and the limb edema was resolved within 30 minutes. By 10 minutes postdelivery, the mother's facial attack had almost completely resolved. Ten months after birth, genetic analysis confirmed that the infant had type I HAE. This is the first documented case of an HAE attack in utero.

(Mayo Clin Proc Innov Qual Outcomes, Aug 2020)

HAE Due to C1-Inhibitor Deficiency in Romania: First National Study, Diagnostic and Treatment Challenges – *by Gabriella Gabos, George Emil Palade University of Medicine, Romania, et al.:*

A cross-sectional observational study of patients from the Romanian HAE Registry show significantly lower delay in children suggesting an improvement in the awareness of C1-INH-HAE among physicians in recent years. The management of HAE in Romania has been somewhat enhanced as the majority of HAE patients have recently gained access to pdC1-INH, rhC1-INH, and bradykinin B2-receptor antagonist.

(Iran J Immunol, Sep 2020)

HAE in children and adolescents - A consensus update on therapeutic strategies for German-speaking countries – *by Volker Wahn, Charité Universitätsmedizin, Germany, et al.:*

Currently, plasma-derived C1-INH concentrates have the broadest approval status and are considered the best available option for on-demand treatment of HAE-C1-INH attacks and for short- and long-term prophylaxis across all pediatric age-groups in German-speaking countries. For on-demand treatment of children aged two years and older, recombinant C1-INH and bradykinin-receptor antagonist icatibant are alternatives. For long-term prophylaxis in adolescents, the parenteral kallikrein inhibitor lanadelumab has recently been approved and can be recommended due to proven efficacy and safety.

(Pediatr Allergy Immunol, Nov 2020)

HAE patients would prefer newer-generation oral prophylaxis – *by Daniela Geba, KJT Group, the United States of America, et al.:*

An online survey conducted in 2018 among adult patients in the United States of America diagnosed with Type I or II HAE shows that most patients would prefer a newer generation oral prophylactic medication that would decrease treatment burden and allow them to live fuller lives.

(J Drug Assess, Jan 2021)

HAE: Special considerations in children – *by Douglas T. Johnston, Asthma and Allergy Specialists, and Christina Smith, Levine Children's Hospital, the United States of America:*

Young children are uniquely vulnerable as attacks may be subtle, resemble other diseases, and often lead to a delay in diagnosis. Misdiagnosis contributes to significant delays in treatment, painful attacks, increased emotional stress, unnecessary procedures, and a potential risk of death. Older children may hide their symptoms due to anxiety or fear of social isolation. Attacks typically become more severe and more frequent during and after puberty. The impact of HAE attacks on school attendance and school performance may prevent future career or education opportunities. Living with HAE poses significant psychosocial stress on children and their families. Physicians should screen all children with a family history of HAE, appreciate the dynamic nature of the disease during adolescence, proactively assess the psychosocial impact of disease, and continually reassess the treatment plan.

(Allergy Asthma Proc, Nov 2020)

HAE: Special considerations in women – *by Elizabeth Yakaboski, Massachusetts General Hospital, the United States of America, et al.:*

The disease course during pregnancy is unpredictable, but studies show that plasma-derived C1-INH is effective and safe for treatment of attacks as well as long-term prophylaxis in select patients. Vaginal deliveries are preferred to caesarean sections, and epidural anesthesia is preferred to general anesthesia in lowering the risk of an acute attack. Lactation postpartum may increase HAE attacks. With regard to contraception, combined oral contraceptive pills that contain estrogen exacerbate symptoms. Similarly, estrogen-replacement therapy in menopause may increase attacks and is contraindicated. Fertility is not impacted by HAE itself or by HAE medications. The risk of breast cancer and female reproductive cancer in women with HAE is comparable with that of the general population, but, in patients with HAE and breast cancer, long-term prophylaxis with androgens is contraindicated. Estrogen modulators, e.g., tamoxifen, should be used with caution.

(Allergy Asthma Proc, Nov 2020)

HAE with and Without C1-Inhibitor Deficiency in Postmenopausal Women – *by Aurore Billebeau, Hôpital Port Royal, Université de Paris, France et al.:*

Following menopause, most women with HAE remain stable but some worsen. Improvement was mainly observed in patients with previous estrogen sensitivity.

(J Clin Immunol, Jan 2021)

Long-term health-related quality of life in patients treated with subcutaneous C1-inhibitor replacement therapy for the prevention of HAE attacks: findings from the COMPACT open-label extension study – *by William R. Lumry, AARA Research Center, the United States of America, et al.:*

Long-term subcutaneous C1-INH replacement therapy in patients with C1-INH-HAE leads to significant and sustained improvements in multiple measures of health-related quality of life.

(Orphanet J Rare Dis, Feb 2021)

Quality of life in patients with HAE in Canada – *by Erika Yue Lee, St. Michael's Hospital, University of Toronto, Canada et al.:*

HAE continues to impair quality of life in Canadian patients despite receiving recommended treatment. Although the frequency of attacks affects quality of life, patients' experience with their HAE care also affects quality of life substantially.

(Ann Allergy Asthma Immunol, Jan 2021)

Oral berotralstat for the prophylaxis of HAE attacks in patients in Japan: A phase 3 randomized trial – *by Isao Ohsawa, Saiyu Soka Hospital, Japan et al.:*

Orally administered, once-daily berotralstat 150 mg significantly reduced the frequency of HAE attacks and was safe and well tolerated, supporting its use as a prophylactic therapy in patients with type 1 or 2 HAE in Japan.

(Allergy, Nov 2020)

The diagnosis and treatment of HAE patients in Japan: A patient reported outcome survey – *by Kazumasa Iwamoto, Hiroshima University, Japan et al.:*

There is a long gap between first attack and diagnosis of HAE, and the number of non-treated attacks is high in Japan. Therefore, steps are needed to improve the diagnostic and treatment environments.

