DECEMBER 2021

Global perspectives:

HAEi MAGAZINE · ISSUE 4/2021

93 Member countries

Global perspectives:

Global Perspectives
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December 2021

Cover photo
Conference attendees at the 2021 Scandinavian Conference installing the HAE TrackR app and using it right away. Photo: Trine Dahl-Johansen.
Read more on page 16.

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

DEAR HAEi FRIENDS,

We are happy to bring you the final edition of *Global Perspectives*, which signals the end of another year marked by travel restrictions and many other challenges posed by the ongoing COVID-19 pandemic.

Nevertheless, news from member organizations and HAEi Regional Patient Advocates, featured in each 2021 edition of this magazine, showed that HAEi friends in our 93 member countries continued to enthusiastically and effectively raise HAE awareness and improve quality of life for people with HAE.

Throughout the year, HAEi served the global HAE community with kindness, compassion, and a robust offering of programs, services, and activities. Highlights include:

- The first HAEi Virtual Regional Workshop for the Middle East, North Africa and Sub Sahara Africa,
- Virtual Regional Workshops held in Central Eastern Europe and Benelux, and South America, Mexico, Central America and the Caribbean,
- Virtual visits to member organizations across the globe to celebrate the 10th anniversary of **hae day :-)**
- Launch of HAE TrackR – our new app to help HAEi friends track their HAE and overall health status,
- Convening Regional Advisory Groups to ascertain the top 5 challenges facing our community,
- Designing and offering new courses in HAEi Academy (our proprietary e-learning platform) that address the challenges identified by the Regional Advisory Groups,
- Continued expansion of the HAEi Youngsters' Community and Youngsters Advisory Group,
- Medical Journal publication of an HAEi/US HAEA pharmaco-economic study showing the value of modern medicines for preventing HAE attacks, and
- Significant growth in the number of GA2LEN/HAEi accredited ACARE Centers.

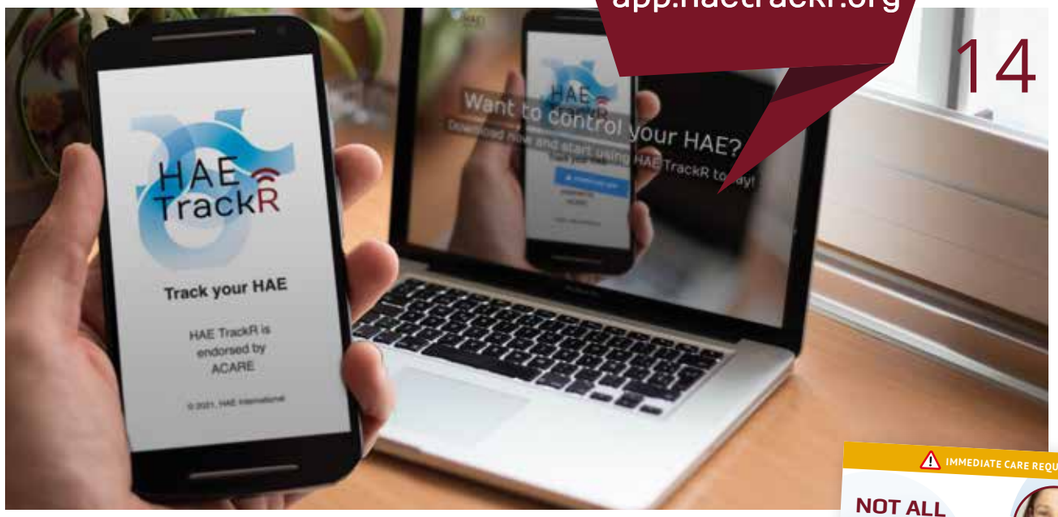
We congratulate our member organizations for their successes in 2021 and look forward to easing of travel restrictions leading to even greater accomplishments in 2022.

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

Tony

Anthony J. Castaldo
President and CEO, HAEi

IN THIS ISSUE OF GLOBAL PERSPECTIVES



NEWS FROM THE HAEi REGIONAL PATIENT ADVOCATES

As the Chief RPA I have the opportunity to see the great progress being made by so many of our member organizations. I am observing continued growth in productive interaction between member organization leaders and their RPAs. The resulting increase in advocacy efforts has led to more countries winning access to modern HAE medicines, although we still have a long way to go.

Developing state-of-the-art tools and services to further enhance advocacy skills is one of HAEi's highest priorities. I am pleased to report that the input our RPAs received from conducting Regional Advisory Group (RAG) meetings, has resulted in creating and adding highly relevant advocacy training courses to the HAEi Advocacy Academy, our proprietary e-Learning platform. The heads of our member organizations serve as the RAGs representatives.

Our RPAs have a special ongoing role to ensure HAEi's programs and services respond to the challenges and needs faced by our member organizations. As I write this message, the RPAs are gearing up for a new round of outreach sessions with the RAGs. We will once again use the information and advice provided by the RAGs to continue creating and refining our advocacy tools and resources. This round of RAGs meeting will also focus on how best to serve and involve our HAEi Youngsters.

The RPAs are always ready to help you and your member organization by providing you with their expertise and support. Please reach out to them for any assistance you may need.

Fiona Wardman
Chief Regional Patient Advocate

JØRN SCHULTZ-BOYSEN
NORDICS, GERMANY, AUSTRIA AND SWITZERLAND

The Regional Medical Advisory Panel (RMAP) is still taking form for the region. While some doctors have already agreed to participate, some countries are still in dialogue. The first dialogue is ongoing for the panelists who have joined, and interesting work and findings are already coming in. I look very much forward to finalizing the work in gathering the RMAP and learning from all the experience accumulated amongst the people on the panel.

