


Global perspectives:

HAEI MAGAZINE · ISSUE 4/2020

 92 Member countries



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DEAR HAE INTERNATIONAL FRIENDS,

We are happy to bring you the final edition of *Global Perspectives* for this most unusual and challenging year.

Despite the unprecedented disruptions caused by the worldwide pandemic, HAE International continued to grow, and we now have member organizations in 92 countries. In addition, our community maintained a high level of enthusiasm and creativity that enabled the continuation of the global HAE advocacy movement. For example, when forced to cancel the 2020 HAE Global Conference in Frankfurt, Germany, we switched gears and delivered the meeting in a virtual format. Similarly, Regional Workshops scheduled for this year have been transformed into a virtual form.

You will find a summary of the 2020 HAEi Virtual Regional Workshop South Eastern Europe in this magazine. The 2020 HAEi Virtual Regional Workshop Central Eastern Europe & Benelux held in mid-December will be summarized in our next issue. Also, HAEi friends can access materials from the Global Conference and Regional Workshops through our website at www.haei.org.

It is also a pleasure to see how our member organizations around the world have been able to find new ways to keep up their level of activity while fighting the coronavirus challenges.

With less travel to fewer international activities, we have been able to invest a considerable amount of our energy in the services and activities we offer our members. For instance, we have further developed **HAEi Connect** (our cloud-based membership database and communication platform for member organizations). We are also excited about the introduction of **HAE Companion** (our new smartphone app for patients and caregivers) that now is available on both Apple's App Store and Google Play, and **HAEi Advocacy Academy** (our free online advocacy e-learning platform). Furthermore, we are happy to see the expansion of the **ACARE** network and the huge interest we experience from centers who want to become an ACARE. We have also seen much activity and growth within the **HAEi Youngsters' Community**. You will find further information on much of this on the following pages.

On behalf of HAE International's Board of Directors, leadership, and staff, I wish you a happy and healthy holiday season! Please stay safe.

Warm regards,

Henrik Balle Boysen
Executive Vice President & Chief Operating Officer
HAE International

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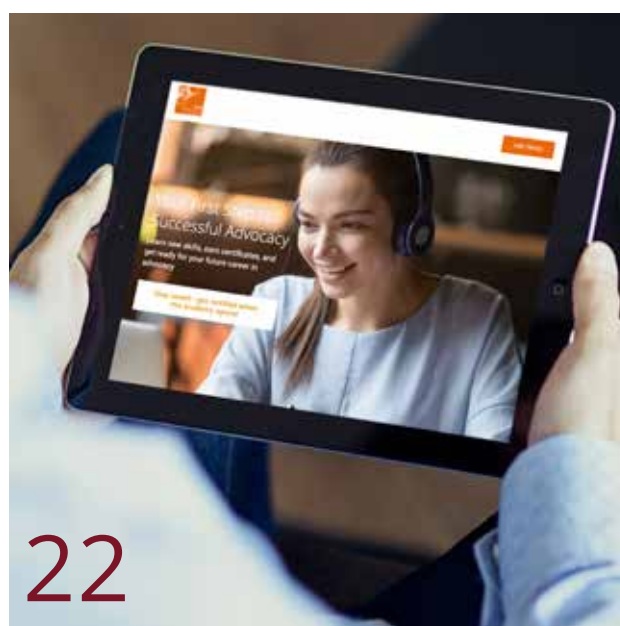
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NEWS FROM THE HAEi REGIONAL PATIENT ADVOCATES

As the end of the year is closing in on us, I think it's a good time to reflect on how well our HAE International Regional Patient Advocates (RPAs) and our member organizations have adapted to a very unpredictable year.

With all of the challenges that COVID-19 has thrown at us, everyone has continued advocating, educating, and moving things forward by adapting to the changing times and restrictions.

The past couple of months have been busy in the South Eastern European and Central Eastern European regions in organizing the 2020 HAEi Virtual Regional Workshops. It has been an outstanding effort by everyone involved to produce such meaningful and great content. You can view the videos from the regions' workshops at haei.org/resources/advocacy/haei-virtual-regional-workshops.

Aside from the virtual workshops, the RPAs have continued the rolling out of the various HAE International projects and programs throughout their regions. With the continued passion and drive from the RPAs working with their member organizations, more countries have gained modern treatment access.

We are now working on plans for 2021. We look forward to continuing our partnership next year with each country, member organization, patient group, physician, and anyone wanting to improve HAE patients' lives around the globe.

Fiona Wardman
Chief Regional Patient Advocate





MICHAL RUTKOWSKI
CENTRAL EASTERN EUROPE,
BENELUX & MIDDLE EAST



The September-October period was intense in terms of my involvement in various activities in the regions. First of all, the main activity was the preparation of the 2020 HAEi Virtual Regional Workshop Central Eastern Europe & Benelux, which is extremely time-consuming. With the global pandemic limitations, the HAEi Regional Workshops will go virtual, and this form of the event is way more challenging to prepare than face to face meetings. Preparing scripts, coordinating HAE International member organizations, recording interviews, translating and creating transcripts, video production and finally watching each recording dozen times can be exhausting. But I am happy to announce that we are aligned with the production plan and will be ready to deliver high-quality HAE sessions for our regional community on time. Having this opportunity, I would like to thank the entire HAE International team, member organizations from Central Eastern Europe and Benelux, as well as HAE experts for their support and brilliant cooperation in organizing this event.

Naturally, in addition to the workshop preparations, I spent a lot of time in contact with member organizations and health care professionals from Benelux, Central Eastern Europe and the Middle East. The main subject of these contacts was the provision of information about the new ACARE global network, as well as the search for potential new patient leaders.

It is with great pleasure that I can inform you that we continue to increase commitment to patient advocacy among our Middle East member organizations. As a result of our activities, the HAE **UAE** now has a new patient lead, Mrs. Shradha Singhania, and we are about to introduce a new patient lead in **Kuwait**. Also, more and more physicians/clinics/hospitals are interested in joining the ACARE global network, and currently, I work with **Estonia, Jordan** and Kuwait on implementation of this specific project there.



MARIA FERRON
MEDITERRANEAN, NORTH AFRICA & BRITISH ISLES



Mauritania: Our new HAE International Poster has been sent for translation to the only contact we currently have in the country. This poster can be quite helpful to localize possible HAE patients as we are not in contact with any yet.

Spain: HAE Spain (AEDAF) had their annual – this time virtual – meeting on 19 September with around 50 attendees. The first part of the two-hour meeting was dedicated to the General Assembly, and in the second hour, we had Dr. Gozalez Quevedo (Sevilla), Dr. Caballero (Madrid) and Dr. Lleonart (Barcelona) as speakers. Among other things, they presented on the repercussion of COVID-19 on HAE patients as well as new treatments.

Portugal: HAE Portugal (ADAH) requested to have their website hosted under the HAE International umbrella. ADAH has also asked to join HAEi Connect – they are currently working on it, and it should be fully running in the following weeks.

Algeria: I am happy to announce that the Algerian patient group has managed to get the final approval from the local administration to become an official association. HAE Algeria is currently in active communication with the Ministry of Health. HAEi Connect is now running in Algeria – and the patient group is working on creating a brochure, an Emergency Card and maybe a patient diary.

Libya: I have been working on possible ways to get access to HAE modern therapies for Libyan patients while national contact Ahmed Ali Abudahair has been investigating how to create an association in the country.



FERNANDA DE OLIVEIRA MARTINS
SOUTH AMERICA & MEXICO



I organized a conference call for member organization leaders on 10 September 2020. Present were representatives from **Argentina, Brazil, Chile, Ecuador, Mexico, Peru, Uruguay, and Venezuela.**



Furthermore, I have used the Instagram account created for my region to share information (in Spanish and Portuguese) on HAE Advocacy Academy, events for patients, *Global Perspectives*, and useful information for patients.



I have requested updated information on the number of patients, medication status etc., and at this point, I have received updates from Brazil, Peru, Venezuela, and **Paraguay.** The idea is to make Instagram posts based on the information received – please see www.instagram.com/haei_south_am_and_mexico.



HAE **Colombia** is the next organization to have its website hosted under the HAE International umbrella – please see <https://colombia.haei.org>.

HAE Peru has been involved in the publication of a Clinical Practice Guide: Screening, Diagnosis and Management of Acute Episodes and Prophylaxis of HAE. I have shared the guide – published by the Peruvian Society of Allergy, Asthma and Immunology – with HAE contacts in the region since it has excellent information and can help countries in developing its own guide on HAE.



JAVIER SANTANA CARIBBEAN AND CENTRAL AMERICA



During the month of December, we are hosting another webinar in Spanish with Dr. Rafael Zaragoza on HAE and COVID-19 in order to update the HAE community from the region on the latest medical information. We expect this event will be well attended.

We are also excited that the new patient group from **the Dominican Republic** already has its website up and running and that the leaders are working hard to identify more patients in their country and educate doctors on HAE.

Additionally, HAE **Costa Rica** has identified a new patient who is proving to be an invaluable resource. Diana Madrigal Fernández is a marketing specialist with strong media relations and has offered to

develop a communications plan for the group. She will also support national contact Angie Leiton in the development of an action plan focusing on high-level government advocacy.

Finally, HAE **Panama** has joined a coalition of rare disease organizations to create a new working group called “RedER Panama”. The intention is to promote live discussions on social networks about different rare diseases in Panama during the COVID-19 lockdown. The group has already rolled out several digital media campaigns such as: “Cultivate your Rarity”, and “I am Different, but I am not absent”. They have also held live events on social media platforms featuring doctors specializing in rare diseases so that the community can ask them questions about the diseases.



PATRICIA KARANI SUB-SAHARA AFRICA



The COVID-19 situation in Sub-Saharan Africa is still the main focus of this region. However, I am taking advantage of any small step I can to move things forward where possible in countries like **Zimbabwe, Kenya, Sudan, Nigeria, and Ghana**.

HAE International was able to raise awareness in Zimbabwe during the Angioedema Awareness month in November through the concerted efforts of Child and Youth Care Zimbabwe. This organization supports children with rare diseases in Zimbabwe. The month was dedicated to raising awareness amongst the

general public as well as the health care professionals in the country.

I have been in touch with HAE **South Africa** to work on a project to help raise awareness of HAE with physicians in the country.

A Zoom meeting has taken place with the Rare Disease Ghana organization to talk about HAE in this country. Rare Disease Ghana has shared a link on HAE on its website to assist with raising awareness.



JØRN SCHULTZ-BOYSEN
NORDICS & DACH



Having recently started up the RPA task for DACH and Nordics, I had the pleasure to meet face to face with Lucia Schauf of HAE **Germany** in September. I should also have met with Adelheid Huemer and Christian Müllner of HAE **Austria** as well as Helene Saam of HAE **Switzerland**. Unfortunately, COVID-19 yet again caused travel restrictions, so these two meetings were moved to be online instead.

Regardless, it was great to meet with the three associations to hear about all the work they have been and are doing, the current state in their countries, and to talk about some of the news and offerings from HAE International.

Some of the key points discussed with the three countries were HAEi Connect, web hosting, the Emergency Card in German, the HAE Companion app, and ACARE. Not least one of the main purposes was to get introduced to each other and to talk about the role of the RPAs and how this can be a beneficial link for all parties; how we can stay updated on activities and help each other.

Also, we have already been successful in kicking some of the tasks off that we discussed. Hence, I am happy to mention that the work of moving HAE Austria's website to HAE International's web hosting setup has been decided and we are taking the first steps now. Also, a demo of HAEi Connect is being set up for HAE Germany to visualize the benefits of this tool. As a very practical and very important task, we got the Emergency Card translated so that it is now available in German both on www.haei.org and in the HAE Companion app.

Furthermore, it's wonderful to see that we have ACARE centers in both Austria and Germany – several in Germany, actually.

In the Nordic region, we are currently working on moving the website of HAE **Finland** to the hosted setup of HAE International.

For **Norway** and **Sweden** regional patient meetings are normally held in the autumn and in **Denmark** in late spring/early summer. Due to COVID-19, these regional meetings will be virtual instead with a lot of interesting and relevant information being shared. The planning and recording for these event are currently ongoing with a planned go live in the first quarter of 2021.

In Denmark, the first ACARE center has been accredited, and dialogue with this center is currently ongoing.

Last but not least, a callout: If you are a patient, care giver 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.



NATASA ANGJELESKA SOUTH EASTERN EUROPE



I have participated in Takeda's External Stakeholder meeting on 13 October 2020 upon invitation from the Head of the Takeda representative office in Belgrade, Aleksandar Bjelski. I was one of two patient representatives invited to speak about living with HAE, as a caregiver, but also as a patient advocate. My talk was 5-7 minutes to introduce some of the aspects of challenges and needs of HAE patients, as well as support and initiatives undertaken as Regional Patient Advocate. Among others Giles Platford, the President of Europe & Canada Business Unit for Takeda, Jiri Smejkal, Hrvojka Kostelac and other Takeda representatives were present during this meeting.

I accepted an invitation from NORBS (the National Organization for Rare Diseases) in **Serbia** to be a speaker at a virtual regional conference "CARE FOR RARE" held on 23-24 October 2020. I presented the project in which I was involved in the course of 2019 implemented by the National Alliance for Rare Diseases Macedonia (NARBM) where we have partnered with patient representatives for different rare diseases to create a National Strategy for Rare Diseases in cooperation with the Ministry of Health. This document is still not adopted by the Government, due to the crisis caused by the pandemic. Nonetheless, we plan to re-initiate our demand for adoption as it regulates very important aspects from the health care field (diagnostics, treatment, and patient involvement) as well as social care and education.

I have spent most of the time in the course of September and October to prepare the 2020 HAEi Virtual Regional Workshop South Eastern Europe. Among many other things, the preparations for the workshop involved scheduling and recording individual interviews with patient leads from **Bulgaria**, Serbia, **North Macedonia**, **Croatia**, and **Turkey**, who accepted to participate in the patient track. Please see the article on the workshop later in this issue of *Global Perspectives*.

With some of the patient leads from my region, I have been discussing the implementation of the Regional Medical Advisory Panel initiative designed to integrate into HAE International's operations. The aim is for the Regional Medical Advisory Panel to provide the global organization with better insight into challenges at the regional and local levels and to assist HAE International in adapting existing programs and designing and implementing new initiatives. I have asked the patient representatives to nominate a physician from each country to the HAEi Regional Medical Advisory Panel.

Dr. Vesna Grivcheva Panovska from North Macedonia prepared a survey called "Perception of the Current Status and Expectations of the Long-term Impact of COVID-19 on HAE Management from the perspective of HAE Patients and HAE Treating HCPs". HAE International and HAE Macedonia, as well as other patient organizations, assisted in sharing the link to the survey that was translated in multiple languages to enable collecting a variety of responses. Dr. Grivcheva Panovska was very satisfied with the response rate gathered.

Dejan Angjeleski, a youngster from North Macedonia, was featured in a book called "A Day in my Life" with 30 stories of people with different conditions and disabilities. In his story, he explains about his life with HAE. He talks about his wish to be like everybody else, to work and travel independently, hoping that new therapies will result in improvement of the quality of his life.

The network of ACARE centers is spreading in South-Eastern Europe. Accreditation of the ACARE center in Bulgaria was announced in November, and we expect more applications for new accreditations to be submitted over the coming months.



FIONA WARDMAN
ASIA PACIFIC



The past few months have been busy in the Asia Pacific region with some exciting projects going on with the member organizations. I always enjoy catching up with each of the patient leads from all the member organizations to discuss plans and how to create awareness and education opportunities and build their capacity.

I have been working with the member organizations to roll out the HAEi Regional Medical Advisory Panel (RMAP) project. Together, we are inviting physicians to take part in the Asia Pacific panel.

The member organizations are also working on rolling out the emergency room poster project where we hope to have as many hospitals and clinics as possible displaying the poster with vital information on HAE.

I have taken part in various workshops and meetings and have been part of focus groups for the Asia Pacific region with umbrella organizations such as Asia Pacific Alliance of Rare Disease Organisations (APARDO), Rare Disease International (RDI), and Eurodis in partnership with the WHO. These workshops are essential to gain information on work being done in the region. They are a great way of collaborating and catching up with other rare disease umbrella organizations and patient groups from within the region. We work together to create awareness and look at ways of overcoming the region's challenges.

I have also written a case study on HAE in the Western Pacific region, which will be included in a report early next year to highlight HAE in this region and beyond.

HAE **Bangladesh** organized a call with an organization called Platform Medical and Dental Society, where we discussed raising awareness of HAE and working on ways to educate physicians on HAE in the country. The platform has access to physicians and medical students, and they will be a valuable partnership. We look forward to working with them on a number of projects very soon.

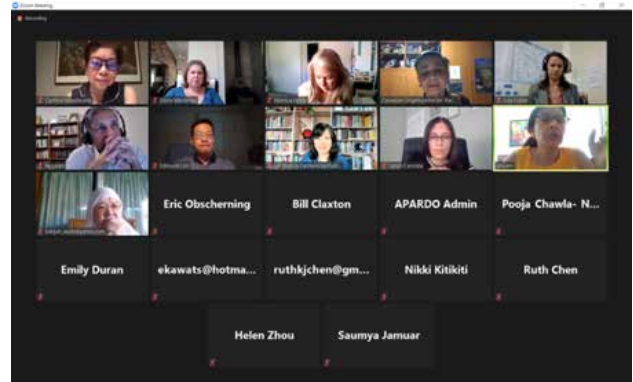
The HAE **India** survey has closed, and we have gained a fantastic insight into patients living with HAE in India. We had good participation response in the survey. Our next step is to report our findings and leverage the information for gaining access to modern treatments.

HAE **Korea** have held a patient meeting in Seoul during November. You can read more about this in the News from Member Organizations around the Globe section.

HAE **China** have been busy with various initiatives; you can read more about this in the News section.

HAE **Indonesia** now has a dedicated Facebook page. 'Like' the page so you can be updated at <https://www.facebook.com/haeindonesia>.