(Allergol Int, Nov 2020)

US HAEA Medical Advisory Board 2020 Guidelines for the Management of HAE – *by Paula J. Busse, Mount Sinai School of Medicine, the United States of America, et al.:*

Advances in HAE treatment now allow the development of management plans that can help many patients with HAE lead a normal life. Achieving this goal requires that physicians be familiar with the diagnostic and therapeutic transformations that have occurred in recent years.

(J Allergy Clin Immunol Pract, Jan 2021)

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 multicenter, double-blind, randomized, placebo-controlled, parallel-arm study to investigate the efficacy and safety of subcutaneous administration of CSL312 (garadacimab) in the prophylactic treatment of HAE

– recruiting in Canada, Germany, Hungary, Israel, Italy, the Netherlands, Spain, and the United States of America

A multicenter, randomized, placebo-controlled, parallel-arm study to investigate the efficacy, pharmacokinetics, and safety of CSL312 in subjects with HAE

– recruiting in Australia, Canada, Denmark, Germany, Israel, and the United States of America

An Open-Label study to Evaluate the Long-Term Safety of Daily Oral BCX7353 in subjects with Type I and II HAE

– recruiting in Australia, the European Union, Hong Kong, Israel, New Zealand, North Macedonia, Serbia, South Africa, South Korea, Switzerland, and the United States of America

An Open-Label Extension Study of ISIS 721744 in Patients with HAE

– recruiting in the Netherlands, the United Kingdom, and the United States of America

A Phase II, double-blind, placebo-controlled, Randomized, cross-over, dose-ranging study of oral PHA-022121 for Acute treatment of angioedema attacks in Patients with HAE due to C1-Inhibitor Deficiency type I and II

– recruiting in Belgium, Canada, France, Germany, Hungary, Israel, Italy, the Netherlands, Poland, Spain, and the United Kingdom

A randomized, double-blind, placebo-controlled, phase II, cross-over clinical trial evaluating the efficacy and safety of KVD900, an oral plasma kallikrein inhibitor, in the on-demand treatment of angioedema attacks in adult subjects with HAE type I or II

– recruiting in North Macedonia and the United States of America

A Randomized, Double Blind, Placebo Controlled, Phase 2a Study to Assess the Clinical Efficacy of ISIS 721744, a Second Generation Ligand Conjugated Antisense Inhibitor of Prekallikrein, in Patients with HAE

– recruiting in the Netherlands, the United Kingdom, and the United States of America

A Study of Icatibant (TAK-667) in Japanese Children and Teenagers with Acute Attacks of HAE

– recruiting in Japan

Biomarker for HAE Disease

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

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

CSL312 (Garadacimab) in the Prevention of HAE Attacks

– recruiting in Canada and the United States of America

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

– recruiting in Canada

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

– recruiting in Japan

Efficacy and Safety of Lanadelumab for Prevention Against Acute Attacks of Non-histaminergic Angioedema with Normal C1-Inhibitor (C1-INH)

– recruiting in the United States of America

Epidemiological Analysis for HAE Disease

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

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

Patient Registry to Evaluate the Real-world Safety of Ruconest

– recruiting in the United States of America

Pharmacokinetics and Safety of Human Pasteurized C1-Inhibitor Concentrate (Berinert/CE1145) in Subjects with Congenital C1-INH Deficiency and Frequent HAE Attacks

– recruiting in Italy

Prospective, open-label, single arm, multicenter, pharmacokinetic, and safety study of a single dose intravenous human plasma-derived C1 Esterase Inhibitor (C1-INH) concentrate in patients with congenital C1-INH deficiency and HAE

– recruiting in Belarus, Bulgaria, Czech Republic, Germany, Hungary, Poland, the Russian Federation, Serbia, and Ukraine

Spring Study: An Open-Label, Multicenter, Phase 3 Study to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of Lanadelumab for Prevention Against Acute Attacks of HAE in Pediatric Subjects 2 to <12 Years of Age

– recruiting in Canada, Germany, Hungary, Spain, and the United States of Americ

Study to Evaluate the Real-world Effectiveness of Lanadelumab in Participants with HAE

– recruiting in Canada, Puerto Rico, and the United States of America

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 Long-Term Safety and Efficacy of Lanadelumab for Prevention of Acute Attacks of Non-histaminergic Angioedema with Normal C1-Inhibitor

– will be recruiting in the United States of America

Japan Expanded Access Program with Lanadelumab for Japanese Patients with HAE

– will be recruiting in Japan

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

– will be recruiting (countries will be disclosed later)

Read more about these and other clinical trials at

clinicaltrials.gov

clinicaltrialsregister.eu

apps.who.int/trialsearch

NEWS FROM THE INDUSTRY

10 December 2020

China's National Medical Products Administration (NMPA) has approved Takhzyro (lanadelumab) subcutaneous injection for prophylaxis to prevent attacks of HAE in patients 12 years and older. Takhzyro from **Takeda Pharmaceutical Company Limited** is a fully human monoclonal antibody (mAb) that inhibits the activity of plasma kallikrein, an enzyme which is uncontrolled in people with HAE, to help prevent HAE attacks.

"The approval of Takhzyro is exciting news for the HAE community in China", says Fiona Wardman, the Chief Regional Patient Advocate at Hereditary Angioedema International. "Until now, no modern therapies have been available to HAE patients in the country, and people with HAE rely on anabolic androgens and tranexamic acid for prophylaxis, and fresh frozen plasma for emergencies. The availability of Takhzyro to help prevent HAE attacks represents significant progress for those living with this chronic condition."