Launching the HAE TrackR app has been exciting – and it is available in many languages. For my region, it is already present in German, Norwegian, Swedish and Danish. And two more languages spoken in the region (French and Finnish) are planned to be available soon. The HAE TrackR app is easy to use – and safe to store your data in – and it will help the patient and physician in their dialogue on current and future treatment options. I can only urge everyone to check it out and start using it. The member organizations also let their members know of the opportunity to use the HAE TrackR app – this is really great.

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

Switzerland has released the 5th newsletter – a very comprehensive and interesting edition covering amongst other items new available medicines, the treatment methods, and a historical walkthrough of the past 20 years with HAE in Switzerland and the Swiss HAE organization.

During the weekend of 12-14 November 2021, HAE Scandinavia, covering Norway, Sweden and Denmark, hosted their 4th Scandinavian conference, this time in Copenhagen, Denmark. At the same time, the conference marked the 20th anniversary of the Scandinavian organization. The theme of the conference was "The Power of Prophylaxis", focusing on the value of having the option of prophylactic treatment in Scandinavia. It was the first time since corona that patients, caregivers, health care professionals and industry representatives from all over Scandinavia were able to meet. More than 120 people gathered to learn more about the latest treatment options as well as how HAE is handled in the countries. Of course, there was time set aside to network; after all, it was great for people to meet face to face. Also, HAE TrackR was presented and caused a lot of interest amongst the participants. HAE Scandinavia had set up a stand to explain more and help the patients download the app and start using it. It was a great opportunity to speak with the patients about the benefits of the app – and to answer questions about getting started. At the same time, it was a good chance to talk with patients and caregivers about the HAE Companion app.

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

MARIA FERRON
MEDITERRANEAN, NORTH AFRICA AND BRITISH ISLES

I have been advising all the member organizations in my region about the new Advocacy Academy courses developed by HAEi. This is an excellent opportunity for national organizations to take advantage of this wonderful tool to learn how to run an organization and advocate for patients. Please don't hesitate to have a look at https://haei.org/resources/haei-advocacy-academy/.

HAE Portugal (ADAH) has been working on getting funding from the industry to print and distribute the poster developed by HAEi to support the awareness campaign that the association is working on. The HAEi poster will be distributed in hospitals and health centers. ADAH has also organized the annual patient meeting to take place virtually due to the current COVID-19 situation.

The HAE group in Tunisia is in the final stage of being an official member organization. The group is just waiting for the authorities to provide them with the accreditation that will allow them to hold their first General Assembly and patient meeting. Once everything is in place, we will start implementing all HAEi resources needed to boost the organization.

In Spain, a survey created thanks to CSL Behring's annual EU Lead Grant Programme should be closed during this month. A survey – or rather two: one for patients and one for doctors – was created to understand the differences in access to and availability of modern HAE treatments depending on place of residence. After its closure, it will take a couple of months to perform the data analysis and preparation of the final report. This report will allow HAE Spain (AEDAF) to understand where they should focus the most and raise awareness on differences in access with the authorities so that they can make the necessary changes in local regulations.

I am thrilled to announce that the Spanish Ministry of Health has approved three so-called CSUR (Reference Centers, Services or Units of the National Health System) for HAE (children and adults). These are the first officially designated national centers of reference for HAE in Spain – please see more under the "News from member organizations around the globe" section.

FERNANDA DE OLIVEIRA MARTINS
SOUTH AMERICA AND MEXICO

I keep encouraging leaders from the member organizations in my region to follow the HAEi Advocacy Academy exclusive courses – lately, I have been sending them information on course updates.

I have supported Carla María Goachet Boulanger, President of HAE Peru, with some points regarding the children's storybook they are developing. In addition, Lisa Facciolla from US HAEA has shared the Spanish version of Brady Club, and I have shared this ready-to-use material with the member organizations and encouraged them to use it with children in their countries. Also, I have sent the member organizations the Brady Club coloring page for the Christmas season.

I have supported HAE Peru and HAE Brazil (ABRANGHE) regarding some technical issues and updates in HAEi Connect. Also, we have provided HAE Peru with an emergency room poster translated into Spanish and with the organization's logo.

Dr. Calderón from Peru has been looking to provide better support to children and pregnant HAE patients. I have put him in contact with CSL for possible opportunities.

I have replied to two patients from Mexico and one from Chile seeking local HAE support. They came in contact with me via HAEi and US HAEA.

On 23-24 November 2021, I attended a virtual Takeda workshop titled "Amplifying the voice of the patients".

Also, I have been discussing with Chief Regional Patient Advocate Fiona Wardman and President Sandra Agustina Nieto-Martinez of HAE Mexico about applying the Burden of Illness survey in Mexico.

Finally, I would like to mention the Instagram account for my region – please see postings at www.instagram.com/haei_sudamerica_y_mexico.

JAVIER SANTANA
CENTRAL AMERICA AND CARIBBEAN

Thanks to the cooperation with the consulting doctors of the patient groups in the Central American region, new doctors from Honduras and Nicaragua have been contacted. In both countries, patients with HAE have been identified, and the necessary efforts are being made to help them understand the disease, educate them and give them tools to have a better quality of life. We hope that new patients from both countries will join the two patient groups.

The patient groups in the Central American and Caribbean region have welcomed the new tool HAEi Advocacy Academy which will help them and their members to educate themselves and develop skills that benefit patient groups.

Doctors in the region are also in the evaluation and analysis to create specialized ACARE centers. It is expected that by 2022 countries such as Panama and Costa Rica will be able to have this type of center.