HAE **Japan** and I are working on a project that will benefit all countries in the Asia Pacific region and beyond. More information is coming soon.



DRIVE, ENERGY, IDEAS AND OPTIMISM HELPS GROW NETWORK OF SPECIALIZED ANGIOEDEMA CENTERS

Just before the end of 2019, HAE International and GA²LEN – the non-profit organization of leading clinical and research facilities in the field of allergy and asthma – established GA²LEN/HAEi Angioedema Centers of Reference and Excellence.

The joint venture regarding these ACARE centers fulfills HAE International's longstanding goal of establishing a worldwide network of accredited angioedema care centers.



Professor Marcus Maurer, who is the HAE International Chief Medical Advisor as well as the GA²LEN /HAEi ACARE Coordinator, explains the important task of the ACARE Centers:

“The ACARE centers are specialized centers for angioedema. They are the place to go when everything else fails, but they are also second opinion centers. The ACARE centers are there for patients; they are there to increase research, knowledge, advocacy, and awareness – but most of all they are there to provide the best care and they do that by seeing patients. They also do that by helping other physicians, such as general practitioners by educating them and helping them with bringing good treatment to patients.”

What requirements have to be met before a hospital or a clinic should consider applying to become an ACARE center?

“The requirements are clearly laid out. There are 32 of them. It sounds like a lot but what's behind this is that we want a high standard of quality both in the care for patients but also in research, clinical trials, advocacy, and awareness. The centers are hospital-based, they provide care for adults and children with angioedema, they follow the guidelines, they know the nomenclature, they know the state-of-the-art treatment, they apply the modern treatment options to help their patients, they do research and clinical studies, they educate physicians, patients and each other. These requirements are meant to make sure that the members of the ACARE network bring the best game to angioedema that we can imagine.”

What is the process to go through to become an ACARE center?

“That is actually very simple: Go to the ACARE website and download the application form. It takes no more than three minutes to complete. Then send it to the ACARE office, and we will find an auditor to do the audit visit. Once that is complete, and the Steering Committee has approved the new member to become an ACARE center you will receive a certificate that states that you are now part of this network eligible to participate in ACARE projects.”

More than 50 centers have completed the process in this year alone – a period that Professor Maurer describes as “a year of a horrific pandemic”, but still the applicants have shown “a lot of energy, a lot of interest” that has led to the fast growth of the network.

What actual role can the ACARE centers and the programs of the ACARE network be expected to play in further HAE basic and clinical research?

“There are a lot of things going on. Regarding the basic research, the centers are now getting organized to work on the identification of novel mutations. For

example, one project that has just started works with dried blood spot cards to do genetic analysis across the globe so even at places where it may be difficult with the regular resources available to get genetic testing ACARE will do this. We will work together to identify and characterize these mutations. Also, we need to get rid of the old prophylactic androgens that are still so widely used and move patients to modern treatment options. Yet, there is very little information on how to do this best, so in another ACARE project, we will look at exactly that: What's the best way to stop the androgens and the best way to introduce modern treatment options? It goes beyond that. We also introduce webinars in these times of COVID-19 – that's super important because patients with HAE have lots of questions and we know that across the globe what is being provided in terms of consultation hours has been reduced during the pandemic. We are moving to remote treatment rather than face to face and we as a network will help to overcome these challenges with education, with providing answers, and with providing new solutions from the research, we do together.”

What in your experience can we learn from UCARE, that is the comparable network of Urticaria Centers of Reference and Excellence?

“We can learn so much from UCARE, our twin network, as a lot of things that they do are very educational to us. We don't need to make the same mistakes that they make, and we can benefit from the insights that they had while they were first developing their network. The way we run projects, the way we bring centers on board, the way we make sure that those who are interested in joining the network get the information they need to work towards completing these criteria. Really, the UCARE and ACARE can work closely together.”

How do you think ACARE can best integrate with the HAE patient community?

“One of the criteria of becoming an ACARE center is to work with patient organizations – to help patients to organize themselves and where they are organized already help them to increase the impact that they have, the voice that they have; to empower patients, to be true partners of patients in their drive to make things better for the patient community. We also ask centers to work with patient organizations for advocacy and awareness events. To bring it out there that the disease is still under-researched, undertreated, underdiagnosed – that we still need in most parts of the world better ways to diagnose patients, better ways to treat patients.

I am grateful to HAE International for being a partner in this, for being a father of this network. Together with GA²LEN, you have brought so much drive, energy, ideas and optimism to this network and we are all benefiting from this. We hope that this network of physicians and researchers working with the HAE International network of patient organizations and patient advocates will make a strong force to improve the care of patients with angioedema and to develop better treatment options for patients with HAE.”



The global network of ACARE centers is growing at high speed. Today, there are ACARE centers – either already accredited or in the pipeline – in Argentina (2), Austria, Brazil (8), Bulgaria (2), China (2), Denmark, France (3), Georgia, Germany (6), Greece (2), Hungary, India (3), Italy, Japan (3), Kenya, Kuwait, the Netherlands, Oman, Peru (2), Poland (3), Portugal, Qatar, Russia (2), Slovenia, Saudi Arabia, South Africa, South Korea, Spain, Thailand, Turkey (3), the United Arab Emirates, and the United Kingdom.



Please see www.acare-network.com for an updated list of ACARE centers across the globe.

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





The HAE Companion app is ready for you

In the previous issue of *Global Perspectives*, we introduced the upcoming HAE Companion – an app providing an easy way to access and store the popular HAE International emergency card that has currently been a paper document.

“I am happy to say that the app is now available on both Apple’s App Store and Google Play for the Android platform. One of the key elements for our app is the excellent emergency card project that our Regional Patient Advocates have undertaken over the last couple of years. People may, however, find it cumbersome having to complete, download, and print the emergency cards – and that is one of the reasons for introducing HAE Companion. The app features our full range of emergency cards and allows smartphone users to download these cards to their device”, says Henrik Balle Boysen, HAE International Executive Vice President & COO.

Thanks to the app, the user can store as many emergency cards as needed. When planning a trip, the user can download relevant languages for the locations he or she is going to visit. The emergency cards are very easily added to Apple Wallet and PassBook – and can be removed just as easily.

“If you accept that HAE Companion knows your location, the app also offers geofencing. This means that the app can send push messages to you when you are on the move – for instance, “We can see that you are near a Spanish speaking country. Do you want to download the HAE Emergency Card in Spanish?”. HAE Companion also links to the HAE International database with contact information on ACARE Centers as well as HAE knowledgeable hospitals and physicians worldwide. Therefore, you can always ask the app to show the nearest HAE knowledgeable center, hospital or physician. Using GoogleMaps or Apple Map, the app also indicates directions and distance to the nearest place”, says Henrik Balle Boysen.



apple.co/33Qn4ZK



bit.ly/3osxkzm

WELCOME TO THE 2020 HAEi VIRTUAL REGIONAL WORKSHOP SOUTH EASTERN EUROPE

By Natasa Angjeleska, Regional Patient Advocate for South Eastern Europe

It was never planned that we should be living in a time with restrictions regarding travel, gatherings, limited physical contact, and keeping distance due to the global pandemic caused by COVID-19. It has indeed changed our daily routines. It has made us more worried and at the same time, more careful. On the other hand, it has also forced us to start thinking that limitations only live in our minds – that if we use our imaginations, our possibilities become limitless.

Regarding the planned regional workshop for South Eastern Europe, we decided to start where we are. Use what we have. Do what we can! This is how the idea for the 2020 HAEi Virtual Regional Workshop South Eastern Europe developed. We knew that the prospect of having a virtual workshop was not as exciting as it was in the past when we could really see and hug each other and experience so many wonderful things together. However, we decided to make the best of the situation we were in.

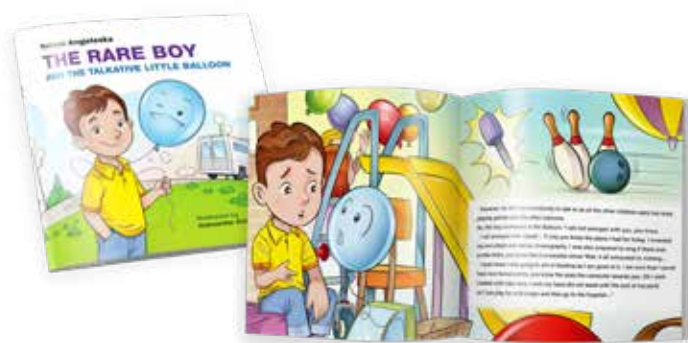
Preparations for the virtual workshop started at the end of August when I sent out information and invitations to representatives from member organizations from the region. The aim was to participate in a discussion on how they feel in these dire life circumstances and what actions they are proud of and would like to share. Also, where do they see their country in the future in

terms of having a strategy and what steps they would like to take in order to set certain things in motion? Furthermore, we would discuss if there have been any breakthroughs in the countries within diagnostics and therapy.



Interviews for the Patient Track of the conference were scheduled with five patient leads: Danail Dimov from Bulgaria, Jovana Cvetkovic from Serbia, Verce Jovanovska Jankovska from North Macedonia, Mihaela Shogoric from Croatia, and Ersan Sevinc from Turkey to share their thoughts, experiences and plans. The Patient Track also contains a video conversation with a licensed psychologist, Radmila Zivanovic from Psihoterapika, with whom we discussed questions received from patients via e-mail and social media.

Furthermore, a group of youngsters were invited to record a Youngsters' Track video in which young patient representatives from Greece (Eirini), Romania (Maria Monalisa), Serbia (Sofija), Turkey (Ersan), and North Macedonia (Dejan) discussed their personal experiences of life with HAE. We also had a guest youngster from the United States of America (Emma) in this video covering the caregiver's perspective of life living with a sibling with HAE.



The children's storybook "The Rare Boy and the Talkative Little Balloon" was posted via ISSU and thus made available for anyone interested – this was also part of the Youngsters' and Children's Track of the workshop. I wrote the story some time ago as I always thought that younger patients and their parents need something that they can use to start a conversation with other children and their parents about this condition. I am amazed about all the positive reactions that this story initiated, and I received excellent feedback via e-mail and comments on social media.

The Regional Expert Track of the workshop included five videos recorded by experienced physicians from Serbia (Dr. Slagjana Andrejevic and Dr. Radovan Mijanovic), Romania (Dr. Noemi-Anna Bara), Turkey (Dr. Ozge U. Soyer) and North Macedonia (Dr. Vesna Grivcheva Panovska). They provide valuable information about the statistics, research results and data from studies, case studies and alike from their everyday work with HAE patients and family members in their respective countries.

In addition, we had three videos in the HAE International Track presenting the latest developments in the global organization: "Decentralization of HAE International in practice" recorded by Chief Regional Patient Advocate Fiona Wardman, "Building the foundations for the future" with President and CEO Anthony J. Castaldo and Executive Vice President and COO Henrik Balle Boysen, as well as a video explaining the ACARE centers' aim, operation and procedures. This was a conversation between Anthony J. Castaldo and Marcus Maurer, Professor of Dermatological Allergology and Director of Research at the Clinic for Dermatology, Venerology and Allergology of the Charité Universitätsmedizin Berlin, Germany.

We had also invited two international experts who cordially accepted to record their presentations for the International Expert Track. Marc Riedl, Professor

of Medicine and Clinical Director of the US HAEA Angioedema Center at the University of California San Diego, gave a presentation titled "We had a dream – New Therapies on the Horizon". And Marcus Magerl, Professor of Medicine at the Charité Universitätsmedizin Berlin, Germany presented on "Other medical conditions and management of HAE".

The launch of the 2020 HAEi Virtual Regional Workshop South Eastern Europe was on 13 November 2020 with the welcome videos containing warm greeting messages from Anthony J. Castaldo, Henrik Balle Boysen and Fiona Wardman as well as Natasha Jovanovska Popovska, representing the HAE International Board of Directors. Also, this section included my video welcoming all to this semi-jubilee of the regional workshops in South Eastern Europe and guiding the participants through the different tracks.

A total of 15 videos has been uploaded to the regional workshop website. They are available in eight languages: English, Macedonian, Albanian, Bulgarian, Turkish, Greek, Romanian and Serbian/Croatian/Bosnian/Montenegrin.

I believe that the translation of the videos has helped to attract patients, physicians, and the general public who are not necessarily fluent in English and thus make the content available to more people interested in HAE awareness and advocacy.

VIDEOS IN EIGHT LANGUAGES

You can access the full content of the 2020 HAEi Virtual Regional Workshop South-Eastern Europe at haei.org/2020-haei-virtual-regional-workshop-see

All 15 videos are available in eight languages: Albanian, Bulgarian, English, Greek, Macedonian, Romanian, Serbian/Croatian/Bosnian/Montenegrin and Turkish.

TWO DECADES OF REMARKABLE HAE DEVELOPMENT

At times it can seem hard to keep track of all that has evolved in and around HAE over the years. Here is an overview – at least when it comes to the development of HAE International.

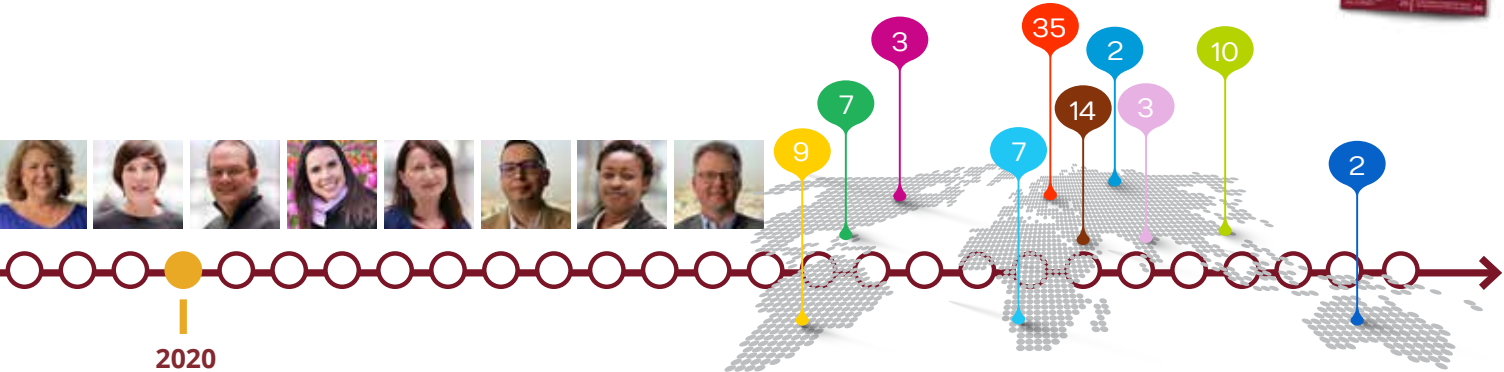
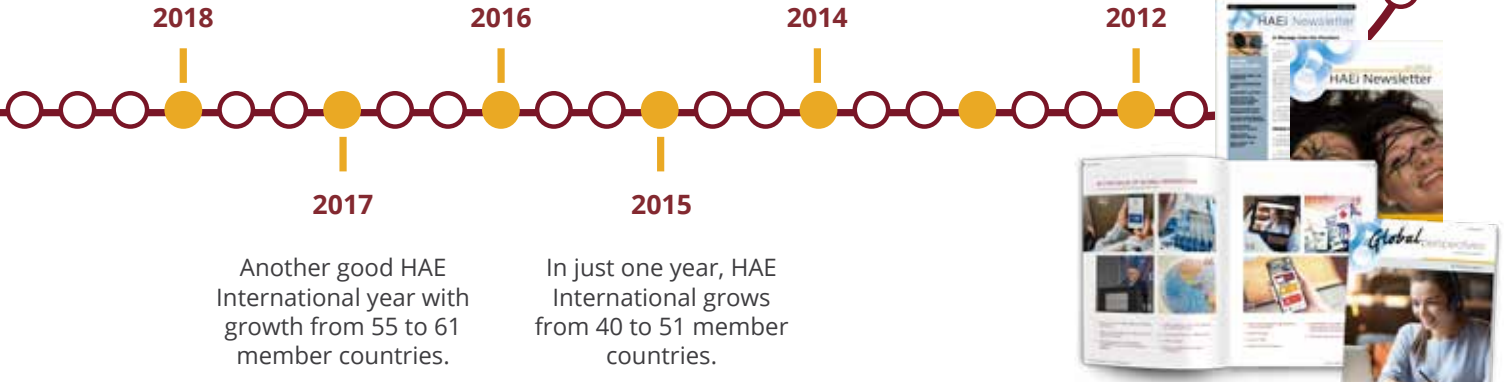
2019

- HAE International is registered as a non-profit corporation in Virginia, the United States of America.
- The initial shipment of modern HAE medication is delivered to South Africa under our Global Access Program (GAP) offering a regulatory compliant process that allows healthcare professionals to secure treatment for their HAE patients.
- The first HAE Youngsters' Advocacy Workshop takes place in Atlanta, Georgia, the United States of America.
- We partner with GA²LEN (a non-profit organization of leading clinical and research facilities in the field of allergy and asthma) to establish the GA²LEN/ HAEi Angioedema Centers of Reference and Excellence.
- We kick off the HAE Heatmap Project with the primary aim to test the viability of a survey research approach to estimate the incidence of people with undiagnosed HAE visiting Health Services in countries around the world.
- The growth continues from 69 to 84 member countries.

Alarmed at the potential consequences of the inadequate methodology chosen for a poorly designed C1 inhibitor concentrate clinical trial, renowned HAE researcher Professor Marco Cicardi calls a meeting of HAE experts and patient representatives to coincide with the International Complement Congress held in Palermo, Italy – the idea for a global HAE organization is born.