"This milestone demonstrates Takeda's ongoing commitment to support the HAE community globally, as we work to expand access to Takhzyro and potentially 14 more highly innovative Takeda medicines to China's patients over the next five years," says Sean Shan, President of Takeda China. "The Chinese government's recent healthcare reforms play an evolving role in reaccelerating the delivery of important therapies like Takhzyro to as many patients as possible through their efforts to increasingly reward innovation."

Takhzyro has a half-life of approximately two weeks and may be self-administered as one subcutaneous injection every two weeks, only after training by a healthcare professional. The recommended starting dose is 300 mg every two weeks. A dosing interval of 300 mg Takhzyro every four weeks is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than six months. In clinical trials, the majority of patients took within 10 to 60 seconds to administer the injection.

Takhzyro is currently available in more than 20 countries and additional regulatory submissions are ongoing worldwide.

(Source: Takeda)

10 December 2020

The first patient has been enrolled in a randomised, open label, parallel group, controlled, pilot clinical trial in up to 120 patients hospitalized with confirmed COVID-19 treated with Ruconest (recombinant human C1 inhibitor) for the prevention of severe SARS-CoV-2 infections at the Valley Hospital in Ridgewood, New Jersey in the United States.

Initially based at Valley Hospital in Ridgewood, New Jersey, this trial is planned to include patients at multiple centres in the US. This clinical trial follows an ongoing investigator-initiated, multinational, multicentre study, led by Dr. Michael Osthoff from the University Hospital Basel, into the use of Ruconest in the prevention of severe SARS-CoV-2 infections in patients hospitalised with related severe pneumonia. **Pharming Group N.V.** announced the enrolment of the first patient in that trial in August 2020.

Systemic hyperinflammation is a hallmark of more severe stages of COVID-19 leading to acute respiratory distress syndrome, mechanical ventilation and ultimately death. Treatment with Ruconest may; 1) dampen uncontrolled complement activation and collateral lung damage; 2) reduce capillary leakage and subsequent pulmonary edema by direct inhibition of the kallikrein-kinin system; and 3) reduce the generation of microthrombi by inhibiting MASP-1 induced clot formation and factor XII amplified thrombo-inflammation.

C1 inhibitor is an acute phase reactant, meaning that the body naturally increases production during inflammatory conditions, such as infections. Despite this, a relative deficiency may occur and complement activation continues unchecked, often leading to a cytokine storm, a dangerous biochemical process that worsens the complications of COVID-19 infection, such as organ failure and death.

These clinical studies in hospitalized patients with confirmed COVID-19 seek to identify if the administration of additional C1INH can control or stop the systemic hyperinflammation syndrome or cytokine storm. Headline data will be made publicly available following either an interim analysis or after all patients have been treated.

(Source: Pharming)

10 December 2020

In the operational update and financial results for the second fiscal quarter ended 31 October 2020 CEO Andrew Crockett of **KalVista Pharmaceuticals, Inc.** says:

"We have completed the patient treatment phase of our KVD900 Phase 2 trial and are in the process of wrapping up that study. Data from this trial evaluating KVD900 as an oral on-demand treatment for HAE is expected in the first quarter of 2021. The formulation data recently shared for KVD824, our oral prophylactic treatment candidate for HAE, showed concentrations that we believe can lead to efficacy levels competitive with approved injectable therapies. We expect to submit an Investigational New Drug Application to the FDA for a Phase 2 clinical trial of KVD824 as a potential twice-daily oral treatment in the prevention of HAE attacks in the first quarter of 2021."

Second Fiscal Quarter and Recent Business Highlights:

- Completed treatment of the planned target of 50 patients in a Phase 2 clinical trial intended to evaluate the safety and efficacy of KVD900 as an oral on-demand treatment of HAE attacks. This trial is expected to provide data in the first quarter of 2021. A Pediatric Investigational Plan (PIP) has also been approved by the European Medicines Agency (EMA) for KVD900.
- Provided data on KVD824 as a twice-daily oral candidate for prophylactic treatment of HAE. Work to optimize the exposure profile of KVD824 yielded a formulation that maintains the plasma concentrations KalVistabelieves are required to compete with approved injectable therapies, while showing an encouraging safety and tolerability profile in up to 14 days of dosing. An Investigational New Drug Application (IND) submission to the U.S. Food and Drug Administration (FDA) for a Phase 2 clinical trial is expected in the first quarter of 2021.
- Announced a novel oral Factor XIIa inhibitor program as the next area of development focus. KalVista's internal research team has discovered multiple series of oral Factor XIIa inhibitors, initially being advanced with the potential to provide the next generation of HAE therapeutics. IND-enabling studies for potential oral Factor XIIa inhibitor candidates are expected in 2021.

(Source: KalVista)

16 December 2020

BioCryst Pharmaceuticals, Inc. announces that oral, once-daily Orladeyo (berotralstat) is now available for shipment to patients with a prescription in the United States.

Orladeyo was approved by the U.S. Food and Drug Administration (FDA) on 3 December 2020 for prophylaxis to prevent attacks of HAE in adults and pediatric patients 12 years and older. Optime Care, Inc., the exclusive specialty pharmacy provider for Orladeyo, has begun shipping to patients today.

"Access to medicine is critical to HAE patients. Many patients have been waiting for an oral option and I am very pleased that they have support from BioCryst to access Orladeyo so quickly following FDA approval," says Douglas R. Lotz, M.D., senior partner, Family Allergy & Asthma, Louisville, KY.

BioCryst is committed to supporting HAE patients taking Orladeyo through a new program designed to streamline access to therapy. Through EMPOWER Patient Services, each HAE patient and their healthcare provider will have a single point of contact for access to Orladeyo. A dedicated care coordinator will support access for each patient with comprehensive financial support tools and reimbursement support.