Since October, the purchase of medicines for HAE has been authorized in Costa Rica, which was received with great joy by patients who have been waiting for years for approval and access to some treatment. Unfortunately, the Department of Pharmacology has not purchased the medicines, but we continue to monitor the situation and are in constant communication. Representatives of several pharmaceutical and distribution companies have already contacted government officials, and we hope that soon the specific HAE medications will be accessible to patients, specifically children who suffer attacks on a monthly basis.

The girl Samantha "Sammy" Madrigal from Costa Rica, who suffers from severe HAE attacks monthly, has developed a fundraising platform to pay for the purchase of medical treatments and services. People who wish to cooperate can do so through https://gofund.me/992a008e.

Because the COVID-19 pandemic continues, several countries in the region still maintain exit restrictions to control infections. This has made the efforts of patient groups to advance the approval of treatments in their respective countries a little more complicated.

As a global organization, we continue to provide the necessary resources and help to patient groups in the Central American region. And we are sure that by the year 2022, there will be new advances.

NATASA ANGJELESKA
SOUTH EASTERN EUROPE

In October, I was focused on stirring up the countries' interest in HAEi resources. I invited patient representatives to a member organization online meeting for my region, where we had an opportunity to discuss the situation regarding access to therapies, new initiatives, challenges etc. in the past period. I also promoted and explained a bit more about the use of HAE TrackR and HAEi Advocacy Academy and reminded the national representatives about the benefits of these resources. I told them that Advocacy Academy each month has new courses in the Exclusive Access area for member organizations as well as an open-access section and that more courses are regularly added. Again, I encouraged the member organization representatives to use their Exclusive Access code to register a profile and offered my help should they need any.

The meeting was attended by 14 participants from 11 countries. They were all very excited about the opportunity to see and discuss. Unfortunately, the representative from Bulgaria was unable to participate. Still, we had an additional discussion in November and added new aspects regarding organizing joint webinars with experts with a focus on genetic therapies.

Ersan Sevinc from HAE Turkey reported that they had two big online meetings with patients in the past period and now see younger patients participating. He added that the President of HAE Turkey, Gökben Yurdakul, will meet with paediatricians to discuss all therapies. He also reported that 90% of patients have been vaccinated for COVID-19 as they belong to the prioritized group. The patient representative from Bosnia and Herzegovina said that patients received a medicine donation from Takeda, and together with the physician are pursuing to secure access to modern therapies in their country.

HAE Montenegro reported more good news: They have managed to regain access to Firazyr for all patients and are awaiting approval for one patient to receive preventive therapy due to many health issues and complications.

In Serbia, three new patients are included in the preventive treatment after good results experienced in one patient and approval from health authorities. In Bulgaria, six adult patients are now receiving prophylactic therapy. HAE Bulgaria informed that throughout the year, they have arranged that all doctoral meetings (pediatricians, immunologists, anaesthesiologists, geneticists, etc.) included a session for HAE. This has contributed to increasing information and awareness among doctors about HAE.

I have participated in the project Education for Macedonian Patients initiated by Dr. Grivcheva, logistically supported by HAE Macedonia and financed by Takeda. The first part of the project happened on 29 November 2021. It started with a lecture by Dr. Emel Aygoren Pursun on "The burden of living with HAE ". This lecture was followed by a presentation from Dr. Marcus Maurer on "The aims of treatment of HAE and how to achieve them" while Dr. Avner Reshef spoke on "Angioedema Therapy: What's in the Horizon? "The event was chaired by Natasha Jovanovska Popovska and Vesna Grivcheva Panovska, which was a nice example of patients and doctors working together. Simultaneous translation was provided for the event so that Macedonian patients who are not fluent in English could follow. The lectures sparked the interest of patients and their caregivers from North Macedonia who attended it, and after the meeting they discussed it extensively.

HAE TrackR is being continuously translated into more languages in my region; most recently, it has become available to users in Greece and Croatia.

MICHAL RUTKOWSKI
CENTRAL EASTERN EUROPE, BENELUX AND MIDDLE EAST

Despite the difficult global pandemic situation, I hope you are keeping safe, healthy and have been already vaccinated.

Firstly, happy birthday to HAE Belarus and HAE Kazakhstan, who recently celebrated the 4th and 3rd anniversaries. The organizations and patients strive to have the first modern HAE treatment reimbursed, and the latest advocacy activities make this possible more than ever before. Also, HAE Poland was celebrating 16 years of advocacy activities, and access to the first preventative HAE medicine has been the icing on the cake.

September, October and November have been incredibly hectic, and I have so many things to share with you.

I was privileged to organize and attend numerous virtual meetings with patients' organizations from Belarus, Egypt, Georgia, Hungary, Iraq, Jordan, Kazakhstan, Kuwait, Lebanon, Lithuania, the Netherlands, Qatar, Poland, Russia, Saudi Arabia, the United Arab Emirates and Ukraine. Furthermore, I was honored to present at the HAE Ukraine Virtual General Assembly as well as the HAE Belarus and HAE Hungary Virtual Summits, sharing HAEi's experience and motivation with fellow patients. As if this was not enough, I had online meetings with individual HAE patients and caregivers from Belgium and Iran, participated in the Takeda HAE Global Expert Patient Council meeting, and took part in the Takeda Business Review online meeting.

Together with the HAEi Team, we launched the 2021 HAEi Virtual Regional Workshop Middle East, North Africa, and Sub Sahara Africa. The enormous effort of all people involved in the preparations resulted in the outstanding educational virtual event available in Arabic, English and French. I highly recommend you watch the workshop at https://haei.org/2021-haei-virtual-regional-workshop-mena_ssa/. Jointly with my fellow RPA Maria Ferron, we launched the HAEi Regional Website Middle East & North Africa – please have a look at https://mena.haei.org.