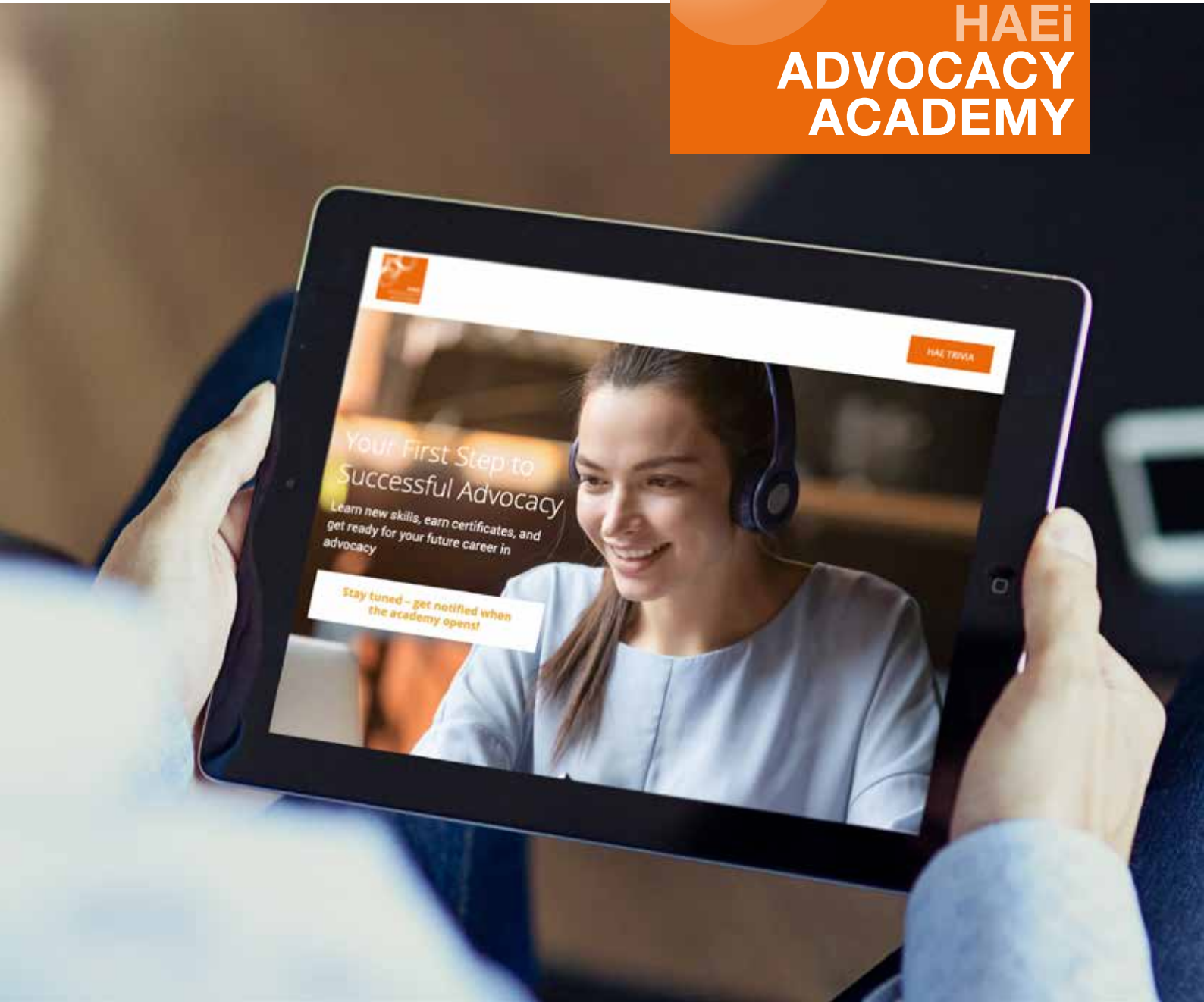
After overcoming a series of bureaucratic obstacles, the organization is registered – the seven founding members are the national HAE organizations of Argentina, France, Italy, Hungary, Spain, the United Kingdom, and the United States of America.

A group of HAE patient advocates establishes an international patient organization.



- We provide an update of our State of Management Report.
- Due to coronavirus COVID-19 the 2020 HAE Global Conference in Frankfurt, Germany is transformed into a virtual conference.
- HAE International is now serving as the global non-profit umbrella organization for 92 national HAE member organizations.





HAEi ADVOCACY ACADEMY

– LIVE AND AVAILABLE GLOBALLY

HAE International is very excited about the great success of the HAEi Advocacy Academy since the launch at the end of October 2020. In just two months, a lot of global HAE friends have joined the academy and are enrolling in the courses available.

“HAEi Advocacy Academy has been an innovative initiative for HAE International. Our main focus has always been building awareness and advocating for people with HAE around the world, and that is exactly what we aim to do with our online e-learning platform. We want to share our experience and inspire anyone interested in advocacy take their first steps towards becoming a successful HAE advocate”, says Nevena Tsutsumanova, HAE International’s Operations Manager.

Currently, there are a total of six courses available in the academy, separated in course series covering different topics.

The Advocacy Toolkit course series is for everyone beginning to think about advocacy and interested in learning more about how to plan and carry out an advocacy project. In these courses, you will find the right tools to help understand and choose your topic, plan your advocacy campaign and carry out the advocacy efforts.

“HAE South Africa and Hana Faulds have worked on creating a wonderful and educational toolkit for the young HAE patients in South Africa. HAE International is thrilled to have had the chance to collaborate with both Hana and HAE South Africa in making their toolkit a course series for the HAEi Advocacy Academy and help them reach more youngsters in our global community”, says Nevena Tsutsumanova.

The HAE Youngsters Toolkit course series is where you will find a lot of information and tips about HAE during puberty, dealing with school and growing up. Each course has a specific subject and a resource section with tools to help and prepare young HAE patients when talking about HAE at home, school or with friends and partners.

If you believe that advocacy is a force to change the world, then this is the place for you! Hope to see you in class.

HAE TRIVIA

If you are looking for a fun way to introduce the subject of HAE to your friends or simply want to test how much you and your family know about HAE, then join the HAE Trivia Challenge.

The rules are simple:

- You can be in a team or by yourself
- If you are in doubt about an answer, you can always find hints
- And last but not least, remember to have fun

Once you have completed the challenge, make sure to share your score with HAE International by using the #haetriviachallenge. Don’t forget to tag your friends and challenge them too.

You can find the HAE Trivia Challenge on the HAEi Advocacy Academy website at www.academy.haei.org

HAPPY QUIZZING ...





HAEi YOUNGSTERS

**CONNECTED BY HAE.
UNITED AS A FAMILY.**

Check out the new look and feel of the HAEi Youngsters website

From the HAEi Youngsters Advisory Group

Haven't you had a look yet? Well, once you've finished reading this, head over to youngsters.haei.org and check out our brand-new website. The HAEi Youngsters Advisory Group and HAE International have collaborated on this project to revamp our online presence – and we're delighted with the results, and hope you like them too.

So why do this now? And what does it mean for us as a Youngsters Community? Let us start by going back in time.

The year is 2018. The place is the HAE Global Conference in Vienna, Austria. Those were some awesome times, especially because people were allowed to be together (#thankyoucorona). This was the conference that saw the official launch of the HAEi Youngsters Community – and to do this, we created our own website and magazine (the Youngsters Voice) over the weekend. It was such an amazing activity to be a part of. We all worked together and let our creativity go wild!

Since then, the HAEi Youngsters Community has grown in numbers and enthusiasm. It has been such a joy to see our community developing and connecting more, especially now, and we felt the time was right to bring our webpage up to date.

Our goal was clear – to build on the great work already done by our Youngsters Community and make the website a tool that will serve the Youngsters Community even more.

So, "What is so different?" you might ask. The first update is obvious: A fresh new look. And behind the scenes, we've added a lot of new functionality as well as content.

"Events" has now joined the navigation tab, and from there you can really easily sign up for our HAEi Youngsters Online Meetups! The first one was held in November and was a lot of fun – we hope you'll join us for a Meetup in the future!

You can read more about the members of the Youngsters Advisory Group under "Meet the team" and join the #togetherApart project. Another update is our easy to complete membership form that you'll find under the "Join us" button. There is now no excuse for getting involved ;-)) and we look forward to developing our membership and being able to keep in touch with Youngsters around the world.

And last, but definitely not least, we have the "Resources & Tools" tab. This is where you can find loads of helpful information; from tips and tricks for when you are travelling abroad, to how to talk to your friends and partners about HAE and much more.

We want to say a big thank you to HAE International, for helping us with implementing our vision and believing in the power of young HAE advocates. And to all of the youngsters in our global HAE community – this website is dedicated to all of you!

Whether you are newly diagnosed with HAE, starting school, university, moving abroad or starting a new job, the website is the place for you. Here you can find resources and tools that can help you, and your family and friends, learn more about HAE. Whether you want to build awareness about HAE in your community or become an HAE advocate, or simply need a way to explain what HAE is at school – we got you covered!

Our goal is to learn, stay connected, grow our global community, share our experiences and have fun together. Join us, and together we can make memories to last us a lifetime!



The importance of our global community

By Morag Faulds

We all know how difficult it can be to get the right emergency treatment and medical advice for HAE, even in our own country. Being so rare, most doctors and nurses do not even know HAE exists, let alone know how to treat it. This is why our global HAE community is so important. Staying connected online and at international conferences gives us the opportunity to share experiences, advice and support each other through it all.

A particular challenge for people with HAE is travelling. Being away from our family, friends and our local HAE doctor - as well as potential differences in language - means that we might not be able to easily and promptly access the support we need if there is an emergency relating to HAE. I recently realized just how important and life-saving our global HAE family can be.

While on holiday in Italy this year, I suddenly had a severe abdominal attack that developed extremely quickly. I am on prophylactic treatment, so this was

unexpected, and most likely triggered by the stress of travelling and being very active, every day. I had no emergency medication, and after a few hours, the pain was unbearable and had caused fainting and vomiting. I contacted hospitals in the area but as a tourist and foreigner no-one wanted to treat me, and they did not know what HAE was. By this time, I couldn't walk or speak much. I was doing my best to try and manage the pain as well as try and find medication nearby - but with no success. My sister, who was at home in South Africa, knew what was happening to me and posted to the HAE International social media platforms: were there any Italian HAE patients who could help? Within minutes we were in contact with fellow HAE patients nearby. These Italian HAE patients contacted their own HAE doctor at a hospital in Milan and alerted them to my emergency situation. I was able to get to the hospital and meet the HAE doctor. Thanks to the HAE patients contacting their doctor, he was ready when I arrived, and I received emergency treatment straight away.

Without the global community, I wouldn't have been able to get the care I needed in this emergency, and my attack would have progressed to much worse.

I would like to say a very special thank you to Marco Roffia and Martina Perera, two amazing HAE friends who jumped to help as much as they could. You went above and beyond to make sure that I got the help I needed in time. You are all amazing, and I appreciate it so much!

Let's keep supporting each other worldwide and never be shy to reach out when you need help; we are in this together!



Will you be the next member of the HAEi Youngsters Community?



... and say hello
- we look forward
to meeting you!

The HAEi Youngsters Community has gone from strength to strength in the last couple of years, and it's all thanks to the members: young people aged between 12 and 25 from all over the world.

The members share experiences, support each other, take part in specific activities to develop and support the Community and have a lot of fun doing it.

You can read all about HAEi Youngsters Community on the new website, Instagram and Facebook:



Follow us on Instagram:
[@haeiyoungsters](https://www.instagram.com/haeiyoungsters)



Join our group on Facebook:
[HAEi Youngsters Community](https://www.facebook.com/HAEiYoungstersCommunity)



Visit our new website:
www.youngsters.haei.org

Anyone aged between 12 and 25 can join the Youngsters Community. Those who have joined and want to take a more active role might like to ask about being a part of the Youngsters Advisory Group. You'll find more info on the updated Youngsters' website.

Don't just take our word for why it's great to be part of the HAEi Youngsters Community. Nathan Galarraga, a member of the Youngsters Community and Youngsters Advisory Group, had this to say:

"What I like about the HAEi Youngsters Community is being able to stay connected and interact with people of the same age that understands our illness. The feeling of having a community to support you makes it easy to overcome any situation; suddenly you don't feel alone anymore."

The HAEi Youngsters Community would love meeting new youngsters so drop by the website, Instagram or Facebook and say hello.

HAE International is delighted that our global community were able to help Morag so quickly when she experienced an HAE attack when travelling. Please do talk to your HAE doctor before travelling and ensure to bring enough emergency/acute medication with you to cover you in case of an attack. To help our community prepare for travel within your country or to another country, HAE International has developed these free resources:

- **The HAE Companion app:** Download from App Store www.apple.com/app-store or Google Play <https://play.google.com/store/apps>
- **The HAE International Emergency Cards:** Download either directly from the HAE Companion app or from <https://haei.org/resources/emergency-cards>
- **Before travelling abroad:** It is always a very good idea to familiarize yourself with HAE knowledgeable hospitals and physicians in the country or countries you are going to visit. Please use the HAE Companion app or the HAE International world map with an updated overview of ACARE centers, hospitals and physicians around the globe: <https://haei.org/about-haei/globally>.

NEWS FROM MEMBER ORGANIZATIONS AROUND THE GLOBE



SOUTH AFRICA

*From Adrienne de Jongh,
President of HAE South Africa*

Growing up with HAE comes with many challenges, some of which are not easy to talk about. We wanted to open up the conversation during these crucial years to allow youngsters to feel comfortable and united through it all. Additionally, the teen years are essential for taking control of your HAE and establishing our own personal patient care that best works for our individual circumstances.



We at HAE South Africa noticed the gap in conversations happening among HAE youngsters, even though most patients share similar experiences. We set out to create a youngsters' toolkit to encourage young patients to discuss all challenges they may face with HAE, without feeling any shame or embarrassment. We want to unite our HAE youngsters, so they never grow up feeling alone in this journey.

The youngsters' toolkit is set to serve as a model for managing and advising young HAE patients through issues which usually are left unspoken, such as dealing with mental health challenges particular focused on body image and confidence, sexual health and wellbeing, as well as social issues pertaining to HAE in the younger years.

We acknowledge the need for increased support and resources for youngsters as they experience extreme physical and emotional changes and challenges throughout their journey to adulthood. Additionally, we have realized the lack of knowledge and advice available to HAE youngsters regarding many of the challenges we hope to address in this toolkit.

The toolkit has successfully been launched at www.southafrica.haei.org. Thanks to Operations Manager Nevena Tsutsumanova, we have also recently collaborated with HAE International to transform the original toolkit into free online courses with loads of helpful resources, tools and fun activities!



PERU

HAE Peru has registered one more HAE knowledgeable hospital, this time Hospital Nacional Arzobispo Loayza in Lima. Please see further information at <https://haei.org/location/hospital-lima-peru>. Also, several HAE knowledgeable physicians have been added to the map in Peru – please see <https://haei.org/hae-member-countries/peru>.

HAE Peru is yet another organization to have its website hosted with HAE International. Please see <https://peru.haei.org>.



CANADA

From the HAE Canada Team

We are kicking off this update with an exciting announcement: Canada now has a representative on the HAE International Youth Advisory Group. We would like to formally introduce Jacob Collins, who lives on Canada's west coast, in beautiful British Columbia. We are thrilled a Canadian will help this fantastic group connect young HAE patients, who will ultimately grow the global HAE community.



We are confident that Jacob, who hopes to become a nurse one day, will be a positive and helpful addition to the team. We would like to thank Operations Manager Nevena Tsutsumanova for inviting a young Canadian to join the Youth Advisory Group. The group is in great hands with Nevena at the helm.

We are also happy to share that HAE Canada associates, between ages 0 and 8, are now able to join the Brady Club, an online safe space created for children diagnosed with HAE. We are grateful that US HAEA has opened registration to Canadian children associates so they can better understand and cope with their disease in a fun, interactive way. We would like to extend a special thank you to Lisa Facciolla, US HAEA's Patient Advocate/Children & Youth Programs. Lisa was amazing to work with, and we appreciated all the work she did to facilitate Canadians joining the Club.

Canadian HAE patients are one step closer to gaining equal access to treatments across Canada. Takeda Canada completed negotiations for Takhzyro (lanadelumab injection) with the pan-Canadian Pharmaceutical Alliance (pCPA), a negotiating body that helps keep drug prices affordable in Canada. This

means that Takeda Canada is now able to start working with different payers across Canada to implement public funding of Takhzyro for eligible HAE patients. We are very excited about this new development and grateful of the time and energy spent by our President, Jacquie Badiou, VP, Tina McGrath, along with Takeda's staff, that helped to allow this to happen.

As mentioned in a previous issue of *Global Perspectives*, Jacquie Badiou, along with our talented contract workers, Bob Bick and Dr. Suzanne Kelly, along with summer intern Maggie Dao, worked hard on our second National Report Card survey over the summer. We are happy to share this survey was launched, and our members across Canada will have a few months to complete this important survey. The data will allow HAE Canada to understand patient product use, symptoms and needs so we may continue to advocate for improved access to new safe, and effective, therapies and treatments for Canadians living with HAE, as well as retain access to current treatments. We look forward to sharing the results.

HAE Canada recently had the privilege of attending the 75th Annual Canadian Society of Allergy and Clinical Immunology (CSACI)'s Scientific Meeting. Three Board members, Jacquie Badiou, Anne Rowe, Lorraine Coumont and staff, Daphne Dumbrille, joined other participants online to view interesting and informative sessions. One presentation that was particularly interesting was by Dr. Hilary Longhurst of the United Kingdom, titled, "Practical Management of Immune diseases – HAE Guidelines and Management with and without COVID-19". HAE Canada submitted a virtual "booth" that provided participants with HAE Canada's various handouts on HAE. It was wonderful to have an effective way to share HAE information to the Canadian and international participants digitally.

As we enter into the winter season, HAE Canada will continue to stay busy with different projects and events, including organizing another virtual patient information update and attending our Annual General Meeting.

We are certainly grateful we are able to continue to function as an organization during these COVID-19 times, but hopeful there will be a vaccine very soon so we can be social once again.



INDONESIA

HAE Indonesia now has a Facebook page – please visit and “like” www.facebook.com/haeindonesia.