"Our goal is to provide a best-in-class partnership that enables an individualized approach for physicians and their patients," said Charlie Gayer, chief commercial officer of BioCryst. "Through our dedicated care coordinators, we offer a single point of contact to assist patients and healthcare providers throughout the treatment journey. From the transition to Orladeyo, coordination of deliveries, to ongoing patient support, EMPOWER puts the HAE patient at the center."

Orladeyo is the first and only oral therapy designed specifically to prevent attacks of HAE in adults and pediatric patients 12 years and older. One capsule of Orladeyo per day works to prevent HAE attacks by decreasing the activity of plasma kallikrein.

(Source: BioCryst)

10 January 2021

Intellia Therapeutics, Inc. outlines its expected 2021 milestones and strategic priorities regarding HAE therapy:

"Since our founding, we set out to develop modular platform components that could serve as the engine powering an expansive portfolio of curative therapeutics. We have paved a rapid and reproducible development path for both in vivo and engineered cell therapies to address serious genetic diseases and cancers. Over the next 12 months, we anticipate first-in-human regulatory submissions for NTLA-2002," says Intellia President and CEO John Leonard, M.D.

NTLA-2002 aims to prevent attacks and eliminate the current, significant treatment burden for people living with HAE after a single course. Intellia is applying its modular LNP delivery system to develop NTLA-2002 to knock out the KLKB1 gene in the liver to permanently reduce plasma kallikrein activity.

- Intellia plans to submit an IND or equivalent regulatory application in the second half of 2021.
- The Company is applying insights gained from NTLA-2001 to expedite clinical development of NTLA-2002.

(Source: Intellia)

14 January 2021

A recent Harris Poll, commissioned by CSL Behring, asked patients who have HAE to assess how the unpredictable condition affects them. In the survey, patients also gave their thoughts on treating the condition, which causes dangerous swelling episodes.

Here are some highlights from the survey, which also included responses from physicians:

More than 40% of patients said the condition had a significant impact on daily activities, but doctors were much less likely to say the same. More than 75% of patients said they worry every day about having an HAE attack. Both patients (94%) and physicians (91%) agree that a reduction in the number of attacks is the leading driver when making treatment decisions, followed closely by the importance of safety. The vast majority of patients (94%) said it's important their preventive therapy specifically corrects C1 esterase inhibitor (C1-INH) deficiency.

(Source: CSL Behring)

22 January 2021

The Ministry of Health, Labor and Welfare (MHLW) in Japan has granted marketing and manufacturing approval for **BioCryst Pharmaceuticals, Inc.**'s oral, once-daily Orladeyo (berotralstat) 150 mg for prophylactic treatment of HAE in adults and pediatric patients 12 years and older.

Orladeyo is the first and only prophylactic HAE medication approved in Japan. One capsule of Orladeyo per day works to prevent HAE attacks by decreasing the activity of plasma kallikrein.

Orladeyo will be commercialized in Japan by BioCryst's partner, Torii Pharmaceutical Co., Ltd. OrphanPacific, Inc. is BioCryst's representative partner in Japan and holds the marketing authorization.

Torii will launch Orladeyo in Japan following the successful completion of BioCryst's pricing negotiations with the Japanese National Health Insurance System (NHI).

"Until now, HAE patients in Japan had no therapies approved to prevent attacks, so the approval of Orladeyo marks a significant advance in HAE treatment," says Goichi Matsuda, President of Torii. "We are pleased to have the opportunity to bring the first oral treatment option to Japanese HAE patients and are actively preparing for the commercialization."

"The approval of Orladeyo in Japan represents important progress towards our goal to bring an oral, once-daily treatment to HAE patients around the world," says Jon Stonehouse, President and CEO of BioCryst. "Thank you to the HAE patients who participated in our APeX-J trial, to the investigators who conducted it, and to Torii and OrphanPacific for their partnership to achieve this milestone to offer a much-needed new treatment option to HAE patients and physicians in Japan."

BioCryst received Orphan Drug and Sakigake designation for Orladeyo in Japan and the approval is based on data from the APeX-J and APeX-2 clinical trials. The APeX-J trial in Japan met its primary endpoint (p=0.003) of a reduction in HAE attacks from baseline for Orladeyo 150 mg compared to placebo, and Orladeyo was safe and generally well-tolerated in the trial. In APeX-2, Orladeyo also met its primary endpoint (p<0.001) for Orladeyo 150 mg compared to placebo and was safe and generally well-tolerated.

In December 2020, the U.S. Food & Drug Administration (FDA) approved Orladeyo in the U.S. In Europe, the European Medicines Agency (EMA) validated its marketing authorization application (MAA) submission for Orladeyo and formal review of the MAA under the centralized procedure is underway. The company expects an approval decision in Europe in the second quarter of 2021.

(Source: BioCryst)

28 January 2021

From its Phase 1 multiple-ascending-dose study demonstrating PHA121's pharmacokinetics and tolerability **Pharvaris** announces that PHA121 was well tolerated at all doses studied, with approximately dose-proportional exposure.

"We are encouraged by these results to continue development of PHA121 as an oral treatment for HAE," says Berndt Modig, CEO and co-founder of Pharvaris. "In 2021, we will explore the therapeutic potential of PHA121 for both acute and prophylactic treatment of HAE. Our upcoming Phase 2 studies will utilize PHVS416, a soft capsule formulation containing PHA121."

The Phase 1 randomized, double-blind, placebo-controlled, multiple ascending dose trial examined the safety, tolerability, and pharmacokinetics of PHA121 in healthy volunteers. The trial included 38 healthy subjects dosed twice daily (BID) for 10 days in four sequential dosing cohorts, ranging from 12 to 50 mg. During the study, PHA121 was well tolerated up to the highest dose of 50 mg BID. All reported treatment-emergent adverse events (TEAEs) were mild in intensity and resolved completely. The total incidence and type of TEAEs were similar between active drug and placebo groups. Lab safety, vital signs, and ECG parameters remained well within normal limits in all subjects. The pharmacokinetic profile suggests that therapeutic drug levels of PHA121 were achieved in day 1 and steady-state plasma concentrations were reached within 72 hours.