Speaking of the Middle East countries, it should be mentioned that the following on-demand therapies have recently been registered: C1 Inhibitor esterase (Cinryze) in Egypt and the United Arab Emirates and Icatibant (Firazyr) in Kuwait, Oman, Saudi Arabia, and the United Arab Emirates.

In recent months, I have also established in-depth contact with healthcare professionals and HAE patients from Iran. The representative of Immunology, Asthma and Allergy Research Institute (IAARI) at Teheran University of Medical Sciences has joined the HAEi Regional Medical Advisory Panel (RMAP) for the Middle East, which is extremely important for this RMAP structure and work. I look forward to further mutual collaboration.

More RMAP panelists have confirmed their availability in their respective regions. So far, there are 16 HAE expert advisors from 15 countries within the RMAP for Central East Europe and Benelux and 11 HAE expert advisors from 11 countries within the RMAP for the Middle East.

The ACARE project is growing fast, and so far, centers have been established in these countries from my regions: Georgia, Hungary, Kazakhstan, Saudi Arabia, Kuwait, the Netherlands, Oman, Qatar, Poland, Russia, and the United Arab Emirates.

I am delighted to inform you that the HAEi electronic patient diary HAE TrackR now is also available in Arabic, Polish and Ukrainian. Soon, we can expect more languages to come. Also, HAEi Advocacy Academy is available in any language from my regions, and more countries have been logging in to use Advocacy Academy "exclusive access".

I successfully established contact with the rare disease organization from Luxembourg (ALAN – Maladies Rares Luxembourg) and had a videoconference with its Director, Daniel Theisen. Also, I identified centers in Luxembourg where HAE patients are treated. Hopefully, it will help identify more HAE patients in this country and increase awareness among health care professionals.

Finally, after 17 years of service as the member organization patient lead and later as the President of HAE Ukraine, Helena Mykal decided to step down, which happened at the HAE Ukraine Virtual General Assembly on 2 October 2021. Many of you know Helena from HAEi events held over the years. On behalf of myself and HAE patients from Central Eastern Europe, I would like to thank Helena for her dedication, professionalism, and expert knowledge in her advocacy activities for the benefit of HAE patients. Also, I would like to introduce to the international community the new President of HAE Ukraine, Natalia Formaniuk.

FIONA WARDMAN
ASIA PACIFIC

There have been a few focused tasks and projects in the Asia Pacific region over the most recent months, including the rolling out the new member only access courses in Advocacy Academy.

During this period, I have attended virtual conferences and symposiums for the region, including the APAAACI Conference, with presentations on HAE, and Pinnacle Workshops for Taiwan, South Korea, and India. I also presented in the Alnylam Pharmaceutical Patient Advocacy Leadership Workshop as a panelist with Lisa Foster (RDNZ) and Ruth Chen (TFRD) on the "Patient Voice in Drug Development and Policy in Asia Pacific".

Patients in Hong Kong and Taiwan will have an opportunity to participate in a clinical trial for preventative therapy.

I have had meetings with member organizations in China, Bangladesh, South Korea, India, Japan, Hong Kong, Taiwan, and South Africa to work through issues and assist them in their projects.

The data collated from the HAEi Burden of Illness Study in India will be used to strengthen the message of disease burden to access treatments in India. We also plan to present a poster during a suitable conference.

I have been involved with new resources for patient awareness and education of HAE for Asia Pacific.

There has been a hive of activity around meetings with pharmaceutical companies in various countries to discuss access to medications, clinical trials, and the challenges patients face with diagnosis and treatment. It's great to see some interest in the Asia Pacific region which has not been focused on for many years.

There is continued uptake of the HAEi TrackR app, and translations have been completed for Taiwan and Hong Kong. Also, we are in the process of translating simplified Chinese for patients in China.

The Emergency Room poster is another HAEi resource that is being utilized and made accessible in the region. We are working towards the translations, ensuring more doctors in countries within the region will have more awareness of HAE.

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

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- Developed by patients for patients and is product and company neutral.
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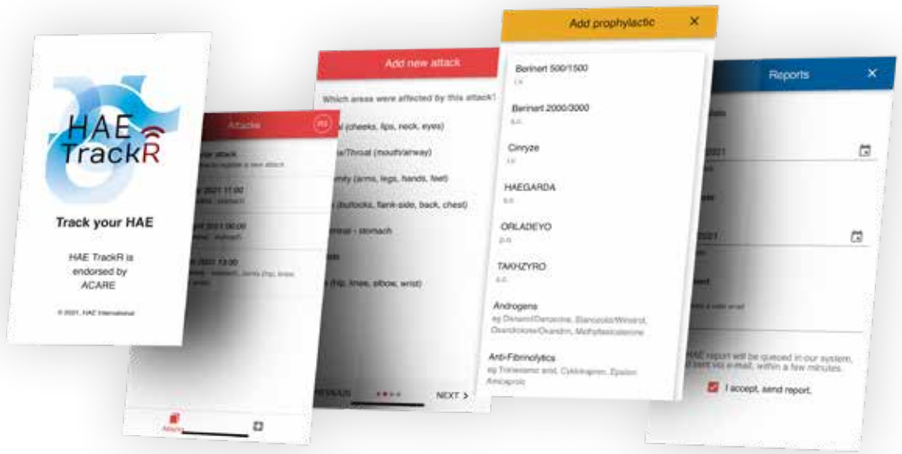
- Endorsed by the ACARE network (Angioedema Centers of Reference and Excellence)
- Can be accessed from a computer, tablet, or smartphone.
- Presently available in Arabic, Brazilian Portuguese, Croatian, Danish, English, German, Greek, Macedonian, Norwegian, Polish, Portuguese, Romanian, Serbian, Spanish, Swedish, Turkish, and Ukrainian – more languages will be added over the coming weeks