COLOMBIA

HAE Colombia is yet another national HAE organization to have its website hosted with HAE International – please see www.colombia.haei.org.



RUSSIA

*From Chairman Elena Bezbozhnaya,
HAE Russia*

During the challenging time of the COVID-19 pandemic, HAE Russia keeps in touch with patients and supports its members through all available means. In the fall, we have ensured several important events, both online and offline.

In early September, when the coronavirus rate slowed down, the School of Patients with HAE held a face-to-face session for residents of Moscow and the Moscow region in the Radisson-Slavyanskaya Hotel conference hall. The discussion covered new clinical guidelines for patients with HAE and vaccination issues:

- I revealed new trends in therapy and prevention of HAE, reviewed prolongation medications that are currently under clinical trials, and addressed the difficulties faced by patients with HAE
- Ilya Ushankov, lawyer of HAE Russia, PhD, presented patient routing “Legal status of patients with HAE” and performed a training business game with the participants, simulating the situation of an HAE patient interacting with doctors
- Tatiana Latysheva, Doctor of Medical Sciences, Professor, Head of the Department of Immunopathology of the Federal State Budgetary Institution SSC Institute of Immunology of the Federal Medical and Biological Agency of Russia,

observed changes in clinical guidelines for HAE treatment and prevention

- Andrey Prodeus, Doctor of Medical Sciences, Professor, Head of the Department of Pediatrics at the Moscow Faculty of the Russian State Medical University named after N.I. Pirogov focused on the current spread of coronavirus infection in Russia and the world, answered questions regarding vaccination as patients with HAE can get vaccinated against seasonal influenza and COVID-19 according to the national vaccination calendar.



On 19 September 2020, HAE Russia conducted an online school, which brought together members from Russia and representatives of patient organizations from Ukraine and Belarus.

I presented an electronic model of an HAE patient’s passport developed by the Institute of Immunology of Russia. Ilya Ushankov, lawyer, informed about the main legal documents that can guide patients in establishing a diagnosis, entering data into the federal register, passing the medical commission, prescribing treatment and medical provision. Then, Ekaterina Viktorova, allergist and immunologist of Dmitry Rogachev

National Research Center of Pediatric Hematology, Oncology and Immunology of the Ministry of Health of the Russian Federation, discussed the situation with COVID-19 in the world and Russia, and the impact of the virus on people suffering from various diseases. The doctor pointed out no data available on the increase in severity or number of cases among patients with HAE, but COVID-19, like any other infection, may become a trigger for swelling. Irina Manto, allergist and immunologist of the Federal State Budgetary Institution SSC Institute of Immunology of the Federal Medical and Biological Agency of Russia, introduced all the medicines currently available for the treatment of HAE in Russia, noting the specifics of their use by women. The doctor also emphasized the pregnancy issue for women diagnosed with HAE.

The event included a new animated video featuring all stages of routing of patients with HAE. In addition, the video gave recommendations to patients with a confirmed HAE diagnosis regarding preferential medical provision.

On 6 November 2020, HAE Russia provided a webinar for patients from different regions of Russia. The discussion brought up routing standards, medical provision, rights and obligations of doctors and patients. The webinar gathered many new members of the organization, so I started my speech with the forms of work of HAE Russia, referring to the three major areas of our activities: Information, psychological and legal support. Also, I informed the participants on the results of the survey conducted in 2020 among members of the organization:

The study revealed fatal cases of HAE-related attacks in the history of one in three families with HAE patients. Seventy-five percent of the interrogated stated having laryngeal edema. Most patients, particularly 65 percent, do not feel protected in everyday life. First of all, they associate such situation with insufficient knowledge of doctors about the course and the specifics of the disease. Eighty-one percent of respondents noted the extremely low level of awareness about the disease in Russia. Thirty-two percent consider the negative impact of HAE diagnosis on educational opportunities, while 49 percent of patients reported on the negative influence of the disease on their professional activity. Sixty-one percent of respondents believe that the condition limits their daily and travel activity. As for the HAE issues to be addressed first, 93 percent of respondents expected new up-to-date medicines to

be registered in Russia and made available. Besides, 70 percent of respondents suggested that the level of diagnostics should be improved.

Legal adviser Ilya Ushankov reported on providing legal assistance to patients, including the judicial practise of protecting the interests of HAE Russia members, and introduced the mechanism for obtaining the required medications.

Doctor of Medical Sciences, Professor, head of the Department of Immunopathology of the Federal State Budgetary Institution SSC Institute of Immunology of the Federal Medical and Biological Agency of Russia, Tatiana Latysheva devoted her speech to the nature of the disease, symptoms and the course of HAE. Dr Latysheva covered in detail abdominal attacks and long-term preventive measures. She noted that 30 percent of HAE patients in the Russian regions do not have access to the latest medications, and 43 percent of patients do not receive long-term preventive care for various reasons.

During the meeting, patients with HAE could share their concerns with the speakers and get qualified answers from the experts.

During the autumn of 2020 HAE Russia has continued to provide legal assistance to members who do not receive effective medicines. We ensured support for such patients in court proceedings, drawing public attention to the current issues and publishing articles on the subject in the federal and regional media.



BRAZIL

HAE Brazil (ABRANGHE) has added yet another social media to its means of communication – please look for @abranghe on Instagram.



SOUTH KOREA

From Soo Jin Min, Chairman of HAE Korea

HAE Korea took a meaningful first step as a non-profit, voluntary organization on 7 November 2020 after a year of activities, starting with its first meeting of friends on 9 November 2019. We elected vice-chairman and general secretary and delivered emergency medical cards for Korean patients.



The meeting that took place on the 31st floor of Lotte Tower in Seoul was attended by ten patients as well as nine people from the Songseok Foundation and pharmaceutical companies.



After a word of welcome and an update from myself, the participants heard about topics such as the HAE Korea hospitalization website, our 2020 Business Report as well as medical support and consultation. Furthermore, we introduced the HAE Korea Emergency Medical Card and Professor Kang Hye-ryeon of the Seoul National University Hospital gave a lecture on “HAE Diagnosis and Management”.



USA

From Patient Advocate/Social Media Manager Ianice Viel, US HAEA

HAE Research: The US HAEA continues to sponsor, produce, and disseminate scientific information that leads to better care for people with HAE. Some of our recently completed projects are highlighted below.



Hereditary Angioedema Primer: The US HAEA joined forces with the prestigious medical journal Allergy and Asthma Proceedings and HAE physician-experts to develop a special supplemental edition on HAE diagnosis and management. The recently published (1

November 2020) supplement contains 14 peer reviewed articles on a range of 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.

US HAEA Medical Advisory Board 2020 Guidelines: We are excited to announce that the US HAEA Medical Advisory Board 2020 patient-centric guidelines for healthcare professionals have been approved for publication! These guidelines provide the 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. You can view these downloadable guidelines in advance of final printing in the *Journal of Allergy and Clinical Immunology—In Practice* at <https://bit.ly/MAB-guidelines>.

US HAEA and Angioedema Center at UCSD Study of COVID-19: The US HAEA and the US HAEA Angioedema Center at UCSD are conducting a survey to help determine if

1. people with HAE are at greater risk of contracting COVID-19, or
2. having HAE or taking HAE medicines affect the duration and/or severity of an infection?

The goal of the study is to safeguard the HAEA community's wellbeing by understanding the interaction of HAE and the virus. Almost 1,400 members of the US HAEA have already responded, and the survey will remain open for the indefinite future so that responses can be updated if someone is unfortunate enough to contract COVID-19.

HAEA Study of Insurance Reimbursement Challenges Faced by People with HAE: We have completed a major research initiative designed to help people with HAE and physicians who prescribe our medicines to obtain insurance reimbursement for HAE medicines. We have conducted detailed surveys of those with HAE, reimbursement specialists in the offices of prescribing physicians, and also conducted structured interviews with a representative sample of health insurers to gather their perspectives on HAE medicines. Based on this data, we are preparing separate guidebooks for people with HAE and physicians who prescribe HAE medicines to help navigate the complex and often frustrating process for obtaining reimbursement for

HAE medicines. Such guidebooks will be available within the next coming weeks.

Medical Journal Publishes US HAEA Health Economics Study Demonstrating the Value of New HAE Preventive Medicines:

The US HAEA in collaboration initiated a study in response to research published by a group of economists who receive funding from the insurance industry. Their economic research concluded that the new preventive HAE medicines are not cost effective. The US HAEA and HAE International questioned the methods and conclusions of this publication and performed a comprehensive analysis to assess the financial and quality of life impact of the new preventive medicines. The data provided by the US HAEA community (through the largest survey of people with HAE ever conducted) reveals that the new preventive therapies yield substantial economic value in light of (1) remarkable decreases in attack frequency and (2) statistically significant improvements in patient quality of life.

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

We are 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. Scientists at the US HAEA Angioedema Center at UCSD San Diego now have in-house genetic testing for several genes that are believed to be implicated with a deficiency in C1-Inhibitor. Physicians and scientists at the Center are committed to expanding the knowledge of this condition and working tirelessly to the development of suitable treatments.



2020 US HAEA Virtual Events: In response to the global COVID-19 pandemic, the US HAEA quickly adapted and found a way to seamlessly provide its programs and services in a virtual format. The shift to online communication has been embraced by members of

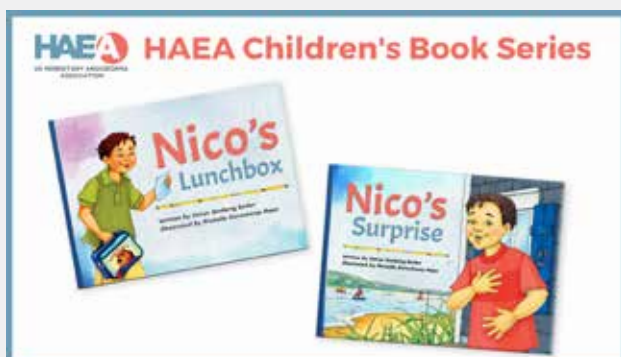
the community and provides special opportunities to engage in programs that promote HAE awareness, HAE-specific learning, and advocacy training.

HAEA Community Steps up for hae day :-) 2020: This year we celebrated **hae day :-)** by hosting a Stepping Forward Together Virtual Walk. During the entire month of May, our community celebrated the awareness day by raising awareness through the Virtual Walk. This exciting event brought together over 280 participants who joined the HAE community in logging over 15,000 miles for HAE Awareness.

HAEA Meet & Greet events: Before the COVID-19 pandemic, we had scheduled a robust lineup of in-person Meet and Greet events planned over the course of 2020, however, we quickly transferred these popular events into a virtual platform to keep our constituents healthy while allowing them to still connect with us and with each other.

2020 HAE IN MOTION Virtual Challenge: We are grateful to the over 500 participants from across the United States and Puerto Rico who joined us, both individually and as teams, for the 2020 HAE IN-MOTION Virtual Challenge! This exciting event brought together the HAE community in logging over 28,000 miles.

2020 HAEA Virtual Capitol Hill Day: The HAEA community joined forces and participated in the 2020 HAEA Virtual Capitol Hill Day. With over 100 registrants committed to having their voices heard by policymakers, this event is sure to create lasting change for the HAE community. Together, we are sending a powerful message in favor of health care coverage, charitable assistance programs, and access to therapies to our elected leaders.



HAEA Children's Book Series - Nico's Surprise: The second book in the HAEA Children's Book Series, "Nico's Surprise", is now available! If your family enjoyed reading Nico's Lunchbox, you'll love "Nico's Surprise". The HAEA Children's Book Series is a timeless resource for children learning to cope with their HAE.

"As a four-year-old with HAE, my daughter doesn't know another child that is going through what she goes through. Nico felt relatable to her and gave her the feeling that she wasn't alone in her experiences!" – John.

Attention all Spanish speaking HAE friends, we have exciting news for you! The second book of the series, "Nico's Surprise", is currently being translated for publication in Spanish. Stay tuned to the US HAEA social media channels and emails for the announcement of when "Nico's Surprise" is officially available for order in Spanish.



US HAEA Webinar Briefs provide useful and timely information: We have developed a series of educational webinar briefs, hosted by President and CEO, Tony Castaldo, that presents information on issues that are important to the HAEA community. The webinar briefs, which are easily accessible through the US HAEA webpage and social media outlets, cover a wide array of topics and are a great way to stay updated with the latest developments affecting the HAE community, including COVID-19. Webinar topics include:

- COVID-19 and HAE, with Dr. Marc Riedl, Clinical Director at the US HAEA Angioedema Center at University of California San Diego
- COVID-19 and Insurance with HAEA Health Advocate, Troyce Venturella, MPH, RN, CCM
- COVID-19 recovered HAE Patient Scott McCoy
- HAEA Scholarships Support Education for our Youth, with HAEA Patient Advocate, Lisa Facciolla
- Why People with HAE Should Not Fear the Dentist, with Dr. Jonathan Bernstein
- Clinical Trial Update: BioCryst's Oral Medicine for Attack Prevention
- Clinical Trial Update: Kalvista's Clinical Development Program for Oral HAE Therapies

Watch these webinar briefs through the US HAEA YouTube Channel ([ushaea](https://www.youtube.com/channel/UCshaea)).



2020 US HAEA Youth Events: We work hard to provide effective and meaningful programming and support for youth members throughout the year. In 2020, some of the US HAEA Youth programs included:

- **Social Media Internship:** The HAEA Social Media Internship is designed to provide young people in the HAEA community with an opportunity to gain professional development and advocacy skills. The internship offers patients and caregivers real world experience in social media content and creation, social media strategy and marketing, storytelling and advocacy, and more! Find us on Instagram by searching for @HAEAYouth. This internship is currently exclusive to HAEA community members living in the United States between the ages of 14 and 25.
- **HAEA Comfort Kits:** This year we launched an exciting new program for Brady Club members, HAE Comfort Kits! Each kit is designed to offer support to children who are struggling with HAE attacks or administering medication. Since children can face unique challenges in coping with the diagnosis of a rare chronic illness, these kits help them to understand their HAE and know that the HAEA is here to help. HAE comfort kits are currently only available to HAEA members in the United States.
- **The Brady Club:** The Brady Club is an international initiative working with HAE International member organizations around the globe to provide kids with a fun platform where they can learn about HAE, complete interactive activities, and read about other kids in the HAE community. Registered members receive quarterly activity books that include interactive activities for your child to complete, HAE facts, collectable stickers, and more!
- **Virtual Legislative Advocacy Training Program:** This year, we developed a program to engage young HAEA community members in legislative advocacy. This six part training program led participants through the completion of a series of activities to help them become more effective advocates. Participants learned how to effectively tell their personal HAE story, research and learn about their congressional

representatives, identify their representatives' stance on health care, and develop a pitch to invite their representative to support the HAE community.

- **BeyondHAE Coloring Contest:** The HAEA's #BeyondHAE Coloring Contest invited children, ages 14 and under, who either have HAE or love someone who does, to create a picture that illustrates what a life #BeyondHAE looks to them! We really enjoyed seeing all the beautiful artwork that was submitted by our community!
- **#BeyondHAE Podcast:** The #BeyondHAE Podcast is a youth produced podcast series dedicated to amplifying the voices and stories of young people affected by HAE. Topics range from sibling support, advocacy, disease management, stories of independence and perseverance, and more! Search for #BeyondHAE on all major podcast platforms!
- **HAEA Youth Instagram Page:** Follow @HAEAYouth on Instagram to get youth program updates, read patient stories, learn about upcoming events, read interesting HAE facts, participate in fun giveaways, and more.



UNITED KINGDOM

From CEO Laura Szutowicz, HAE UK

Much to my surprise, I am already writing another report for *Global Perspectives*. At the time of the last one, we in the UK had come out of lockdown, and there was a gradual return to normal. I was kicking myself, thinking we had decided to make the UK Patient Days virtual. The Patient Days are an enormously important part of our calendar, and they are hugely enjoyable, a chance to catch up with old friends and an opportunity to involve the new ones. We had kept in touch with our members via very successful Zoom meetings, and our wonderful expert panel gave freely of their time to give presentations and answer questions, but I was not sure that the virtual event would work.

Well, I am so happy to have been proved wrong! The virtual event has been a massive success, due in no little part to Rachel Annals, who collated and edited the various presentations. Our fabulous panel of experts proved how we have clinical support that is absolutely top class, and the patients who were kind enough to share their patient stories yet again showed how having HAE does not stand in the way of living your best life.

We started with the 'virtual cocktail party' on Friday evening. The evening pre-meeting reception has

become a feature of the physical Patient Days, and I was a little worried that it might be Rachel and me staring at one another over a glass. However, lots of friends turned up, notably Furkhanda (who is always a major support at all our events) drinking something that I think was vaguely berry-flavored (hence part of her “five a day” fruit and veg!), Nikki Pitt with an enormous red wine...



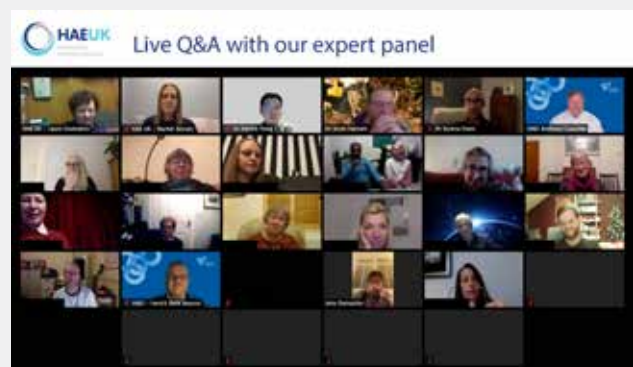
One of our Trustees, Tim Crouch and his wife Sue, definitely won the “best turned out” prize both being in immaculate evening dress. We had circulated a menu of cocktails and snacks, and it was wonderful to see everyone enjoying themselves. Seeing everyone in the little Zoom boxes is a bit like a box of chocolates – don’t know who to pick!