PHVS416 is a soft capsule formulation containing PHA121 (PHA-022121), a highly potent, specific, and orally bioavailable competitive antagonist of the bradykinin B2 receptor. Pharvaris is developing this formulation to provide rapid exposure of attack-mitigating medicine in a convenient, small oral dosage form.

PHA121 (PHA-022121) is a highly potent, specific, and orally bioavailable competitive antagonist of the human bradykinin B2 receptor currently in Phase 1 clinical development for the treatment of HAE. PHA121 utilizes the same mechanism as icatibant, the leading therapy for on-demand treatment of HAE. Pharvaris is developing this novel small molecule for on-demand and prophylactic treatment of HAE and other bradykinin-mediated disease through formulations optimized for each setting.

(Source: Pharvaris)

29 January 2021

Sandoz Inc. has launched its generic Icatibant injection pre-filled syringe to treat acute attacks of HAE in adults 18 years and older. It is available immediately for US patients.

Sandoz has signed a US commercialization deal with Slayback Pharma, a company focused on producing complex generic and specialty pharmaceutical products, for this medicine, which is a generic equivalent to Takeda's Firazyr (icatibant injection).

"We are eager to see the positive effects of making generic Icatibant available immediately to people living with this painful and disabling rare disease," says Keren Haruvi, President, Sandoz. "This collaboration aligns with our goal to build our injectables portfolio and provide US patients access to affordable generic medicines that work the same as brand-name products."

"With our strong developmental capabilities and Sandoz's industry-leading commercialization of its extensive portfolio of generic medicines, we couldn't be more excited to collaborate with Sandoz and help people living with HAE," says Ted Smolenski, Vice President of Business Development at Slayback Pharma.

(Source: Sandoz)

1 February 2021

After the acquisition of **Quellis Biosciences Inc.**, Catabasis Pharmaceuticals, Inc. expects to enable the completion of IND-enabling studies, Phase 1a, and Phase 1b/2 clinical trials for the lead program QLS-215 in HAE.

"Our mission has always been to bring life-changing therapies to patients and families affected by rare diseases. We look forward to progressing QLS-215, a differentiated and potential best-in-class new therapy for patients affected by HAE", says Kenneth Bate, Chair of the Catabasis Board of Directors.

The vision for QLS-215 is to develop the best-in-class monoclonal antibody inhibitor of plasma kallikrein for HAE with infrequent dosing and sustained blood levels. QLS-215 is a humanized monoclonal antibody targeting plasma kallikrein that has demonstrated potent inhibition of plasma kallikrein as well as extended plasma half-life in non-human primates. Catabasis expects to file an Investigational New Drug application for QLS-215 in the first half of 2022 and plans to initiate a Phase 1 clinical trial with initial results anticipated by the end of 2022. Subsequently, Catabasis expects to initiate a Phase 1b/2 trial in patients affected by HAE in 2023 with initial results anticipated by the end of 2023.

(Source: Catabasis)

9 February 2021

KalVista Pharmaceuticals, Inc. announces positive topline data from a Phase 2 clinical trial demonstrating statistically and clinically significant efficacy of KVD900 as an oral on-demand treatment for HAE attacks.

"We are very excited to share this positive data which shows that KVD900 is the first oral therapy to achieve clinical efficacy results comparable to current injectable therapies, while also demonstrating a promising safety and tolerability profile. The rapid onset of symptom relief and significant reduction in the use of rescue medication show that patients can confidently take KVD900 at the earliest signs of an attack and avoid the burden and discomfort of injections," says Andrew Crockett, CEO of KalVista. "We look forward to working with regulatory agencies to bring the many advantages of KVD900 to patients as quickly as possible. In parallel, we remain committed to advancing our oral HAE franchise, with submission of an IND this quarter for KVD824 as a prophylactic treatment and ongoing preclinical work on our oral Factor XIIa program."

The KVD900 Phase 2 was a randomized, double-blind, placebo-controlled, crossover clinical trial evaluating the efficacy and safety of KVD900 as an on-demand treatment for HAE attacks. The trial completed 53 adult HAE patients from 25 clinical sites in the United States and Europe. The trial included type 1 and type 2 HAE patients who had three attacks in 90 days prior to enrollment. During the first part of the two-part trial, patients received a single, open label 600 mg dose of KVD900 to evaluate pharmacokinetic and pharmacodynamic properties. All patients then entered part two of the trial, which was a double-blind investigation to assess the efficacy of KVD900 compared to placebo in a two-attack, crossover design. During part two of the trial, patients took a single dose of 600 mg of KVD900 or placebo within one hour of the start of the first attack. The second attack was dosed with the alternative crossover treatment. Patients were able to use their conventional rescue treatment, as required.

Topline Phase 2 Results

- Attacks treated with KVD900 significantly reduced use of rescue (p=0.001), with 15% of KVD900 treated attacks rescued compared to 30% on placebo at 12 hours.This efficacy benefit of KVD900 was maintained at 24 hours (p=0.0005).
- KVD900 significantly reduced time to onset of

symptom relief (p=<0.0001) on a Patient Global Impression of Change scale (PGI-C), with a median time of 1.6 hours versus 9 hours for attacks treated with placebo.
- KVD900 treated attacks achieved symptom relief more quickly than placebo treated attacks (p<0.0001) when assessed using a composite Visual Analogue Scale (VAS) score.
- Within 12 hours of oral administration, KVD900 significantly increased the number of stabilized or improved attacks when assessed by a Patient Global Impression of Severity scale (PGI-S) or use of rescue (p<0.0001).
- Additional exploratory endpoints were also statistically significant and favored KVD900 treatment over placebo.
- There were no serious adverse events reported in the trial and no patients withdrew due to adverse events. In the open-label phase, 8 on-treatment drug-related treatment emergent adverse event (TEAE) were experienced by 5 patients. In the crossover phase of the trial, 3 on-treatment drug-related TEAEs were experienced by 3 patients (5.2%) following administration of KVD900, and 2 on-treatment drug-related TEAEs were experienced by 2 patients (3.6%) following administration of placebo.