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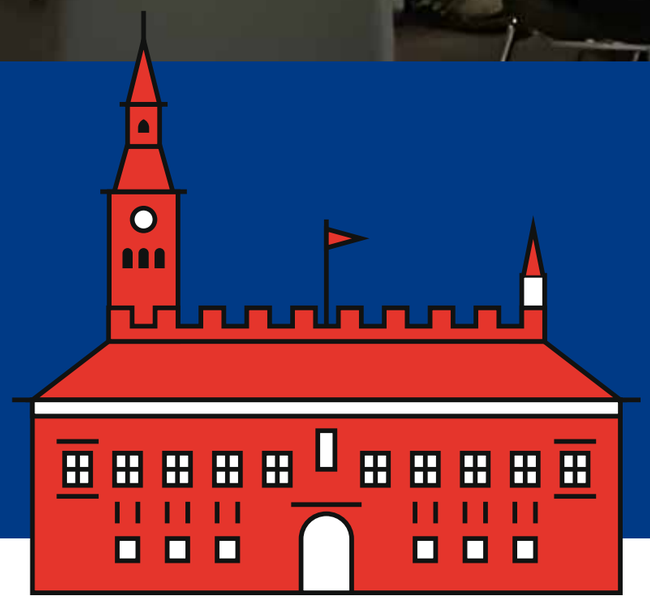
HAE TrackR is easy to use – find tutorials on haetrackr.org and get started!



Scandinavian
Conference

2021 · Copenhagen

Finally together again for HAE Scandinavia's 2021 Scandinavian Conference and 20th anniversary

No matter where people with HAE gather in large groups – for example, at national or international meetings and conferences – there is joy of getting together with HAE friends old and new.

This was also the case when HAE Scandinavia held their combined 2021 Scandinavian Conference and its 20th anniversary in mid-November. The conference took place in a beautiful and very convenient setting at the Clarion Hotel Copenhagen Airport. The joy of meeting was both visible and audible – and it was made even greater by the fact that it was the first time the Scandinavian HAE community could assemble after a long period of corona restrictions. More than 125 Scandinavians seized this amazing opportunity to meet again.

After a word of welcome from HAE Scandinavia President Henrik Balle Boysen, the first guest on the podium was Anthony J. Castaldo, President and CEO of HAEi. Under the heading "HAE – a Global Perspective", he gave a comprehensive update on the development of recent years and said, among other things: "We now have multiple modern medication options, and more are coming. There are currently eight HAE medicines approved worldwide, and five companies are underway with gene therapy options while others are developing next-generation treatments."

Despite the many treatment advances, Anthony J. Castaldo stressed the need for active patient organizations as it "is essential for preserving current and future access to medication". He stated that "nothing is more powerful than patient advocacy". At the same time, Anthony J. Castaldo called for even a well-established organization such as HAE Scandinavia to continue to find more people and build strength in numbers: "Much has been gained, but we should take nothing for granted".

Prof. Markus Magerl from Charité - Universitätsmedizin Berlin, Germany, also linked to the conference theme "The Power of Prophylaxis". He asked, "What is the best drug – who is the winner?" and answered the question himself: "The patient is the winner as there is now a chance to find the right individual drug." Prof. Magerl pointed out that everybody who wants prophylaxis should have it. In this context, he said that it is crucial that we move from a "12 attacks per year" assessment to a view of the individual with HAE and look at when there is "insufficient disease control".

Among the other speakers at the conference was Dr. Olav Rogde Gramstad from Oslo University Hospital, Norway, who focused on "How to prepare children and young people with HAE for treatment", while Dr. Kåre Steinar Tveit from Haukeland University Hospital, Norway, talked about follow-up on HAE patients in his home area of Bergen. Sweden was represented by Dr. Maria Karlsson from Karolinska University Hospital in Stockholm, who talked about HAE and family planning. The HAE patients Nathalie Berne (Sweden), Karina Langsager (Denmark), and Trine Balle Boysen (Denmark) discussed the same topic, not least based on experiences with and considerations about in-vitro fertilization. The participants in the conference also had the opportunity to hear the nurses Tine Skov Andreasen and Karin Pia Henriksen from Odense University Hospital, Denmark, on their experience with preventive treatment.

After a Q&A session with the majority of the participating physicians that mainly focused on how to solve the continued differences in access to therapies in the three Scandinavian countries, breakout sessions followed with a particular focus on Denmark, Norway, Sweden, and the HAE youngsters.

The full academic program ended with a conversation between Prof. Anette Bygum from Denmark and HAE Scandinavia President Henrik Balle Boysen, who have both been involved in the organization since its inception 20 years ago.

Of course, there were also breaks in the program, where the participants had ample opportunity to talk to each other. These breaks also provided an occasion to visit the exhibits of the sponsoring pharmaceutical companies and to visit HAEi' stand, where HAE TrackR was promoted. Here conference attendees were introduced to how easy it is to download and use this new app from HAEi. HAE TrackR was unveiled from the stage, and many conference attendees chose to install the app and started using it immediately.

20 YEARS 2001-2021

HAE Scandinavia

Photos by Trine Dahl-Johansen

"THE POWER OF PROPHYLAXIS"

HAEi-SPONSORED RESEARCH FOCUSES ON DATA TO SUPPORT ADVOCACY FOR MODERN THERAPY AND IMPROVED QUALITY OF LIFE

By Anthony J. Castaldo, HAEi President & CEO

Access to modern HAE medicines is the key to improving our community's quality of life. HAEi's experience working with member organizations shows that having robust and reliable real-world data is a key component winning approval for a therapy. HAEi conducts targeted, scientific based research designed to provide data that our member organizations can use in their advocacy efforts to convince Health Ministries to approve HAE therapies.