Other events were running over the weekend. People were reminded about the event by being sent an invitation card which was actually full of lovely flower seeds to plant for next year. We thought this was a better way of remembering the event than something that might get thrown away. The youngest members of HAE UK were sent a Percy the Pufferfish bag with a copy of the Percy book, “Nico’s Lunchbox”, some crayons and a coloring competition. The winners of each age group of the coloring competitions were Dean Harber, Charlena Goodier and Charlie Hill. Well done to them! And many thanks to all the other entrants.

Then on to the Patient Day itself. There were many presentations, some introducing the various people involved in HAE UK and what HAE UK can do for members. There was an excellent presentation by Ann Price, the founder of HAE UK, Henrik Balle Boysen and Hilary Longhurst detailing the background of why there was a need to start an organization and how they went about setting it up. We then had excellent presentations by various of our clinicians about topics:

- “HAE – Why? How?” with Dr. Schuab Elkhalfa as the Superhero C1-INH
- “Keeping Fit and Healthy with HAE” by Specialist Nurse John Dempster
- Patrick Yong gave a reprise of his History of HAE as well as an update on the activities of the HAE Clinical Network
- Scott Hackett was his usual expert self on dealing with children and young adults with HAE
- Sorena Kiani gave a very interesting presentation on current treatments for HAE and what might lie in the future
- Hilary Longhurst transmitting all the way from New Zealand presented on HAE and women
- Mark Gompels and his Specialist Nurse Lisa Smith told us how important clinical trials are to furthering treatment and knowledge of HAE
- Immunology Nurse Specialists Fran Ashworth and Christine Symons brought us up to date on the work of the nurse specialist – both these ladies have been tremendous supporters of HAE UK right from the start, and we are fortunate to have them!
- Dawn Harper may not be familiar to most of the HAE community, but she is a well-known doctor on TV and radio in the UK, and she told us how to get the most from your GP appointment
- Anthony J. Castaldo gave an update on the worldwide activities of HAE International.

There are also patient stories from Dana Shapiro, one of our Trustees, on how she climbed Mount Kilimanjaro, Scott Weddle and Paul Carroll. Scott and Paul are both amazing fitness people. The most important message from all their presentations is that anyone can do it but take it slowly and gradually build your fitness, don’t think it can all be done at once.



Then on Saturday afternoon, we had a live Q & A with Drs. Hackett, Yong and Kiani, Anthony J. Castaldo and Henrik Balle Boysen. We rather overran time with this, but it was very interesting. One of the topics was around having COVID-19 vaccinations, and the basic message was, discuss it with your care team, but the

results so far are really promising. We also touched on the importance of mental health issues and how we need to recognize these to assist people who might otherwise just say “yes, I’m fine”.



The day finished with a very testing quiz, Rachel is our quiz mistress extraordinaire and never fails. Did you know wombats have cube-shaped poo?

Anyone who wants to view the presentations is welcome to visit www.haeuk/pd2020, and I hope you enjoy them!

A final bit of good news is that berotralstat, the oral prophylaxis treatment manufactured by BioCryst, is available in the UK under an Early Access Medicine scheme. This means that, even though it is not fully licensed, clinicians in the UK can prescribe it where they think appropriate. So, this is yet another product available to our clinicians to use for patients.

Stay safe everybody, best wishes for Christmas and let’s look forward to a better 2021!



AUSTRALIA AND NEW ZEALAND

From CEO Fiona Wardman, HAE Australasia

HAE Australasia held a webinar for patients and carers in New Zealand with Dr. Karen Lindsay, Dr. Hilary Longhurst for physicians and research updates. The webinar was recorded and has been uploaded to our YouTube channel: <https://youtu.be/DsdKUdTDHJQ>.

One of our younger HAE patients from Perth, Western Australia, has shared her personal HAE story as a newly diagnosed patient. The story was shared through our social media and gained positive feedback from her family, friends, and our members.

A lot of hard work has been going on behind the scenes by Olivia (one of HAE Australasia’s Directors) on the website

video project. An agency has been engaged, and the first video on mental health tips and tricks will be recorded in December. We look forward to being able to share the finished product with everyone.

HAE Australasia was included as a panellist for discussion with the Pharmaceutical Benefits Advisory Committee (PBAC), along with the Department of Health and key physicians to discuss HAE patients gaining access to one of the new modern treatments. The discussions were fruitful in helping the decision-makers understand how this treatment would be beneficial to HAE patients.





SWITZERLAND

From HAE Switzerland

Again, the coronavirus has its grip on Switzerland. By the end of October 2020, restrictions and measures against the virus have been reinforced due to increasing infection numbers. Newspapers and online news are only covering one topic.

Despite these very difficult times, we are very pleased to be able to share the 4th edition of our newsletter both in German and French, bringing an update to

our members, the HAE network and others with HAE interest.

Fortunately, the whole world hasn't stopped. It is with pleasure we can announce that Berinert 2000/3000 (s.c.) is now available in Switzerland. And we are already seeing the first results of patients on Takhyro which has been available in Switzerland since 16 December 2019.



DENMARK, NORWAY AND SWEDEN

From HAE Scandinavia

Similar to most other organizations, HAE Scandinavia had to conduct the General Assembly via Zoom. This time we used Zoom Webinar which gave us a lot of functionality when it comes to polls etc. Although everyone in Scandinavia is sick and tired of the corona restrictions, we all adhere and hope for the world to turn normal soon again.

On 8 October around 30 people participated via Zoom Webinar in the 2020 HAE Scandinavia General Assembly. Here the financials were approved, there was an agreement to a minor change of the bylaws, and new board members were elected. After many years of service with the board of HAE Scandinavia, both Bente Egaa and Poul Erik Andreasen decided that it was time for them to retire. We would like to thank both of them for their hard work over the years and their dedication for patients and caregivers in Scandinavia.

The new board of HAE Scandinavia was elected, and we are happy to announce that two young people, who also are active with the HAEi Youngsters, were included on the board. We also had the pleasure of welcoming both Karen Jespersen Hansen and Erik Hovgaard Hansen to the board. As of 8 October 2020, the new board of HAE Scandinavia includes:

- Henrik Balle Boysen (President) – Denmark
- Jørn Schultz-Boysen (Vice President) – Denmark
- Karina Langsager (Treasurer) – Denmark
- Erik Hovgaard Hansen (Secretary) – Denmark
- Karen Jespersen Hansen – Denmark
- Trine Dahl Johansen – Norway
- Camilla Eriksson – Sweden
- Ann Helen Hellevik – Norway
- Cecilia Grahn – Sweden
- Victoria Schultz-Boysen – Denmark
- Nanna Maria Boysen – Denmark

With two youngsters on the board, HAE Scandinavia now is ready to increase the focus on, and helping, our younger patient population, keeping them engaged and motivated to optimize their life's potential further.

Continuing to maneuver in the virtual world, the planned HAE Scandinavia patient meetings for the autumn of 2020 and the spring of 2021, will be converted into an HAE Scandinavia Virtual Meeting that will be launched in the first quarter of 2021. The HAE Scandinavia Virtual Meeting will include presentations from HAE experts, interviews with HAE experts and other health care professionals, a patient session, as well as presentations from our younger board members. There will also be Q&A sessions and other activities during the virtual meeting.

AUSTRIA

From President Adelheid Huemer, HAE Austria

2020 has given us a lot of new challenges, and no real face to face meetings are possible. Therefore, 27 November 2020 HAE Austria went virtual and hosted the webinar “My good life with HAE” for its members.

Prof. Dr. Marcus Maurer from Charité in Berlin, Germany spoke about the latest treatment methods both on-demand and prophylactic – with Takhzyro and Berinert 2000/3000 as new products on the Austrian market. Prof. Maurer is of the impression that HAE patients can only improve their quality of life through the correct prophylactic treatment.

Dr. Clemens Schöffl, an expert from the Uniklinik Graz and Chairman of the Board of HAE Austria, talked about “HAE: Psyche and stress”. Dr. Schöffl is an HAE patient himself and thus has a double role as patient and physician. In his experience, stress – regardless if good or bad – can move the attack frequency in both ways, which was new for all of us. This means that stress can cause zero attacks or especially frequent attacks; both options are possible.

Last but not least Prof. Dr. Werner Aberer, our HAE expert in Austria, shared his experiences on the theme “Every patient needs an individual treatment”. Prof. Aberer presented six patients from the Uniklinik Graz and their different experiences as well as HAE treatments. He also moderated the webinar, which was received very positively by our members.

We were pleased to see so many people from HAE Austria participating in the webinar – and we are thankful to CSL Behring for helping us in arranging the meeting.

innovative projects and provide financial support. The bottom line is to promote projects to benefit the majority of patients with rare diseases.

On the afternoon of 24 October 2020, the award ceremony of the contest sponsored by the Disease Challenge Foundation and guided by the China Rare Disease Alliance was successfully held after the official meeting of the China Rare Disease Conference 2020. We won a seed fund award of 10,000 USD, which will be applied to the operation of the later project.



Rare disease conference: On 31 October and 1 November 2020, the Shanghai Medical Association, the Shanghai Center of Diagnosis and Treatment of Rare Diseases and the Shanghai Children’s Center of Diagnosis and Treatment of Rare Diseases jointly organized a conference on rare disease prevention and control. The meeting focused on and exchanged topics in the areas of rare disease research, related drug development, policy support, and social support for patients with rare diseases.



CHINA

From HAE China

Winner of seed fund: April 2020, the first public benefit innovation competition for rare diseases was officially launched. Through online courses, an offline entrepreneurship camp and project supervision, rare disease organizations are helped to improve their overall operation ability, incubate high-quality,

PATIENT STORY



Having a solid contact with HAE International via the Regional Patient Advocate has made things easier for Angie Dayan Leitón Chacón. For sure, it is not the same to work alone for HAE patients than to have the support and presence that an international organization with the proper resources and global experience can provide.

Patient Story: Angie Dayan Leitón Chacón

PROPER TREATMENT WOULD BE A BLESSING FOR THE CHILDREN OF COSTA RICA

I had my first attack when I was eight years old. It started as abdominal pain, but I didn't know what it was – and obviously, I didn't know anything about HAE at that time. The attack was so strong that I couldn't walk. I was transferred to a hospital because everyone thought it was appendicitis and stress colitis. The doctors decided to operate me at that time, but after some tests, they chose not to and eventually sent me home.

This must have been around 2002. Were you diagnosed at that time?

Oh, no! Many years went by without me knowing what was happening. My parents did their best to try to find out what was going on, and they paid for many doctors trying to come up with the right diagnosis. One day I visited a rheumatologist, and she did several studies. Later on, she saw me with other rheumatologists from my home city to evaluate my case, and they decided to send me someplace else for yet another analysis. That is why I went to one of the hospitals in San José to see doctors specialized in immunology. There a doctor examined me – and to my amazement, she said that she thought she knew what I was suffering from. She sent me to do blood tests outside the country, and when the results came, I had a positive result for HAE. I was then referred to Mexico because the doctor knew that there was a community of patients with the disease in that country, and she understood that they could help me better in Mexico. So, I wasn't officially diagnosed before meeting this immunologist in 2016. Today another doctor – in Costa Rica – is treating me.

How has your childhood and adolescence been affected by HAE?

After that attack, when I was eight, I didn't have another severe one until I was 15 years old. By then the attacks became more frequent, and so it has been to this day. I would say that my adolescence was very difficult. I was attending school, but naturally, my classes were interrupted. On top of that, people were staring at me, so it was indeed a difficult time. Boyfriends, friends – we all want acceptance from the world because it is a challenging age. And it is something that I still have inside because it is very complex. Sometimes I didn't like people to ask me because it was tough to explain. And until I was 18 or 20 years old, I thought my problem was with my body periphery because only my limbs were swollen.

I guess this also affected, for instance doing sports?

You're quite right – I had to stop swimming. I liked swimming. Since I was little in school, I used to enjoy swimming. I competed in this sport but was afraid to swell from the effort or impact with the edge of the pool.

I am a positive person, but I have had to leave many things to avoid swelling or worrying my family. On one occasion, I was in teamwork training with my job, and I had to ask not to participate in an exercise where they threw a ball because I thought that if they hit me with the ball, it could give me an attack and could inflame me.



Sometimes I stop myself doing things with friends for fear of inflammation. For instance, I try to avoid entertainment parks because I cannot jump down slides or use machines where there could be any impact that could create an attack.

What kind of HAE treatment do you have?

None. Whenever I have a crisis, I endure the pain. Only when the attack hits my face, they use hydrocortisone and fresh plasma. During my most recent severe attack, my airways swelled, and fresh plasma was used to reduce the crisis.

Are there any other HAE patients in your family?

According to my doctor, no one else in my family has the condition – I am the only one with HAE type I; with HAE at all, that is. Speaking of family and other people close to me: My husband knows about my condition, and he is very well prepared to help me. That is quite important as when I have abdominal attacks, I go unconscious. My boss and my colleagues are also aware of me being an HAE patient. Indeed, all people close to me – like my husband, my mother, and people at work – have a copy of the information about HAE in case something happens. The family of an HAE patient needs to know everything about the condition.

Could you elaborate a bit on that?

Well, it is essential because when I have a strong attack, my husband supports me in everything. He

combs me, helps me with medications, with food, etc. People must be aware of the disease and what it can do to the patient. Sometimes at work, if I have a seizure in my hands, my colleagues help me – and at home, my husband does the same. My boss and the company have been very good to me. That is why I think it is imperative to keep them well informed.

How would you describe the present HAE situation in Costa Rica?

I feel that for many people, our disease is insignificant because there is only a relatively limited number of identified HAE patients. On the other hand, patients who live with HAE know that it is not a disease or a situation that must be left for tomorrow to solve. This affects us all: work, lifestyle, plans, etc. I think that the case right now in Costa Rica is tragic because it is challenging to get proper treatment. It has been and still is very difficult for the Government to understand our situation. I recognize that the treatment is extremely expensive, but the Government and the health system should help us in some way. I think that the health system should modernize in some aspects. Many things must change for the good of the citizens – and I have faith that someday it will improve.

How is the support from the doctors in Costa Rica when it comes to HAE?

When they first hear about the disease, the majority of the doctors have shown an interest in learning more. But unfortunately, the health system does not allow them to go further than the initial help they provide us. I would, however, like to stress that the doctors have been extremely good with the patients. When for instance, I have needed them, they have always answered me and responded to my emergencies despite their routines, vacations or personal commitments.

For a while now you have been the national contact in Costa Rica with raising of awareness as one of your main focus areas. How do you do that?

Indeed, the job of Asociación de Angioedema Hereditario Costa Rica is to raise awareness about the condition through our testimonies. I don't want other people in the future to have to go through what I've been experiencing. Having to go to a hospital, having to explain what the problem is, and having doctors

look at you with doubtful faces because they don't know anything about this disease. We have to continue working on building awareness in Costa Rica so that more people – both patients, health care professionals, politicians, and the general public – know much more about HAE.

As the national contact in Costa Rica, you work with HAE International. How do you think the global organization can help you and HAE patients in your country?

Since I first met HAE International, I have started to see the good things for us. The fact that the global organization supports us, helps us, and have proper guidance for us is a blessing.

With HAE International on my side, I started to see all the good things I want to do in Costa Rica. For instance, the HAE International Regional Patient Advocate for my part of the world – that is Javier Santana – has proved to me that he is willing to work with me, with our organization and with the HAE patients in Costa Rica.

Having a solid contact with HAE International via the Regional Patient Advocate has made things easier for me. For sure, it is not the same to work alone here in Costa Rica for our disease and to have the support and presence as an international organization with the proper resources and global experience. Working with HAE International has helped us clarify many doubts that we had as patients, and it has given us the support that any group, with any disease in the world, needs from an international organization. Indeed, I am very grateful because from the first moment I met HAE International and the Regional Patient Advocate, I have never felt alone.

What are your short-term tasks in Costa Rica?

Take action as soon as possible – and hold more meetings and conferences to talk about HAE in Costa Rica. With our legally established organization, it will be much easier for us to carry out this type of events. At the moment, it is very hard for us to reach the media, so another short-term task is to get a broader audience via the media and create awareness about the disease.

Let me close with a personal question: What do you think your life will be like the day Costa Rica finally has access to modern HAE treatments?

For me, it will be a dream come true. I would be able to live an everyday life. I can imagine I won't have to live with the anguish of not being able to do what I want. Not having to live with the mystery of not knowing when or how the next attack will hit me. Sometimes, as much as I take care of myself, I don't know why I have an attack, and that saddens me. But to think that modern HAE treatments will arrive for us in Costa Rica is a dream – it is to have won the battle against the disease. I think every day about the children who are hospitalized due to HAE. If proper treatment came to Costa Rica someday, it would be a blessing for them too. I think about how it could change their lives as well as the lives of adult HAE patients.