"Today's data show that KVD900 halts HAE attack progression and also provides rapid relief by shortening the time to symptom resolution," says Dr. Emel Aygören-Pürsün, Principal Investigator for the KVD900 Phase 2 Clinical Trial and Head of the HAE Center at the University Hospital Frankfurt, Germany. "The results are highly encouraging. For patients, easy and efficacious oral on-demand treatment of attacks is now within reach."

(Source: KalVista)

20 February 2021

At the 2021 American Academy of Allergy Asthma & Immunology (AAAAI) Virtual Annual Meeting **Pharvaris** presents clinical data supporting the pharmacokinetic and pharmacodynamic profiles of PHA121 (PHA-022121) for the treatment of HAE.

"The data continue to support our development plans to initiate studies in HAE patients this year," says Berndt Modig, CEO and co-founder of Pharvaris. "There remains an unmet medical need for highly effective oral therapies with favorable safety profiles. We will continue to evaluate PHA121 for both on-demand and prophylactic treatment of HAE through our soft-capsule formulation, PHVS416, and tablet formulation, PHVS719."

Peng Lu, M.D., Ph.D., chief medical officer of Pharvaris, adds: "Orally dosed PHA121 was rapidly absorbed and exceeded projected efficacious therapeutic thresholds within 15 minutes with or without food. Using bradykinin-challenge-induced surrogate markers, pharmacodynamic results suggest that PHA121 may provide longer pharmacological effect with a single oral dose than icatibant. We look forward to exploring the therapeutic potential of this compound in multiple clinical studies this year."

PHA121 was orally administered in two double-blind, placebo-controlled single-ascending-dose studies up to 50 mg, with pharmacokinetic and safety observed for 72 hours. Pharmacodynamic effects were evaluated with a nonlinear mixed-effect pharmacokinetic/pharmacodynamic model using 12 mg and 22 mg doses and compared to historical icatibant data. Pharmacokinetic/pharmacodynamic analysis showed significant inhibition of bradykinin-induced hemodynamic changes with an average composite EC50 of 2.4 ng/mL and EC85 of 13.8 ng/mL. Quantitative modeling indicates that single oral doses of PHA121 will maintain pharmacologically active drug levels for a substantially longer time than 30 mg of subcutaneous icatibant.

Adverse events were reported by 25% of the subjects in the combined group of all subjects treated with PHA121, identical to the 25% incidence with placebo. All adverse events were mild or moderate, and subsided rapidly and completely. No clinically relevant changes in safety laboratory parameters, vital signs, and ECG parameters were observed.

(Source: Pharvaris)

25 February 2021

From March 2021 the Ministry of Health and Welfare in South Korea will grant expanded reimbursement for the acute HAE treatment Firazyr.

The ministry will expand the insurance benefits for Firazyr to two doses per patient from the existing one-dose regimen. The expanded insurance benefit will allow patients with confirmed HAE due to a deficiency of a C1-esterase inhibitor to receive reimbursement for up to two doses.

"As the only treatment for HAE acute seizures in Korea, we are very pleased that the reimbursement has improved the treatment environment for patients with HAE," says Ji Chang-duk, head of **Takeda Pharmaceutical Korea**'s genetic disease business unit. "Patients with HAE, who have a hard time carrying out their daily lives due to unexpected seizures, will now have an opportunity to respond effectively to emergencies."

(Source: Takeda via koreabiomed.com)

25 February 2021

"With two approvals for Orladeyo, our launch in the U.S., and the addition of more than 425 million USD through our May and December financings, 2020 was a transformational year," Jon Stonehouse, President and CEO says at the presentation of the **BioCryst Pharmaceuticals, Inc**. financial results for the fourth quarter and full year ended 31 December 2020. "Using our strong balance sheet as a foundation, we expect to continue this transformation in 2021 with Orladeyo generating revenue in the U.S., Japan and Europe".

Orladeyo (berotralstat): Oral, Once-daily Treatment for Prevention of HAE Attacks:
- BioCryst launched Orladeyo in the United States following U.S. Food and Drug Administration (FDA) approval on 3 December 2020, and product shipments began on 16 December 2020.
- On 22 January 2021, the company announced that the Ministry of Health, Labor and Welfare (MHLW) in Japan had granted marketing and manufacturing approval for oral, once-daily Orladeyo 150 mg for prophylactic treatment of HAE in adults and pediatric patients 12 years and older. Orladeyo is the first and only prophylactic HAE medication approved in Japan and will be commercialized in Japan by BioCryst's partner, Torii Pharmaceutical Co., Ltd. OrphanPacific, Inc. is BioCryst's representative partner in Japan and holds the marketing authorization. Torii will launch Orladeyo in Japan following the successful completion of BioCryst's pricing negotiations with the Japanese National Health Insurance System (NHI).
- In Europe, the Committee for Medicinal Products for Human Use (CHMP) is scheduled to review the Orladeyo marketing authorization application this week. The company expects approval from the European Commission (EC) approximately 60 days following a positive opinion from the CHMP.
- On 30 October 2020, the company announced that the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) had granted Orladeyo a positive scientific opinion through the Early Access to Medicines Scheme (EAMS). Under the EAMS, HAE patients in the UK aged 12 years and older can gain access to Orladeyo for the routine prevention of recurrent attacks of HAE before the drug is granted marketing authorization by the EC.
- On 22 October 2020, the company announced that data from the first 24 weeks of the Phase 3 APeX-2 trial of Orladeyo in 121 HAE patients ages 12 years or older had been published online by the Journal of Allergy and Clinical Immunology.
- On 13 November 2020, the company presented data in several abstracts at the 2020 Annual Scientific Meeting of the American College of Allergy, Asthma & Immunology across HAE patients, caregivers and treating physicians showing many patients experience a significant treatment burden associated with current prophylactic HAE therapies.
- On 30 November 2020, the company announced that the journal Allergy had published data from the APeX-J trial, a randomized, placebo-controlled trial conducted in Japan evaluating ORLADEYO for the prophylactic treatment of HAE.