HAEi has three core methodological approaches for patient-centric HAE studies that we conduct for our member organizations: Heat Map Survey, Pharmacoeconomic, Socioeconomic and Quality of Life Assessment, and Baseline Burden of Illness Study.

Heat Map Survey

HAEi designed our Heat Map Survey methodology to be used for countries where there are few, if any people diagnosed with HAE. The objective is to identify "pockets" of potential HAE so that we can pinpoint areas to concentrate HAE education and awareness campaigns. The Heat Map Survey is currently running in Rwanda, and we are looking at Thailand, Bangladesh, and the Philippines as study candidates.

HAEI-SPONSORED RESEARCH TO SUPPORT ADVOCACY FOR MODERN THERAPY AND IMPROVED QOL

Pharmacoeconomic, Socioeconomic and Quality of Life Assessment

Our Pharmacoeconomic, Socioeconomic and Quality of Life Assessment studies are targeted for countries that already have access to modern HAE therapies. At present, we have completed these studies in the US, the United Kingdom, and the Nordic countries. We are also initiating studies in Australia and New Zealand.

The results of the pharmacoeconomic study conducted in the US were published in March 2021 in the prestigious medical journal Proceedings of Asthma and Allergy.

Baseline Burden of Illness Study

Baseline Burden of Illness study is conducted in countries where a patient organization exists, but no modern HAE therapies are yet available. Surveys are used to quantify the number of attacks, emergency room visits, hospitalizations, and patient quality of life. This study provides data that opens the door to approaching health ministries with real world evidence of a catastrophic unmet medical need. We have conducted the study India and are currently discussing plans for China and several other countries.

HAEi ADVOCACY ACADEMY: A TRAINING RESOURCE DESIGNED AROUND THE NEEDS IDENTIFIED BY OUR REGIONAL ADVISORY GROUPS

By Fiona Wardman, HAEi Chief Regional Patient Advocate

HAEi Advocacy Academy is the premier online learning platform for the HAE Community that supports people living with HAE in their everyday life and offers training to help our HAEi member organizations sharpen their advocacy skills.

The content found in the academy is the direct result of needs identified by the HAEi Community.

The process used to understand and then develop highly relevant learning materials reflects HAEi's decentralized approach that features our Regional Patient Advocates (RPAs) as the "on the ground forces" to working closely with our member organizations.

The "bottom up" development process for HAEi Advocacy Academy began with the RPAs asking each member organization to nominate an Advisor who would be part of the Regional Advisory Group (RAGs). Each RPA then held group or one-on-one meetings with the RAG members and asked a variety of questions to gather information on the challenges and unmet needs being faced in each country and region.

The information generated during the RAGs meetings provided a clear picture of the issues faced by member organizations, which informed development of a "Top 5 Challenges" which served as basis for creating HAEi Advocacy Academy courses.

Besides the academy courses, HAEi has also designed materials to address the issues identified by the "Top 5 Challenges".

In sum, HAEi Advocacy Academy is a sophisticated, practical, and highly informational tool for member organizations to use to help them build their organizations, assist them in their advocacy efforts, and so much more. HAEi Advocacy Academy isn't only for member organizations as there are also open courses for anyone wanting to become a better advocate and assist their efforts.

HAEi will add more courses regularly. Check back often to see what's new. In the meantime, your RPA is always ready to help you with any questions, challenges, or projects.

>> VISIT ACADEMY.HAEI.ORG

Available in multiple languages!

HAEi ADVOCACY ACADEMY AND MATERIALS DEVELOPED BY HAEi TO ADDRESS THE ISSUES IDENTIFIED BY THE "TOP 5 CHALLENGES"

1) LENGTHY TIME TO DIAGNOSIS

- HAEi Emergency Department Poster
- HAEi Emergency Card
- HAE Management Plan
- Learn about ACARE Centers

2) NO MODERN TREATMENT ACCESS OR HOME THERAPY

- HAEi Connect, TrackR app
- Six-part series on Building Your HAE Organization
- Patient-Driven Research
- Working with Pharmaceutical Companies
- HAE Management Plan

3) LACK OF HAE AWARENESS

- HAEi Hosted Websites
- HAE Resources for Kids
- HAEi Youngsters Community
- HAEi Youngsters Toolkit
- HAEi Emergency Department Poster
- Six-part series on Building Your HAE Organization
- Patient-Driven Research
- Learn about ACARE Canters
- HAE Management Plan
- Global Perspectives Magazine

4) MOTIVATING PATIENTS AND CAREGIVERS

- HAE Advocacy Workshop
- HAEi Connect
- Resources for Kids
- HAEi Youngsters Community
- HAEi Youngsters Toolkit
- HAEi Hosted Websites
- Six-part series on Building Your HAE Organization

5) LACK OF RESOURCES

- HAE Companion app
- IT Security
- Regional Patient Advocates (RPAs)
- All of the courses already mentioned above

NEWS FROM MEMBER ORGANIZATIONS AROUND THE GLOBE

UNITED KINGDOM

From Executive Officer Rachel Annals, HAE UK

HAE UK have been working on and supporting a number of projects over the past few months: Our recently launched nurses' program, developed in conjunction with our nurse advisors, has been developed for nurses who have not dealt with HAE before to learn and understand the condition and treatments. It is also beneficial for nurses who need their knowledge refreshed. Another new project at one of our hospitals in Birmingham, is to have a clinical psychologist available for HAE patients. This is a new project being run as a clinical trial, which we hope we could roll out further around the UK to HAE patients in need of support when diagnosed or to manage their condition. We are also supporting a Fitbit project at one of our hospitals in Cardiff, to study the effects of exercise and weight loss on HAE attacks.