ANGIE'S STORY IN BRIEF

- Born in 1994 in Cartago, Costa Rica
- Works within public accounting for a private company in Costa Rica
- HAE symptoms started when she was eight years old; diagnosed in 2016
- Other HAE patients in her family: None

POWERFUL FREE RESOURCES FOR MEMBER COUNTRIES



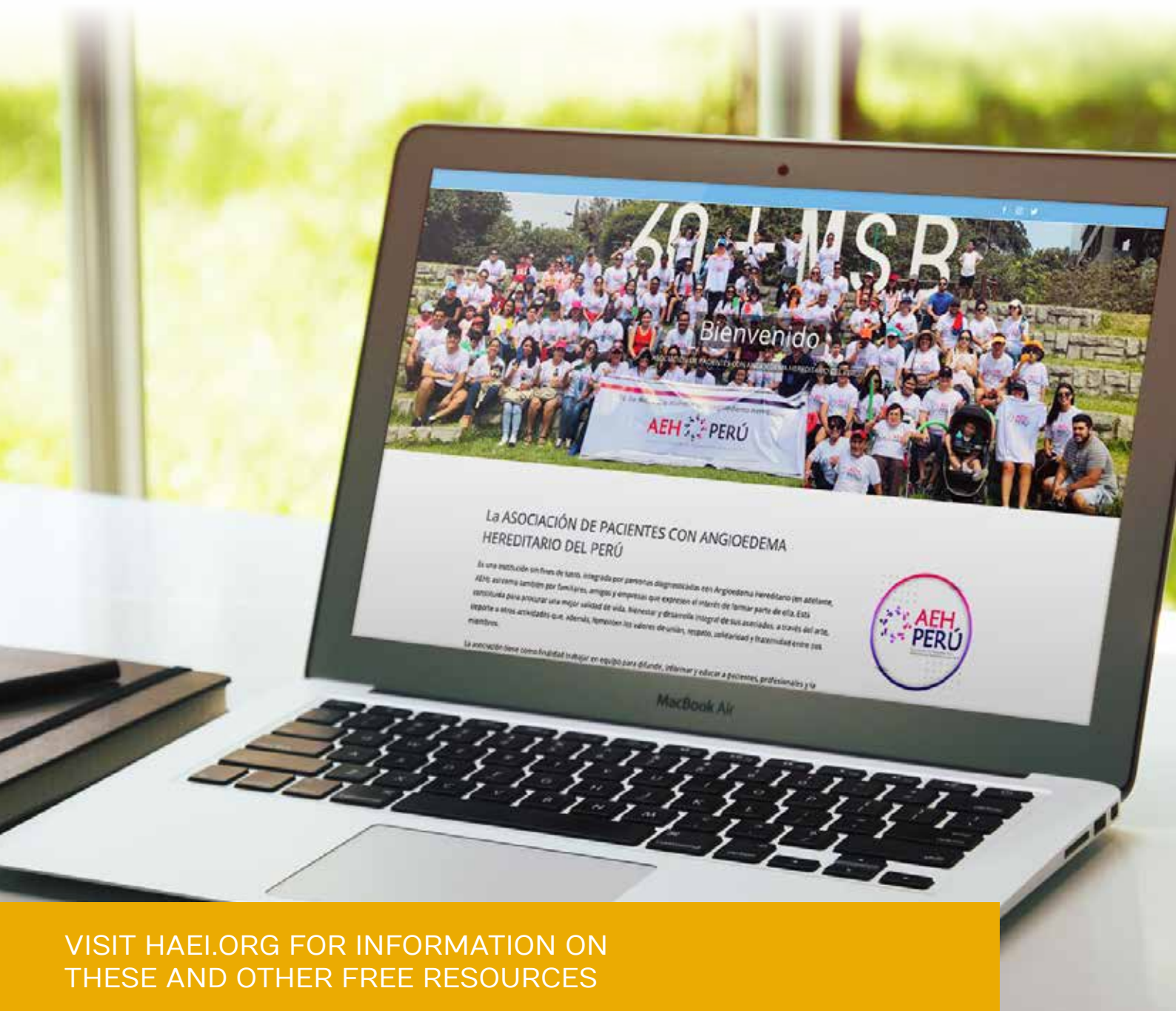
SECURE ONLINE MEMBERSHIP DATABASE AND COMMUNICATIONS PLATFORM FOR THE HAEi MEMBER ORGANIZATIONS

- 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

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- 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



VISIT [HAEI.ORG](https://haei.org) FOR INFORMATION ON THESE AND OTHER FREE RESOURCES

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

Can the neutrophil-lymphocyte ratio predict type 1 HAE attacks? – by Guzin Ozden and Didar Yanardag Acik, Adana City Education and Research Hospital, Turkey:

The neutrophil-lymphocyte ratio – a simple, easily calculated and cheap parameter for the assessment of inflammation – can be used by clinicians as a parameter for prediction of the episode count in patients with HAE.

(Scand J Clin Lab Invest, Sep 2020)

Clinical features of genetically characterized types of HAE with normal C1 inhibitor: a systematic review of qualitative evidence – by Konrad Bork, Johannes Gutenberg University, Germany et al.:

A number of clinical differentiators for the different types of HAE with normal C1-INH have been identified. This may support clinicians to narrow down the correct diagnosis of HAE with normal C1-INH prior to genetic testing and thereby guide appropriate treatment and management decisions. However, confirmation of the causative gene mutation by genetic testing will always be required.

(Orphanet J Rare Dis, Oct 2020)

Clinical presentation of HAE – by Veronica Azmy, Yale School of Medicine, the United States of America, et al.:

Abdominal HAE attacks can cause severe pain, nausea, and vomiting. Bowel sounds are often diminished or silent; guarding and rebound tenderness may be present on physical examination. These findings may lead to unnecessary abdominal imaging and procedures. Fluid shifts into the interstitial space or peritoneal cavity can cause clinically significant hypotension.

(Allergy Asthma Proc, Nov 2020)

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

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

(Ann Allergy Asthma Immunol, Oct 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. A facial HAE attack occurred at week 38 of her pregnancy, and symptoms improved after self-administration of 50 U/kg of recombinant human C1-INH (total dose, 3500 U), but soon after she had an unusual abdominal sensation. Ultrasonography detected fetal lower lip swelling (3 times the normal size) and limb swelling. Physical examination of the mother found cervical dilatation, indicating the final stages of labor. 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. Treatment of the mother with recombinant human C1-INH was effective for the maternal and fetal attacks, with resolution within approximately 2 to 2.5 hours for both patients.

(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:*

The significantly lower delay observed in children suggests 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: Epidemiology and burden of disease – by *William R. Lumry, University of Texas, and Russell A. Settiple, Warren Alpert Medical School, the United States of America:*

The burden of disease for patients with HAE is substantial. Attacks are unpredictable with respect to frequency, severity, and the site of swelling. Feelings of stress, anxiety, and depression can trigger attacks, and begin a cycle of attacks that cause anxiety that, in turn, triggers further attacks. Despite full physical recovery between attacks, patients often experience continual emotional impairment and reduced quality of life. Absenteeism from work and presenteeism at work or educational activities for patients and caregivers increase stress and reduce productivity during and between attacks. Missed opportunities for career development are common. However, significant advances have been made in the past decade to expand both acute and prophylactic treatment options for patients with HAE, lowering the disease and treatment burden, and improving the quality of life of HAE patients.

(Allergy Asthma Proc, Nov 2020)

HAE: On-demand treatment of angioedema attacks – by *Sandra C. Christiansen and Bruce L. Zuraw, University of California San Diego, the United States of America:*

The availability of effective acute treatment for angioedema has been fundamental in reducing the burden of illness for HAE patients. In building on the foundation of scientific advances that elucidate the pathomechanism(s) of attacks related to vascular permeability, novel targeted on-demand treatments have been approved. These therapies have provided the means to arrest episodes of swelling, which, in the past, had the potential to inexorably lead to morbidity, and even mortality, for HAE patients. Access to these medications, along with an emphasis on early administration and guidance that all attacks are candidates for treatment, has shifted the management paradigm for HAE. Although unmet needs remain, these acute therapies and prophylactic treatment have furthered the goal for all HAE patients to live a normal life.

(Allergy Asthma Proc, Nov 2020)

HAE: Special considerations in children –

by Douglas T Johnston, the Asthma and Allergy Specialists, and R. Christina Smith, Levine Children's Hospital, the United States of America:

The onset of swelling is typically in childhood. Unlike adults, this population is uniquely vulnerable; attacks in young children 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 performance may prevent future opportunities. Living with HAE poses significant psychosocial stress on children and their families. In the United States of America, medical treatments for acute attacks in children approved for self-administration are limited to intravenous therapies, which complicates early treatment. To provide optimal care, we suggest that physicians 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 et al., Massachusetts General Hospital, the United States of America:

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 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 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. More research is required in menopausal women with HAE to better understand how to manage climacteric symptoms.

(J Clin Immunol, Oct 2020)

Interactive web-based resource for annotation of genetic variants causing HAE (HADA):

Database development, implementation, and validation – by *Alejandro Mendoza-Alvarez, Universidad de La Laguna, Spain, et al.:*

In agreement with recent recommendations from the International Consensus on the Use of Genetics in the Management of HAE, to facilitate the clinical diagnosis and adapt it to the paradigm of precision medicine and next-generation sequencing-based genetic tests, we aimed to develop a genetic annotation tool, termed HAE Database Annotation (HADA). HADA is built on top of a database of known variants affecting function, including precomputed pathogenic assessment of each variant and a ranked classification according to the current guidelines from the American College of Medical Genetics and Genomics. HADA is provided as a freely accessible, user-friendly web-based interface with versatility for the entry of genetic information. The underlying database can also be incorporated into automated command-line stand-alone annotation tools. HADA can achieve the rapid detection of variants affecting function for different HAE types, and further integrates useful information to reduce the diagnosis odyssey and improve its delay.

(J Med Internet Res, Oct 2020)

Long-term efficacy of subcutaneous C1 Inhibitor in pediatric patients with HAE – by

Donald Levy, University of California at Irvine, the United States of America et al.:

Data from pediatric subjects treated with subcutaneous C1INH for up to 2.55 years and adult subjects revealed similar efficacy. Subcutaneous C1INH is effective and well tolerated as long-term prophylaxis in children, adolescents, and adults with HAE.

(Pediatr Allergy Immunol Pulmonol, Sep 2020)

Management of HAE in Japan: Focus on icatibant for the treatment of acute attacks –
by Michihiro Hide, Hiroshima University, Japan et al.:

In Japan, recognition of HAE within the medical community remains low, and numerous obstacles complicate diagnosis and access to treatment. Multiple factors contribute to delayed HAE treatment (potentially leading to life-threatening consequences), including difficulties in finding facilities at which C1-INH agents are readily available. Recognition of challenges faced in Japan can help promote efforts to address current needs and expand access to effective therapies. Icatibant, a potent, selective bradykinin B2 receptor antagonist, has demonstrated inhibition of various bradykinin-induced biological effects in preclinical studies and has shown efficacy in treating attacks in various clinical settings and HAE patient populations. Icatibant was approved in Japan for the treatment of HAE attacks in September 2018; its addition to the HAE treatment armamentarium contributes to improved patient care. In Japan, disease awareness and education campaigns are warranted to further advance the management of HAE patients in light of the unmet needs and the emerging availability of modern diagnostic approaches and therapies.

(Allergol Int, Sep 2020)

Novel use of fresh frozen plasma in treating HAE: A success story from Pakistan –
by Amber Sabeen Ahmed and Sidra Fayyaz, Aga Khan University Hospital, Pakistan:

The targeted therapy for HAE consists of plasma-derived or recombinant C1-INH, ecallantide, and icatibant or bradykinin receptor antagonist. In the absence of these therapies, it becomes difficult to manage this condition effectively. An HAE patient presented with life-threatening laryngeal edema causing asphyxia and leading to cardiac arrest was (due to a lack of availability of C1-INH concentrate) given fresh frozen plasma. His condition gradually improved, and he was successfully extubated after three days. This is the first time we are reporting a case from Pakistan in which the patient was successfully treated with fresh frozen plasma for an acute attack of HAE.

(Cureus, Aug 2020)

Oral once-daily berotralstat for the prevention of HAE attacks: A randomized, double-blind, placebo-controlled phase 3 trial –
by Bruce Zuraw, University of California San Diego, the United States of America et al.:

Berotralstat (BCX7353) is an oral, once-daily inhibitor of plasma kallikrein in development for the prophylaxis of HAE attacks. Both 110-mg and 150-mg doses of berotralstat reduced HAE attack rates compared with placebo and were safe and generally well tolerated. The most favorable benefit-to-risk profile was observed at a dose of 150 mg/day.

(J Allergy Clin Immunol, Oct 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. Steps are needed to improve the diagnostic and treatment environments to address these issues.

(Allergol Int, Nov 2020)

COVID-19 affecting HAE patients with and without C1 Inhibitor deficiency –
by Anete S. Grumach, Centro Universitario Saude ABC, Brazil, et al.:

To the best of our knowledge, this is the first study to report a series of cases of HAE patients with SARS-CoV-2 infection. In our data, unlike we expected, patients with HAE and COVID-19 did not present severe acute angioedema attacks or severe COVID-19, despite complement system disorder. On the other hand, our population was predominantly female and with a median age below 50 years old, usually reported as less susceptible to severe COVID-19. Also, recognizing the role of the complement and contact systems in SARS-CoV-2 infection could be useful for the therapeutic approach in severe cases of COVID-19. Further real-life registry-based studies are needed to confirm our findings and extend the evidence that HAE patients on prophylaxis are at low risk of developing angioedema attacks and severe COVID-19.

(The Journal of Allergy and Clinical Immunology: In Practice, Nov 2020)



CLINICAL TRIALS

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

A Long Term Safety Study of BCX7353 in HAE

– recruiting in Australia, Austria, Denmark, France, Germany, Hong Kong, Hungary, Israel, Italy, New Zealand, North Macedonia, Poland, Serbia, Slovakia, South Africa, South Korea, Spain, Switzerland, the United Kingdom, and the United States of America

Biomarker for HAE Disease

– recruiting in Armenia, Georgia and Romania

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

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

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 IV Injection of OCTA-C1-INH in HAE

– recruiting in Belarus, Germany, Russia and Ukraine

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

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



National Institutes of Health
Turning Discovery Into Health

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

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

– will be recruiting later

An Extension Study of IONIS-PKK-LRx in Participants with HAE

– enrolling by invitation in the United States of America

Read more about these and other clinical trials at clinicaltrials.gov and apps.who.int/trialsearch.

NEWS FROM THE INDUSTRY

16 October 2020

KalVista Pharmaceuticals, Inc. provides an update on its franchise of oral therapies for treatment of HAE.

“We have completed enrollment of our Phase 2 trial for our oral on-demand HAE treatment, KVD900, and remain on track to deliver data before the end of this year. We are also pleased to announce data from KVD824, our oral program for HAE prophylaxis, and to introduce our oral Factor XIIa program, which we believe represents the next generation of HAE therapeutics,” says Andrew Crockett, CEO of KalVista. “Our ongoing work to optimize the exposure profile of KVD824 has yielded a formulation that maintains the concentrations we believe are required to compete with approved injectable therapies, while showing an encouraging safety and tolerability profile in up to 14 days of dosing. We intend to submit an Investigational New Drug application for a Phase 2 study to evaluate KVD824 in prevention of HAE attacks in the first quarter of 2021. Looking to the future, we are also excited to share early data on our oral Factor XIIa inhibitor program as an additional HAE therapy, with IND-enabling studies anticipated in 2021.”

(Source: KalVista)



18 October 2020

IONIS-PKK-LRx from **Ionis Pharmaceuticals, Inc.** is being evaluated in an investigator-initiated Phase 2 clinical study to determine its effectiveness in reducing the severity of respiratory complications in patients with COVID-19. The trial coordinators are Fernando G. Zampieri, M.D., Ph.D., and Alexandre Biasi Cavalcanti, M.D., Hospital do Coracao (HCor Research Institute), Sao Paulo, Brazil. The study will enroll up to 110 patients at 25 hospitals in Brazil. Ionis has provided IONIS-PKK-LRx and funding to the Brazilian Research for Intensive Care Network (BRICNet) to support the study.

IONIS-PKK-LRx is designed to inhibit bradykinin signaling by halting synthesis of prekallikrein (PKK), a precursor of the enzyme kallikrein, which is involved

in the formation of bradykinin, a protein that promotes inflammation and dilates blood vessels. There is growing evidence that the pulmonary edema (fluid in the lungs) and associated morbidities in severe COVID-19, such as the respiratory distress syndrome, are, in part, caused by a dysregulation in bradykinin signaling, referred to as a “bradykinin storm”. A therapy that prevents or reduces this bradykinin storm could potentially decrease the number of severe cases of COVID-19 in Brazil.

“Bradykinin elevations in the body can cause blood vessels to become leaky, causing inflammation in the surrounding tissue. In the lungs, this is often associated with severe COVID-19 cases. We are hopeful that IONIS-PKK-LRx can alleviate some of the worst symptoms caused by the infection and we look forward to seeing data from the study,” says Kenneth Newman, M.D., M.B.A., Ionis’ vice president of clinical development and leader of the pulmonology and immunology franchise.

In the study, a single dose of IONIS-PKK-LRx or placebo will be administered subcutaneously to hospital patients who present with symptoms consistent with COVID-19. The primary endpoint is the number of days alive and free of oxygen support up to 15 days.

IONIS-PKK-LRx is also undergoing a Phase 2 clinical study in patients with HAE. In September 2020, the New England Journal of Medicine published encouraging data showing safety and efficacy in two patients with uncontrolled, severe HAE. These data support the continued development of IONIS-PKK-LRx as a potential treatment in patients with severe HAE for whom current therapies offer limited therapeutic benefit.

IONIS-PKK-LRx is one of 20 potentially transformative antisense programs in the growing Ionis-owned pipeline that the company is prioritizing and preparing for commercialization.

(Source: Ionis)



22 October 2020

The Journal of Allergy and Clinical Immunology (JACI) publishes data from the first 24 weeks of the APeX-2 trial of oral, once-daily berotralstat in patients with HAE.

APeX-2 was a Phase 3, double-blind, placebo-controlled, parallel-group trial that evaluated the efficacy and safety of oral, once-daily berotralstat versus placebo over 24-weeks in 121 HAE patients ages 12 years or older. In the trial, after 24 weeks, both the 110-mg and 150-mg doses of berotralstat significantly reduced HAE attack rates compared with placebo and were safe and well tolerated, with greater attack rate reductions observed for the 150-mg dose.

The authors conclude that the combination of efficacy, safety, and tolerability with convenient oral, once-daily dosing will make berotralstat an important addition to the HAE-C1-INH therapeutic armamentarium, if approved.

“We are excited to have our results published in JACI, building on the compelling pivotal and longer-term data presented at scientific congresses in the past year. HAE patients are waiting for an oral, once-daily option to control their disease. As the authors have recognized, providing patients with an effective, oral therapy is a major step towards the goal of enabling them to live a normal life,” said Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc.**

On 30 March 2020, BioCryst announced that the European Medicines Agency (EMA) had validated its marketing authorization application (MAA) submission for Orladeyo and begun its formal review of the MAA under the centralized procedure. The company expects an opinion from the Committee for Medicinal Products for Human Use (CHMP) within approximately 12 months from MAA validation.