(Source: BioCryst)

26 February 2021

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending the approval of Orladeyo (berotralstat) for routine prevention of recurrent attacks of HAE in adult and adolescent patients aged 12 years and older.

The European Commission (EC) will review the CHMP recommendation and a final approval decision from the EC on the marketing authorization application (MAA) for Orladeyo is expected in the second quarter. If approved, Orladeyo would be the first oral, once-daily therapy in the European Union to treat patients with HAE by preventing recurrent attacks. The CHMP positive opinion is based on data from the pivotal APeX-2 clinical trial and supporting data from the APeX-S trial. In APeX-2, Orladeyo met its primary endpoint ($p<0.001$) for ORLADEYO 150 mg compared to placebo. Orladeyo showed a positive safety profile and was generally well-tolerated over 48 weeks in both APeX-2 and APeX-S.

"Following the recent approvals in the U.S. and Japan, we continue to focus on bringing our oral, once-daily treatment to HAE patients around the world," says Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc**. "The positive CHMP opinion for Orladeyo is an important step closer to delivering a new option to HAE patients across Europe and our commercial team is in place and ready to launch quickly upon final EC approval."

In December 2020, the U.S. Food & Drug Administration (FDA) approved Orladeyo in the U.S. In January 2021, Orladeyo was approved by the Ministry of Health, Labour and Welfare in Japan. An Early Access to Medicines Scheme (EAMS) for HAE patients has been approved by the Medicines & Healthcare products Regulatory Agency in the United Kingdom.

(Source: BioCryst)

26 February 2021

Intellia Therapeutics, Inc. reports operational highlights and financial results for the fourth quarter and year ended 31 December 2020.

"Intellia's achievements in 2020 reflect important progress on both our full-spectrum strategy and our mission to deliver curative genome editing treatments for people with severe diseases", says Intellia President and CEO John Leonard, M.D. "We are on track to submit first-in-human regulatory applications to begin clinical studies of NTLA-2002 for HAE, and we plan to nominate at least one new development candidate from our research portfolio."

NTLA-2002 aims to prevent attacks for people living with HAE after a single course of treatment. Intellia is applying its modular LNP delivery system to develop NTLA-2002 to knock out the KLKB1 gene in the liver to permanently reduce plasma kallikrein activity. This approach is expected to provide continuous suppression of kallikrein activity and eliminate the significant treatment burden associated with currently available therapies for HAE patients.

Intellia commenced clinical manufacturing activities to support the Company's plans to submit an IND or equivalent regulatory application in the second half of 2021.

(Source: Intellia)

27 February 2021

Pharvaris announces dosing of the first patient in RAPIDe-1, an on-demand Phase 2 study evaluating the efficacy, safety, and pharmacokinetics of PHVS416 in patients with HAE due to C1-Inhibitor Deficiency type 1 and 2.

"The initiation of this trial signifies another step towards developing an oral treatment for HAE patients experiencing acute attacks," says Berndt Modig, CEO and co-founder of Pharvaris. "The importance of providing patients with treatment alternatives to injection cannot be overstated. We hope to confirm in HAE patients the compelling findings of our previous studies. This study will help to determine if our small-dosage oral softgel capsule provides safe, rapid, and convenient on-demand treatment of HAE attacks."

RAPIDe-1 is a Phase 2 study evaluating the efficacy and safety of orally administered PHVS416 for the acute treatment of attacks in patients with HAE type 1 or 2. The study aims to enroll 54 adults, ages 18 to 75, at centers in North America and Europe. Eligible patients are randomized to one of three single doses of active and placebo. The study will compare symptom relief (skin pain, skin swelling, abdominal pain) during HAE attacks and safety of each dose of PHVS416 with placebo. PHVS416 is a softgel capsule formulation containing PHA121, a highly potent, specific, and orally bioavailable competitive antagonist of the bradykinin B2 receptor.

(Source: Pharvaris)

2 March 2021

BioCryst Pharmaceuticals, Inc. has submitted a marketing authorization application (MAA) to the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) seeking approval of Orladeyo (berotralstat) for the prevention of recurrent HAE attacks in HAE patients 12 years and older. The MAA was submitted under the MHRA's new European Commission Decision Reliance Procedure (ECDRP).

On 25 February 2021, BioCryst announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) had adopted a positive opinion recommending the approval of Orladeyo for routine prevention of recurrent attacks of HAE in adult and adolescent patients aged 12 years and older. The European Commission (EC) will review the CHMP recommendation and a final approval decision from the EC on the marketing authorization application for Orladeyo is expected in the second quarter.

When a valid ECDRP submission is made within five days of a CHMP positive opinion, the date of the CHMP positive opinion will be designated Day 0 of the ECDRP, and the MHRA will aim to determine the Great Britain MAA as soon as possible following submission of confirmation of the EC decision.

If approved, Orladeyo would be the first oral, once-daily therapy in the United Kingdom to treat patients with HAE.