We have been working with the pharmaceutical companies and the National Institute for Clinical Excellence on submissions for Berotralstat in England, which was later approved. We are now following this up with The Scottish Medicines Consortium for approval in Scotland.

We have sadly decided not to host a 2021 Patient Day in the UK. After much deliberation, and with feedback from our members who felt unsure about travelling and meeting in a large group, we decided to postpone and will hold a large event next year, when hopefully things are back to normal.

HAE UK are also seeing some further changes in our management: Our Chief Executive Officer, Laura Szutowicz, resigned from her role to take up a position with a pharmaceutical company. Laura says: "I have enjoyed every minute of my six and a half years in the role, mainly due to the terrific support of the Trustees and the members, and particularly due to Rachel who has been my right (and probably my left) hand! We have had some memorable times and I have great memories of all the various patient days and getting to know so many members. I hope I shall still see some of you at meetings in the future."

HAE UK have successfully recruited a new CEO, Angela Metcalfe, who started in the role at the beginning of November. Angela joins HAE UK from both a commercial business background and working together with CEO and Director level within an autism charity, as well as for a charitable foundation. She understands the frustrations that can exist with accessibility to support, especially around medical needs and mental health. Her main focus will be to raise awareness of HAE, to help develop better sharing of information about the illness within the UK Rare Diseases Framework that is currently under development, and to grow the training programs in place throughout the National Health Service.

BRAZIL

Short but sweet from HAE Brazil (ABRANGHE)

Subcutaneous Berinert has been approved in Brazil for prophylactic treatment. It has been available for medical prescription to patients since 1 November 2021.

CROATIA

From Mihaela Šogorić, President of HAE Croatia

HAE Croatia organized a gathering during the weekend 2-3 October 2021 in Tuheljske Toplice. It was the first such encounter in Croatia.

The gathering began with the speech of Ljerka Karadža Lapić, MD of otolaryngology, working in the Clinical Hospital Center Šibenik, who greeted participants in the name of the Supervisory Board followed by the paediatricians' lectures. Irena Ivković-Jureković, MD of Paediatric Allergology andClinical Immunology at the Children's Hospital Zagreb talked about the symptoms and diagnosis of HAE. A lecture about treatment for HAE was held by Nevena Cigrovski, MD at the Paediatric Clinic at the Clinical Hospital Center Zagreb.

She pointed out that HAE is a rare but potentially fatal disease.

On the other hand, the future is bright because there are more and more research including medications for long-term and short-term prophylaxis. Lecture about long-term prophylaxis was provided by Bojana Olujić, MD at the Paediatric Clinic in the Clinical Hospital Center Osijek. Among other information, she presented statistics about how HAE affects the quality of children's life: between 20 to 100 days a year they are not capable of doing normal daily activities and 44 % of children suffering from HAE are absent one or more days from school.

The second day of this gathering, Ante Prgin held a motivational workshop for children where he talked about his life experience with HAE. He pointed out that, for him, this is not a disease, but a restriction. The gathering ended with psychological workshops for children, but also for their parents held by Maja Batista, MD from the Clinical Hospital Center Sestre Milosrdnice in Zagreb. HAE Croatia has begun production of a brochure with the aim to provide psychological support to people suffering from HAE with the help of Maja Batista, MD. The brochure is supposed to be printed at the beginning of next year.

I will endeavor to organize this kind of gathering for children every year. I am acknowledging appreciation to all the doctors for participation, as well as to all donators for financial support of this gathering. The instructive and pleasant weekend included a tour of the castles Mihanović and Veliki Tabor.

Till the next time, I'm sending you my best regards.

JAPAN

From President Beverley Yamamoto, HAE Japan

The non-profit organization Discovery Consortium has been established in Japan to try and lift the diagnosis rate for HAE up to the kind of levels seen in North America and Europe. At the moment we estimate that only 20 % of all Japanese patients have been diagnosed.

The majority of the funding for the project is coming from the pharmaceutical companies, with equal funding from Takeda, CSL and Torii who represent BioCryst in Japan. I am on the Board of Directors along with the leading doctors in the field.

USA

From Digital & Social Media Manager Ianice Viel, US HAEA

2021 has continued to be an incredibly productive year for the US HAEA despite the ongoing pandemic-related challenges. As shown in the examples that follow, our programs, services, and activities continued to generate great enthusiasm and participation.

2021 US HAEA Virtual Summit Series: The 2021 "first ever" US HAEA Virtual Summit series was a resounding success that was enjoyed by over 1,200 participants. The event brought together people with HAE, expert physicians, caregivers, industry partners, health insurance representatives, and the FDA. This "one-of-a-kind virtual" summit series addressed the issues faced by our community and offered ideas on how we can work together to solve them.

2021 Capitol Hill Campaign: The outstanding level of participation in our Virtual 2021 US HAEA Capitol Hill Campaign demonstrates that our community continues to be eager to advocate for people with HAE. The program kicked off with a live event that featured US elected officials and HAEA Advocates who showed support for the HAE community and efforts to improve quality of life. We then held an educational session on best practices for presenting personal HAE stories to elected representatives. Armed with this knowledge, attendees participated in exclusive virtual meetings with the elected officials who represent them in Congress. During these meetings, our HAEA Advocates shared their stories and asked their representatives to vote on issues that directly impact the day-to-day challenges presented to people with HAE. The 2021 HAEA Capitol Hill Campaign is a perfect example of how virtual advocacy can make a difference in the lives of people affected by HAE.