(Source: BioCryst)



23 October 2020

In its annual R&D briefing to investors **CSL Limited** demonstrates how the company is advancing a novel research portfolio across four strategic scientific platforms (Plasma Fractionation, Recombinant

Technology, Cell and Gene Therapy, Adjuvanted Cell and Egg-based Vaccines) across six therapeutic areas (Immunology, Hematology, Respiratory, Cardiovascular and Metabolic, Transplant, Influenza Vaccines) and two businesses (CSL Behring and Seqirus) to help patients lead full lives, protect public health and drive future business growth. It's this scientific capability and diverse portfolio that positioned the company to quickly respond to the COVID-19 public health crisis.

“CSL's acumen in vaccines, monoclonal antibodies, recombinant technologies, manufacturing capabilities and external partnerships, along with a therapeutic area focus and insight that includes Immunology and Respiratory, has supported the growth and progress of our pipeline and has also enabled us to respond quickly to the need for potential solutions in the world's fight against COVID-19,” said Bill Mezzanotte, MD, MPH, Executive Vice President, Head of Research and Development and Chief Medical Officer. “Right across the spectrum of infection and disease, CSL has taken on projects we think make sense both scientifically and that fit our capabilities.”

The company's efforts in the fight against COVID-19 include:

- Accelerating the development, manufacture and distribution of a vaccine candidate pioneered by researchers at the University of Queensland in Australia in collaboration with the Coalition for Epidemic Preparedness. If the vaccine development is successful, CSL anticipates producing the vaccine for Australia and distribution to global markets via the COVAX facility toward the end of 2021. And CSL is also working with AstraZeneca to manufacture, if successful, approximately 30 million doses of its vaccine candidate under development with the University of Oxford (AZ1222) for supply to Australia.
- Co-founding the CoVlg-19 Plasma Alliance, an unprecedented industry partnership of more than 12 plasma industry companies, to develop a hyperimmune for treating COVID-19. The phase 3 study in which the CoVlg-19 Plasma Alliance is participating enrolled its first clinical trial participant in early-October. The study will take several months to complete, but if successful, will be the basis for regulatory submissions.
- Developing an investigational, anti-SARS-CoV-2 plasma hyperimmune product for the Australian market to treat people with serious complications of COVID-19. The company is currently manufacturing its therapy for the clinical trial.
- Conducting a Phase 2 study to assess the safety

and efficacy of garadacimab (Factor XIIIa antagonist monoclonal antibody) to treat patients suffering from severe respiratory distress, a leading cause of death in patients with COVID-19 related pneumonia. The first patient was enrolled in July.

Additionally, the company is partnering with SAB Biotherapeutics to manufacture clinical and early commercial supplies of SAB-185, a potential novel immunotherapy targeting COVID-19, produced without the need for blood plasma donations from recovered COVID-19 patients. SAB-185 is currently in early phase development.

“The same collaborative mindset with which CSL has responded to the COVID-19 pandemic is also reflected in how we are advancing our pipeline,” said Andrew Nash, PhD, Senior Vice President, Head of Research and Chief Scientific Officer. “Across therapeutic areas, strategic platforms and geographies we continue to grow our footprint and capabilities so that we can deliver a significant benefit to patients around the world.”

Other advancements in CSL’s R&D pipeline in the last year include:

Setting the pace in Plasma Product development:

CSL is continuously improving current plasma fractionation processes and developing new therapeutic options, which has shown major relevance in the fight against COVID-19 and is also evident in other therapeutic areas. For example:

- The company continues to advance its AEGIS-II Phase 3 study of CSL112 (ApoA-1), for potential treatment of acute coronary syndrome. More than 10,000 patients have been enrolled to date.
- CSL has initiated the subcutaneous immunoglobulin 20% Dermatomyositis RECLAIM phase 3 trial. Dermatomyositis is a severe autoimmune disease where there is high unmet need.

Advancing its Cell and Gene Therapy research by:

- Agreeing to acquire exclusive global license rights to commercialize an adeno-associated virus (AAV) gene therapy program from uniQure. The EtranaDez (AMT-061) program, currently in Phase 3 clinical trials, if successful, could be one of the first gene therapies to provide potentially long-term benefits to patients with hemophilia B. The deal is subject to regulatory clearances.

- Commencing a Phase 1 trial of CSL200, a stem cell gene therapy for the potential treatment of sickle cell disease.
- Collaborating with Seattle Children’s Research Institute to develop a stem cell gene therapy for primary immunodeficiency diseases – a rare disease area where the company has industry leading capabilities.

Building momentum in Recombinant Technology:

CSL has established a highly differentiated preclinical and clinical stage pipeline of recombinant proteins and monoclonal antibodies from its proficiency in protein biology and innate cell immunity. In addition to using this technology against COVID-19, the company is studying:

- Garadacimab as a new type of once-monthly subcutaneous prophylactic treatment for attacks related to HAE, for which it has received Orphan Drug Designation from the U.S. Food and Drug Administration. The company shared the encouraging phase 2 study data in June and is preparing for the start of the VANGUARD phase 3 trial. Additionally, garadacimab is showing promise beyond HAE, notably in fibrotic, cardiovascular and inflammatory diseases.
- Acquired Vitaeris Inc., which included clazakizumab (CSL300), an anti-interleukin-6 monoclonal antibody in the IMAGINE Phase 3 trial for the potential treatment of chronic active antibody-mediated rejection, the leading cause of long-term rejection in kidney transplant recipients.

(Source: CSL Behring)

CSL Behring

29 October 2020

At the presentation of the financial report for the nine months and third quarter ended 30 September 2020 **Pharming Group N.V.** CEO Sijmen de Vries says:

“We are pleased to announce continued growth, demonstrating consistent progress, despite the impact of the COVID-19 pandemic. We remain focused on, and are delivering against, our strategy for long-term growth. This includes continued sales growth of Ruconest through increasing market share for the treatment of acute HAE attacks.”

Operational highlights

- On 10 August 2020, the Company announced the enrollment of the first patient in a randomized, controlled, investigator-initiated clinical trial in up to 150 patients for treatment with rC1INH of patients with confirmed COVID-19 infections hospitalized with related severe pneumonia at the University Hospital Basel in Basel, Switzerland. This trial continues to recruit and has since expanded to other centers in Switzerland and is in the last stages of preparation in centers in Mexico and Brazil.
- On 17 August 2020, the Company announced the publication of data in the peer-reviewed journal, *Frontiers in Immunology*, from a compassionate use program of five patients with confirmed COVID-19 infections hospitalized with related severe pneumonia that were treated with rhC1INH at the University Hospital Basel, Switzerland.

COVID-19 update

- No impact on the upscaling or continued production of Ruconest
- No impact on the availability or distribution of Ruconest to HAE patients
- The recruitment of new patients in ongoing clinical trials has been temporarily halted; patients already incorporated into ongoing clinical trials are continuing to receive treatment

(Source: Pharming)



30 October 2020

The United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) has granted oral, once-daily berotralstat from **BioCryst Pharmaceuticals, Inc.** 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 berotralstat for the routine prevention of recurrent attacks of HAE before the drug is granted marketing authorization by the European Commission (EC).

Medicines included in the EAMS are those that have a high unmet need, are intended to treat, diagnose or prevent seriously debilitating or life-threatening conditions where there are no adequate treatment

options, and are likely to offer significant advantage over methods currently used in the UK. Under the scheme, the MHRA provides a scientific opinion on the benefit-risk balance of the medicine, based on the data available when the EAMS submission was made.

"There are many patients in the UK that don't have a realistic option for effective HAE prophylaxis. The addition of berotralstat through the EAMS will bring a much-needed option for HAE patients suffering with this debilitating disease," said Dr. Sorena Kiani, Consultant Immunologist at Royal London Hospital, London.

"HAE patients around the world are waiting for an oral, once-daily therapy to prevent attacks and reduce their burden of therapy. With this decision by the MHRA, the wait for many HAE patients in the UK can end sooner," said Jon Stonehouse, CEO of BioCryst.

The European Medicines Agency (EMA) is reviewing the marketing authorization application (MAA) for berotralstat under the centralized procedure. An opinion from the Committee for Medicinal Products for Human Use (CHMP) is expected approximately 12 months from MAA validation, which the company announced on 30 March 2020.

(Source: BioCryst)



5 November 2020

In its financial results for the third quarter of 2020 **Ionis Pharmaceuticals, Inc.** reports the advance in the IONIS-PKK-LRx program:

- Proof-of-concept data from the PKK development program in patients with HAE were reported in the *New England Journal of Medicine*
- Enrollment completed in the IONIS-PKK-LRx Phase 2 study in patients with HAE
- IONIS-PKK-LRx advanced into an investigator-initiated study in hospitalized COVID-19 patients in Brazil

Among the company's upcoming catalysts is the IONIS-PKK-LRx Phase 2 study in patients with HAE.

(Source: Ionis)



5 November 2020

“We are ready to launch ORLADEYO to bring HAE patients the oral, once-daily medicine they have been waiting for to prevent attacks, reduce their burden of therapy and live a normal life,” says Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc.** at the announcement of financial results for the third quarter ended September 30, 2020.

Updates and Key Milestones for HAE Program ORLADEYO: Oral, once-daily treatment for prevention of HAE attacks

- BioCryst expects three regulatory approvals for ORLADEYO in Q4 2020 and early 2021.
- The U.S. Food and Drug Administration (FDA) is reviewing a new drug application for ORLADEYO and has set an action date of 3 December 2020 under the Prescription Drug User Fee Act (PDUFA).
- In Japan, ORLADEYO is being reviewed under Sakigake designation. The Pharmaceutical and Medical Devices Agency (PMDA) has confirmed their regulatory review schedule and the company expects a decision on approval in December 2020.
- On 30 March 2020, the company announced that the European Medicines Agency (EMA) had validated its marketing authorization application (MAA) submission for ORLADEYO and begun its formal review of the MAA under the centralized procedure. The company expects an opinion from the Committee for Medicinal Products for Human Use (CHMP) within approximately 12 months from MAA validation.
- BioCryst has completed the build-out of the commercial infrastructure to support the successful launch of ORLADEYO in the U.S.
- The company has hired and trained accomplished U.S. rare disease sales and market access teams and has deployed a robust patient services support hub.
- The company is well-positioned in terms of product supply and inventory on-hand to support the launch and anticipated demand for ORLADEYO.
- On 30 October 2020, the company announced that the United Kingdom’s Medicines and Healthcare Products Regulatory Agency (MHRA) has granted oral, once-daily berotralstat 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 berotralstat for the routine prevention of recurrent attacks of HAE before the drug is granted marketing authorization by the European Commission. Medicines included in

the EAMS are those that have a high unmet need, are intended to treat, diagnose or prevent seriously debilitating or life-threatening conditions where there are no adequate treatment options, and are likely to offer significant advantage over methods currently used in the UK.

- On 28 October 2020, the company announced it will present five abstracts and one Distinguished Industry Oral Abstract, including 48-week results from the APeX-2 trial and new data on quality of life and the treatment burden of injectable medication administration, at the upcoming (virtual) Annual Scientific Meeting of the American College of Allergy, Asthma & Immunology on 13-15 November 2020.
- On 22 October 2020, the company announced that data from the first 24 weeks of the APeX-2 trial of oral, once-daily berotralstat in patients with HAE have been published online by the Journal of Allergy and Clinical Immunology.

(Source: BioCryst)



6 November 2020

Takeda Canada Inc. has completed the negotiations with the pan Canadian Pharmaceutical Alliance (pCPA) with a Letter of Intent (LOI) regarding TAKHZYRO (lanadelumab injection) for routine prevention of HAE attacks in adolescents and adults (12 years of age and older).

This is an important step to ensure equitable and timely access to TAKHZYRO for eligible patients across Canada. The signed LOI allows Takeda Canada to work with participating jurisdictions to implement public funding of TAKHZYRO for eligible HAE patients.

Stephen D Betschel, HBSc, MD, FRCPC, and Chair of The Canadian Hereditary Angioedema Network (CHAEN): “TAKHZYRO has the potential to transform care for patients and as a physician who treats this chronic condition, I hope to see rapid access for patients who can benefit from this important treatment option.”

Following a priority review, Health Canada authorized TAKHZYRO for routine prevention of attacks of HAE in adolescents and adults (12 years of age and older) in

September 2018. In addition, Health Canada issued the Notice of Compliance (NOC) for the new presentation (300 mg/ 2 mL Prefilled Syringe) in September 2020. In November 2019, TAKHZYRO received a positive recommendation from CADTH's Canadian Drug Expert Committee for the routine prevention of HAE attacks.

"Patients constantly live in fear of their next attack. They avoid social situations, even just going out in public, and this has a significant impact on their quality of life," says Jacquie Badiou, President of HAE Canada: "The HAE community is thrilled with this positive step forward, because having access to a treatment option that can prevent attacks would be life-changing."

As one of the fastest-growing pharmaceutical companies in the country, Takeda Canada is committed to delivering better health for Canadians through leading innovations in medicine.

"At Takeda, we always strive to do more for patients, and we are pleased to reach this important milestone for TAKHZYRO," said Gamze Yüceland, General Manager, Takeda Canada Inc. "With the Letter of Intent in place, this lays the path forward for funding discussions with each of the participating jurisdictions, and we look forward to working with our partners to bring this important therapy to Canadians living with HAE as soon as possible."

(Source: Takeda)



6 November 2020

"We are progressing NTLA-2002 for the treatment of HAE, to a regulatory submission next year," says President and CEO John Leonard, M.D., at the presentation of the **Intellia Therapeutics, Inc.** operational highlights and financial results for the third quarter ended 30 September 2020.

Third Quarter 2020 and Recent Operational Highlights – HAE Program:

NTLA-2002 is a wholly owned, in vivo development candidate for the treatment of HAE. Today, Intellia announced results from its completed non-human

primate (NHP) study of its lead lipid nanoparticle (LNP) formulation for NTLA-2002. Following a single dose, the knockout of the prekallikrein B1 (KLKB1) gene resulted in a year-long therapeutically relevant reduction of serum kallikrein protein levels and activity. Building on Intellia's modular LNP delivery system, NTLA-2002 is designed to knock out the KLKB1 gene in the liver after a single course of treatment. This approach is expected to prevent improperly regulated bradykinin production and therefore reduce HAE attacks. During the third quarter, the Company initiated Good Laboratory Practices (GLP) toxicology studies in preparation for an IND or IND-equivalent submission for NTLA-2002, which remains on track for the second half of 2021.

(Source: Intellia)



13 November 2020

New clinical data that further evaluates the attack rate reductions, patient satisfaction and quality of life of HAE patients in the APeX-2 trial over 48 weeks is being presented by **BioCryst Pharmaceuticals, Inc.**

"The data continue to demonstrate the potential of berotralstat – an investigational treatment for the prevention of attacks in patients with HAE – as a prophylactic medication, if approved by the FDA, with sustained reduction in attacks and meaningful improvements in quality of life seen over 48 weeks of treatment. With its oral, once-daily administration, berotralstat would offer patients a therapeutic alternative for managing this chronic disease," says H. James Wedner, M.D., the Dr. Phillip and Arleen Korenblat Professor of Medicine at Washington University School of Medicine in St. Louis.

Berotralstat Reduces Attacks in Patients with HAE: APeX-2 Trial 48 Week Results:

Patients treated with oral, once-daily berotralstat 150 mg for 48 weeks experienced a sustained reduction in mean investigator confirmed HAE attack rates through month 12.

In patients re-randomized to berotralstat 150 mg after 24 weeks on placebo, there was a marked reduction in

investigator-confirmed HAE attack rates over 24 weeks of treatment. These patients had a mean attack rate per month of 2.5 at baseline, 1.7 at month six (while on placebo), 0.6 at month seven (one month after starting berotralstat 150 mg) and 0.6 at month 12 (six months after starting berotralstat 150 mg).

Berotralstat was generally well-tolerated in APeX-2 through 48 weeks. The safety profile observed from weeks 24 to 48 was consistent with the data observed through the first 24 weeks. The most commonly reported treatment-related adverse events were upper respiratory tract infection, abdominal pain, diarrhea and vomiting.

Berotralstat Positively Impacts Patient-Reported Satisfaction: Results from the Phase 3 APeX-2 trial:

Patient satisfaction with treatment was assessed using the validated Treatment Satisfaction Questionnaire for Medicine (TSQM), which is comprised of three specific scales (side effects, effectiveness and convenience) and is scored on a global satisfaction scale from 0-100.

HAE patients who transitioned from placebo to berotralstat 150 mg at week 24 reported improved overall treatment satisfaction and effectiveness. These patients experienced statistically significant improvements from weeks 24 to 48, with a mean global satisfaction increase of 26 points ($p=0.005$) and a mean effectiveness increase of 29.6 points ($p<0.001$). Convenience scores remained high through week 48, reflecting the positive experiences patients had taking an oral medication.

Berotralstat Improves Patient-Reported Quality of Life Through 48 Weeks in the Phase 3 APeX-2 Trial:

Quality of life was assessed with the Angioedema Quality-of-Life (AE-QoL) questionnaire, a validated tool to measure impairment of QoL based on a total and domain (functioning, fatigue/mood, fear/shame and nutrition) scores. The minimal clinically important difference (MCID) is defined as an improvement of six points.

Clinically meaningful improvements in mean AE-QoL total scores were observed as early as week four, with a mean improvement from baseline of 15 points at week 24. This improvement was sustained through 48 weeks of treatment with berotralstat 150 mg.

Improvements were observed in all four domains (functioning, fatigue/mood, fear/shame, nutrition)

through week 48. Notably, 77 percent of patients exceeded the MCID in total AE-QoL total scores at 48 weeks, indicating the reduction in attacks following berotralstat therapy appears to have a positive impact on patients' quality of life.

(Source: BioCryst)



13 November 2020

BioCryst Pharmaceuticals, Inc. presents data from a cross-sectional study among patients, caregivers and physicians capturing the burden of injectable prophylactic therapy experienced by HAE patients and caregivers, and differences in perceptions between physicians and HAE patients.