"The ECDRP provides an opportunity to accelerate the approval of Orladeyo in the UK following approval by the European Commission. If approved, Orladeyo will provide a much needed oral, once-daily option for many patients and we are excited to be a step closer to making this a reality for them," says Jon Stonehouse, President and CEO of BioCryst.

(Source: BioCryst)

11 March 2021

Providing an operational update and financial results for the third fiscal quarter ended 31 January 2021, **KalVista Pharmaceuticals, Inc.** CEO Andrew Crockett says:

"We are making excellent progress in our commitment to providing those with HAE a complete set of oral options to manage their disease. The data announced last month for KVD900 as an oral on-demand therapy were overwhelmingly positive and show that patients don't have to compromise on efficacy or rely on injectables. We view this data as validation of our work in oral plasma kallikrein inhibition, which also includes KVD824 as a development candidate for an oral prophylactic treatment for HAE. Our next step is to meet with regulatory agencies to finalize the Phase 3 program for KVD900 while we push ahead with preparations to be ready to begin that trial as quickly as possible. We have also filed the IND for a Phase 2 clinical trial of KVD824 and expect to initiate that trial in the second quarter of 2021. The closing of our recent upsized financing puts us in a position to execute on plans across our oral HAE franchise, thanks to a cash balance sufficient to get us to the KVD900 NDA filing."

(Source: KalVista)

11 March 2021

The French National Agency for Medicines and Health Products Safety (ANSM) has granted an Autorisation Temporaire d'Utilisation de cohorte (cohort ATU), or Temporary Authorization for Use, for the use of berotralstat to prevent attacks of HAE in appropriate patients aged 12 and older.

This cohort ATU allows patients with HAE in France to receive treatment with berotralstat before the drug is granted marketing authorization by the European Commmission (EC).

According to the French Code of Public Health, a cohort ATU is dedicated to high unmet medical needs in serious diseases and covers medicinal products of which the efficacy and safety of use are strongly presumed and intended for a group or sub-group of patients treated and monitored in accordance with criteria defined in a protocol for therapeutic use and collection of information.

"HAE is a debilitating and potentially deadly disease so the early access to a new treatment option for patients is exciting news," said Dr. Laurence Bouillet, head of internal medicine, University Hospital Grenoble, Coordinating Reference Centre for HAE in France (CREAK).

"The cohort ATU represents BioCryst's second early access program approved in Europe and provides patients in France with faster access to treatment," says Jon Stonehouse, CEO of **BioCryst Pharmaceuticals, Inc.**

The EC will review the CHMP recommendation and a final approval decision from the EC on the marketing authorization application (MAA) for ORLADEYO is expected in the second quarter.

(Source: BioCryst)

12 March 2021

Takeda Pharmaceutical Company Limited has submitted a New Drug Application (NDA) to the Ministry of Health, Labour and Welfare in Japan for lanadelumab subcutaneous injection, a monoclonal antibody therapy for prophylaxis against attacks of HAE.

In Japan, it is estimated that between 2,000 and 3,000 people are living with HAE, but only approximately 450 have been diagnosed due to low awareness of the disorder.

"Recognition of HAE remains low in Japan, meaning there are significant challenges relating to diagnosis and access to effective therapies," says Naoyoshi Hirota, General Manager, Takeda Development Center, Japan. "Lanadelumab is a fully human monoclonal antibody that specifically binds and decreases plasma kallikrein activity, with a proven efficacy and safety profile as a preventive treatment for HAE attacks. Subject to approval, we are looking forward to providing lanadelumab as a new treatment option for patients in Japan living with HAE.

The submission of the New Drug Application in Japan is primarily based on results of the global Phase 3 HELP (Hereditary Angioedema Long-term Prophylaxis) Study and the Phase 3 HELP Study Open-label Extension (OLE), in addition to interim results of a Phase 3 study evaluating the efficacy and safety of lanadelumab in Japanese subjects. Combined, these studies have demonstrated the efficacy and safety profile of lanadelumab as a preventive treatment for HAE attacks. If approved, lanadelumab will be available to patients in Japan as a pre-filled syringe presentation.

The regulatory submission in Japan will be evaluated by the Japanese Pharmaceuticals and Medical Devices Agency. Following its review, the Agency will issue a report to the Ministry of Health, Labour and Welfare of Japan for a final decision.

Lanadelumab, under the tradename Takhzyro, received its first approval for the prevention of HAE attacks in patients 12 years and older in 2018 and is now available in more than 20 countries with additional regulatory submissions ongoing worldwide.

(Source: Takeda)

12 March 2021

"With our acquisition of Quellis and concurrent financing, we believe **Catabasis** is well positioned to advance the development of our lead program, QLS-215, as a differentiated and potential best-in-class new therapy for the chronic treatment of patients affected by HAE to prevent attacks," says Jill C. Milne, Ph.D., CEO of Catabasis Pharmaceuticals, Inc., at the presentation of a corporate update."QLS-215 is a monoclonal antibody inhibitor of plasma kallikrein in preclinical development, which we believe has the potential to demonstrate clinical proof of concept of its differentiated profile in Phase 1. Our mission has always been to bring hope with life-changing therapies to patients and their families affected by rare disease."

The vision for QLS-215 is to develop the best-in-class monoclonal antibody inhibitor of plasma kallikrein for HAE with infrequent dosing and sustained inhibitory blood levels. QLS-215 is a humanized monoclonal antibody targeting plasma kallikrein that has demonstrated potent inhibition of plasma kallikrein as well as an extended plasma half-life in non-human primates.

Catabasis expects to file an Investigational New Drug application for QLS-215 in the first half of 2022 and plans to initiate a Phase 1a clinical trial with initial results anticipated by the end of 2022. Subsequently, Catabasis expects to initiate a Phase 1b/2 trial in patients affected by HAE in 2023 with initial results anticipated by the end of 2023.

(Source: Catabasis)

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.