"These data are consistent across HAE patients, caregivers and treating physicians showing many patients experience a significant treatment burden associated with current prophylactic HAE therapies. New therapies with easier routes of administration may meet a significant unmet need for HAE patients seeking improved quality of life," says study lead Cristine Radojicic, M.D., assistant professor of medicine at Duke University School of Medicine.

Overall, the burden of treatment reported across all groups surveyed suggests an unmet need still remains in HAE clinical management. These study findings collectively highlight the opportunity to strengthen the shared decision making between patients and physicians with more effective dialogue about the burden of treatment and patients' individual needs and preferences.

The following is a brief summary of the data from the cross-sectional study conducted via three double-blinded surveys with HAE patients (n=75), caregivers (n=30) and physicians (n=109), respectively:

- Almost nine in 10 patients with HAE report they have learned to tolerate difficult aspects of their treatment and 58 percent report they are tired of their injections. Even though patients are satisfied with their current prophylactic medications, 86 percent are still interested in a less burdensome route of administration.

- Over 50 percent of caregivers agree it was challenging to learn how to administer HAE treatment, specifically gaining comfort with using needles and learning how to self-administer. Seventy-one percent of caregivers agree that patients experience needle fatigue with their HAE prophylactic medications, and an even greater proportion of caregivers believe a once-daily pill would provide the patient more freedom (86 percent), independence (85 percent), and reduce caregivers' burden.
- Most physicians (94 percent) and patients (84 percent) agree there is a need for newer and more novel HAE treatments. In addition, 86 percent of caregivers believe that, while their patient is satisfied with current treatment, the patient would still be interested in one that is easier to administer.
- Over 70 percent of physicians surveyed believe that starting prophylaxis treatment was overwhelming, becoming comfortable with needles was intimidating, and learning how to self-administer was challenging for their patients. The study also shows that physicians tend to underestimate time required for preparation and administration of prophylaxis medications. Importantly, despite recognition of the burden with current treatments, there is discordance between patients and physicians regarding the person initiating conversations about medication challenges, suggesting an opportunity to improve the dialogue to help with an individualized approach to the management of HAE.

(Source: BioCryst)



13 November 2020

Takeda Pharmaceutical Company Limited announces the final results from the Phase 3 HELP Study Open-label Extension (OLE) showing that Takhzyro (lanadelumab-flyo) helped prevent and reduce the frequency of HAE attacks long term in patients 12 years of age and older who received treatment for a mean (standard deviation) duration of 29.6 months.

Results are consistent with the safety and efficacy of Takhzyro in the pivotal trial. The mean HAE attack rate was reduced by 87.4% overall versus baseline and in a pre-specified exploratory endpoint, nearly 70%

of patients treated with Takhzyro 300 mg every two weeks experienced an attack-free period of more than 12 months.

“The unpredictability of HAE attacks has a significant impact on the lives of HAE patients. HAE is a lifelong condition, so reducing the frequency and severity of attacks is an important therapeutic goal for many individuals living with HAE,” says Marc A. Riedl, M.D., investigator in the HELP Study OLE and Professor of Medicine and Clinical Director, U.S. HAEA Center at the University of California, San Diego. “The original placebo-controlled HELP Study demonstrated the efficacy and safety of Takhzyro over 26 weeks. The results from the open-label extension study are encouraging as they show that Takhzyro may help prevent attacks over the long term with continued treatment.”

The original Phase 3 HELP Study was conducted in 125 patients aged 12 years and older over 26 weeks, making it the largest randomized, controlled prevention study in HAE, with the longest active treatment duration, to date. The HELP Study OLE was designed to evaluate the long-term safety (primary endpoint) and efficacy of Takhzyro for up to 2.5 years. The complete results were based on data collected between May 2016 and October 2019 and included 109 rollover patients who were originally evaluated in the HELP Study, and 103 eligible non-rollover patients who did not participate in the initial study but had experienced at least one HAE attack in 12 weeks.

“A significant amount of progress has been made in advancing the science to better understand and treat HAE over recent years. In 2018, we received the first regulatory approvals for Takhzyro as a first-of-its-kind monoclonal antibody preventive therapy in HAE, and we have already seen the difference it has made by preventing attacks in many patients around the world,” says Donatello Crocetta, M.D., Global Medical Head, Rare Immunology and Metabolic Diseases, Chief Medical Office, Takeda. “Continued research such as the HELP Study OLE is critical to further build our understanding of the potential of Takhzyro as a long-term preventive treatment option for those living with HAE.”

The complete results from the HELP Study OLE show that the safety profile of Takhzyro is consistent with the original findings from the HELP Study, with treatment-related treatment emergent adverse events (TEAEs) occurring in 54.7% of patients and the most common

being injection-site pain, respiratory tract infection, or headache. In addition, data from the HELP Study OLE show that the efficacy of Takhzyro 300 mg administered subcutaneously every two weeks in rollover patients is consistent with the original findings from the HELP Study. The mean reduction in the attack rate compared to baseline observed in the study population is of 87.4%, with approximately 93% of patients experiencing at least a 70% reduction of the attack rate. Additional pre-specified exploratory endpoints measured attack-free periods.

(Source: Takeda)



14 November 2020

At the presentation of data on the pharmacokinetic (PK), pharmacodynamic (PD), and safety profiles of PHA121 in healthy volunteers **Pharvaris** expects to advance PHVS416 (PHA121 in soft capsules) to provide a rapid and convenient on-demand HAE treatment using a small oral dosage form.

Bradykinin Challenge Provides Surrogate Endpoints for HAE Treatment Using Bradykinin-B2-Receptor Antagonists:

The effect of PHA121 on cardiovascular changes induced by bradykinin (BK) was evaluated in a proof-of-concept study in healthy volunteers. Two doses (12 and 22 mg) of PHA121 were administered orally to 16 healthy volunteers, followed by bradykinin challenges to induce brief hemodynamic responses. The PHA121-mediated dampening of these BK-induced hemodynamic responses was evaluated using a non-linear mixed-effect PK/PD model. The effective treatment duration from both doses of PHA121 exceeds the published duration of subcutaneous icatibant (30 mg), with the duration of 22 mg PHA121 approximately twice as long as icatibant. The plasma concentration producing 50% of the maximum effect of the study drug (EC₅₀) was found to be approximately four-fold more potent than that observed for icatibant in published data.

“When we scale the observed clinical potencies in this human bradykinin challenge by the molecular weight and plasma protein binding for PHA121 and icatibant, we find that PHA121 is 24-fold more potent than icatibant on a molar basis (IC₅₀ of 170 pM versus 4.1 nM, respectively), consistent with our preclinical

in vitro and ex vivo measurements,” observes Jochen Knolle, Ph.D., chief scientific officer and co-founder of Pharvaris. “This agreement between clinical and preclinical studies gives us confidence in the models and approach that Pharvaris has used in developing PHA121.”

Hartmut Derendorf, Ph.D., distinguished professor emeritus of pharmaceuticals at the University of Florida College of Pharmacy, says: “These data show that the BK-challenge test, which was used intensively in the dose-finding of icatibant, allows an estimation of the therapeutically relevant target concentrations of PHA121. Icatibant has good efficacy; however, for some attacks, the effect dissipates after six hours. The investigated doses of PHA121 provide equivalent BK-antagonism for a longer time than the currently approved dose of icatibant, which is therapeutically relevant given the previous use of the BK challenge to predict therapeutic outcome.”

PHA-022121, a Selective Bradykinin-B2-Receptor Antagonist, is Safe and Shows Rapid Oral Bioavailability in Humans:

PHA121 was administered as an oral solution in a double-blind placebo-controlled single-ascending-dose first-in-human study in healthy volunteers. Both PK parameters and safety were assessed until 72 hours post-dosing. PHA121 was very rapidly absorbed and reached peak plasma levels within 30 to 60 minutes after dosing in all subjects under fasted conditions. The systemic exposure was dose proportional with a mean t_{1/2} ranging from 3.5 to 5.6 hours between doses. Plasma levels for PHA121 reached therapeutic efficacious threshold concentration (estimated EC₅₀ 2.4 ng/mL and EC₈₅ 13.8 ng/mL) within 15 minutes, with or without food, and were maintained for approximately 12 hours with doses of 12 and 22 mg. All doses tested in this study were well tolerated. The total incidence and pattern of adverse events (AEs) was similar between active and placebo groups. In total, 17 AEs were reported by 12 out of 52 subjects (23%) on study drug versus 7 AEs in 5 out of 16 (31%) placebo-treated subjects. No serious or severe adverse events occurred. All related adverse events were of mild intensity and resolved rapidly. No clinically significant changes in safety laboratory parameters, vital signs, and electrocardiogram (ECG) parameters were observed.

“PHA121 is an oral bradykinin-B2-receptor antagonist that is rapidly absorbed with dose-proportional pharmacokinetics, and has been well tolerated in studies to date,” says Peng Lu, M.D., Ph.D., chief medical

officer of Pharvaris. “The PK/PD profile suggests that rapid onset of action and prolonged efficacy with a single dose of PHA121 can be expected in the treatment of acute HAE attacks. Pharvaris is preparing to initiate an on-demand study of PHVS416, a soft capsule formulation of PHA121, for the treatment of HAE attacks in 2021.”

(Source: Pharvaris)

PHARVARIS

19 November 2020

Pharming Group N.V. will be building a new facility to expand the company’s downstream processing capacity for its lead product, Ruconest (recombinant C1 esterase inhibitor (rhC1INH)).

The downstream processing facility will include the purification, filtration and concentration of the starting material. Construction is planned to begin mid-2021 at Pivot Park in Oss, the Netherlands. Pivot Park is also the location of BioConnection B.V., Pharming’s contracted fill and finish facility, in which Pharming holds a minority stake.

At Pivot Park, Pharming will move into a new, sustainable, five-story building with a total floor space of approximately 4,000 m². The building has been specially designed for the company and is located in a prominent position on the site. It is the first new building on the campus and CEO Drees hopes many more will follow. Pharming’s arrival at Pivot Park will create at least 40 new jobs in Oss.

Sijmen de Vries, CEO of Pharming: “With an increasing demand for Ruconest® for the treatment of HAE and an increasing need for rhC1INH in our clinical trials in new, large indications, we continue to invest in expanding our in-house processing capabilities as part of our strategy to deliver long-term growth.”

(Source: Pharming)

 **Pharming**

20 November 2020

An online survey conducted the Harris Poll and sponsored by **CSL Behring** show that a vast majority of HAE patients (94%) say it’s important their preventive therapy specifically corrects C1 esterase inhibitor (C1-INH) deficiency. Both people living with HAE (94%) and the physicians who treat them (91%) agree that a reduction in the number of attacks is the leading factor when evaluating prophylactic therapy, followed closely by the importance of safety.

“This data shows that those living with HAE and their physicians place importance on preventing more attacks, with most people living with HAE preferring a prophylactic treatment that is effective in reducing the number of attacks rather than a treatment that offers less frequent administration,” says Jonathan A. Bernstein, M.D., Professor of Medicine, Department of Internal Medicine, Division of Immunology and Allergy Section, University of Cincinnati College of Medicine. “A treatment that may offer less frequent administration may seem appealing, but these findings suggest that many people living with HAE live with daily fear, stress and anxiety related to having an attack. These substantial burdens should be important points of consideration when discussing and developing treatment plans.”

According to the survey findings, physicians do recognize the negative impact of HAE on virtually every aspect of their patients’ lives, but the survey results also show that people living with HAE view the disease as having a more significant impact on their daily activities. For example, 43% of people living with HAE say the disease has a major negative impact on their work or studies, but only 9% of physicians say the same about their patients.

“HAE affects my life daily; with the concerns and stress of not only maintaining my own health as a patient, but also that of my children, both of whom also have HAE,” said Cheryl French, a person living with HAE.

The survey findings demonstrate physicians and people living with HAE are generally aligned when it comes to making treatment decisions, but results also show that physicians and people living with HAE could benefit from improved dialogue on the factors that are most important in selecting a therapy.

Other key findings include the following:

Treatment

- More than 95% of people living with HAE say they are determined to do whatever it takes to avoid HAE attacks and most physicians (82%) agree
- People living with HAE (97%) and physicians (99%) almost universally agree that the best way to manage HAE is to take measures to prevent attacks

Impact of HAE on Lifestyle

- 76% of people living with HAE say they worry about having another attack on a daily basis
- Over 8 in 10 people living with HAE consider managing and recovering from an HAE attack to be disruptive to their overall quality of life
- 70% of people living with HAE rate their HAE attacks as severe/very severe
- 68% of people living with HAE say having HAE has a major or moderate negative impact on their work/studies

(Source: CSL Behring)

CSL Behring

20 November 2020

Pharvaris has closed its oversubscribed 80 million USD Series C financing bringing its total venture funding to over 160 million USD to date.

“Our team is committed to developing and delivering differentiated products to patients – the oversubscription of our Series C highlights broad enthusiasm for our vision for HAE and beyond,” said Berndt Modig, CEO and co-founder of Pharvaris. “The backing from a prominent group of investors will enable us to develop our pipeline of compounds for the treatment of HAE and other bradykinin-B2-receptor-mediated indications. We expect to complete our Phase 1 assessments in healthy volunteers at the end of the year and anticipate announcing top-line data in 2021.”

The proceeds from the Series C financing will fund the clinical advancement of Pharvaris’ pipeline of novel oral bradykinin-B2-receptor antagonists for the treatment of HAE, including both on-demand treatment and prophylactic prevention. Pharvaris’ first

product candidate, PHVS416 (PHA121 in soft capsules), is a potent, orally available bradykinin B2-receptor antagonist designed to block the effects of bradykinin during HAE attacks. Initiation of RAPIDe-1, a multi-center Phase 2 placebo-controlled on-demand study of PHVS416 in HAE patients, is expected in 2021. Pharvaris is also developing an orally available extended-release product containing PHA121 specifically for prophylaxis in HAE patients.

(Source: Pharvaris)

PHARVARIS

30 November 2020

The journal *Allergy* has published data from the APeX-J trial, a randomized, placebo-controlled trial conducted in Japan evaluating oral, once-daily berotralstat for the prophylactic treatment of HAE. The results are consistent with the global phase 3 APeX-2 trial, where berotralstat 150 mg also reduced the rate of HAE attacks compared to placebo ($p < 0.001$) and was safe and generally well-tolerated.

HAE is estimated to affect 2,500 patients in Japan. Although two on-demand treatments are approved, no therapies are currently approved for long-term prophylaxis in Japan.

“Berotralstat would be the first approved prophylactic therapy for HAE patients in Japan and we believe there is a significant opportunity for berotralstat to accelerate the diagnosis of HAE patients and dramatically improve the quality of life for patients,” says Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc.**

A new drug application (JNDA) is under review in Japan for approval of oral, once-daily berotralstat for the prophylactic treatment of HAE. Berotralstat is being reviewed under Sakigake designation and the company expects a decision on approval in December 2020.

(Source: BioCryst)

bioCryst

4 December 2020

The U.S. Food and Drug Administration (FDA) has approved oral, once-daily Orladeyo (berotralstat) for prophylaxis to prevent attacks of HAE in adults and pediatric patients 12 years and older.

“Orladeyo offers people with HAE and their physicians the first orally administered non-steroidal option for preventing HAE attacks and represents an important and welcome step in making more treatment options available to physicians and patients,” says Anthony J. Castaldo, President and CEO of the US Hereditary Angioedema Association (HAEA).

In the pivotal Phase 3 APeX-2 trial, Orladeyo significantly reduced attacks at 24 weeks, and this reduction was sustained through 48 weeks. HAE patients who completed 48 weeks of treatment (150 mg) saw reductions in their HAE attack rates, from a mean of 2.9 attacks per month at baseline to a mean of 1.0 attacks per month after 48 weeks of therapy. In the long-term open label APeX-S trial, patients completing 48 weeks of therapy (150 mg) had a mean attack rate of 0.8 attacks per month.

Orladeyo was safe and well tolerated in both trials. The most frequently reported adverse reactions in patients receiving Orladeyo compared with placebo were gastrointestinal reactions. These reactions generally occurred early after initiation of treatment with Orladeyo, became less frequent with time and typically self-resolved.

“Patients and physicians acknowledge that HAE treatments can add a burden to patients’ lives. As an oral, once-daily option, Orladeyo can provide significant attack reduction and lessen the burden associated with injections and infusions,” says Marc Riedl, M.D., Professor of Medicine and Clinical Director, U.S. Hereditary Angioedema Association Center at the University of California, San Diego, and an investigator in the APeX-2 trial “With this new treatment option, physicians and patients can continue to have collaborative discussions to choose the treatment that meets each patient’s needs, life circumstances and preferences.”

HAE patients note a significant treatment burden associated with existing prophylactic therapy. In addition to reducing HAE attack rate, data from APeX-2 show that patients reported meaningful improvements

in both quality of life and overall patient-reported satisfaction, and significant reductions in their monthly use of standard of care on-demand medicine, while taking oral, once-daily Orladeyo (150 mg).

“The FDA approval of Orladeyo fulfills a promise BioCryst made to HAE patients that we were committed to helping them achieve the dream of an oral, once-daily medicine to prevent and reduce the burden of their attacks,” says Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc.** “Thank you to the HAE patients who participated in our clinical trials, to the investigators around the world who conducted these trials, to the HAEA for their patient advocacy and to our employees who never forgot that patients were waiting. We will stay focused on enabling access and providing personalized support to HAE patients and physicians.”

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.

EMPOWER Patients Services is administered by Optime Care Inc., the exclusive specialty pharmacy provider for Orladeyo. Physicians can begin writing prescriptions for Orladeyo immediately, with direct to patient shipments from Optime Care expected to begin by the end of December 2020.

(Source: BioCryst)





HAE INTERNATIONAL AROUND THE WORLD

Currently there are HAE member organizations in **92** 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 HAE International receives fresh data from the national member organizations.