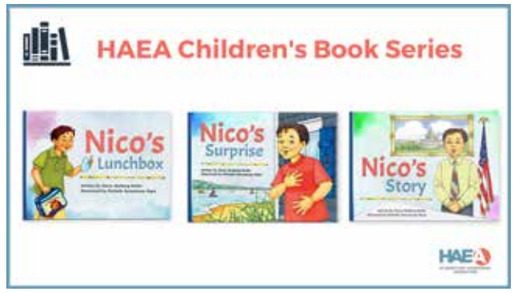
2021 HAE IN-MOTION® Virtual Challenge: The 2021 HAE IN-MOTION® Virtual Challenge was a huge success with over 500 people joining together to raise HAE awareness. By registering over 35,000 miles in various activities, the HAEA community once again came together to take action for HAE. The event also raised funds to support key HAEA programs including the Pam King HAEA Scholarship Program, the Chris Whalen HAEA Compassion Fund, and the HAEA Research Fund.

Virtual Meet and Greets Events: In 2021 the HAEA hosted a series of virtual Meet & Greet events for US HAEA youth and young adults that offered an opportunity to connect with peers while learning about the HAEA's different programs and services, specially tailored for the HAE community.

We also held a large number of virtual Meet & Greet events for adults with HAE. Due to the accessible nature of these Zoom Meet and Greet Events, we reached more members of the HAE community and hosted meetings across more areas of the US than ever before.

US HAEA Podcasts: The US HAEA is proud to host two podcasts for our community: #BeyondHAE and HAE Speaks. The HAE Speaks podcast series presents unique stories of individuals affected by HAE with the goal of connecting our community through shared experiences. The #BeyondHAE Youth Podcast series is produced by and for young people with HAE. The HAE Speaks and #BeyondHAE podcasts are available on all major podcasting platforms.

HAEA.org has been redesigned: The US HAEA community spoke, and we listened. Responses to recent surveys and focus groups helped us reimagine the haea.org website and transform it into an intuitive, dynamic, and mobile-friendly resource. At haea.org, you can find valuable resources such as: educational materials, including everything you need to know about successfully managing HAE; access to our kind and compassionate HAE Advocates; ways to connect to the broader HAEA community; and information about the US HAEA's programs, services, and activities. The new website features enhanced sections tailored to particular groups within our HAE community, such as parents of children with HAE and newly diagnosed individuals. Other important upgrades include easier ways to search for and find information on: FDA-approved treatments, ongoing clinical trials, breaking HAE news, everything you need to know about hosting or participating in a US HAEA event, and much more.



HAEA Children's Book Series: "Nico's Story": All three books in the HAEA Children's book series are now available as e-books for the international community. In the recently released book "Nico's Story", Nico cannot wait to get on the plane and head to Washington, DC. He and his family will join other HAE advocates for Capitol Hill Day. Nico is excited to visit Congress and talk about what it's like to have HAE. Best of all, he will get to see his good friends, Jay and Kai. He has not seen them since the surprise visit at the lake house last summer. Will Nico make new friends at Capitol Hill Day? What will he discover when he explores the nation's capital? Listen to the e-books of the HAEA Children's book series in English and Spanish on our Vimeo channel (ushaea).

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

An HAE-Specific Instrument to Measure Quality of Life: The US HAEA is wrapping up a unique, ground-breaking research study that seeks to accurately show how HAE affects overall quality of life. This research will help us publish a quality of life questionnaire that (1) truly captures the way HAE affects the everyday life of individuals and families, and (2) demonstrates to health insurers and others the value of life-changing improvements in health and quality of life that result from modern HAE medicines.

Shared Decision-Making Tool: We are currently developing a Shared Decision-Making tool that will enable physicians and people with HAE to work together when making healthcare decisions, ensuring that both the physician and the person with HAE have a voice in their treatment plan.

HAE and Aging Study: The US HAEA study on HAE and Aging will help us to better understand the demographic and clinical characteristics, HAE treatment patterns, HAE impact and burden, and perceived health-related quality of life of the aging HAE population. This study is being designed with a comparator population of

people without HAE, and we plan to have these results published in a manuscript when complete in early 2022. This research project is uniquely important to the HAEA community, as current data on HAE and Aging does not exist.

HAEA Study on the Number of People with HAE in the US: The US HAEA is dedicated to offering its unique programs, services, and activities to everyone in the US that has HAE. Estimates regarding the number of people with the condition in the United States have an extremely large range, which means we have no idea if we are reaching the entire population. We have initiated a study using sophisticated data mining techniques and expert HAE physician input to calculate the number of people with HAE in the United States. The results of this study will help the US HAEA to target its outreach efforts to continue building the HAEA community.

RUSSIA

From HAE Russia

We bring good news for juvenile HAE patients and their parents as children with HAE will soon begin receiving advanced pathogenetic medications from the Circle of Good Foundation.

The Circle of Good Foundation is a public non-budgetary charitable organization. Established in January 2021 by presidential decree, the Foundation aims at supporting children with severe life-threatening and chronic diseases, including rare (orphan) diseases. Founded by the Russian Ministry of Health, the Foundation provides assistance to Russian children under the age of 18 diagnosed with diseases included in the Foundation's List of Diseases.

HAE refers to orphan diseases. Until now, in the regions of Russia children with such a diagnosis have not always and regularly been provided with effective medicines intended to treat HAE.

In September 2021 the Board of Directors of HAE Russia applied to the Circle of Good Foundation requesting that juvenile patients with HAE be included in the Foundation's List of Diseases. On 7 October 2021 the Expert Council of the Circle of Good decided to add the underage patients and children diagnosed with HAE to the list of diseases supervised by the Foundation.

Elena Viktorovna Bezbozhnaya, Chairman of HAE Russia, considers this decision very significant: the Circle of Good assumed care for our children diagnosed with HAE, included the HAE disease in the Foundation's List of Diseases, which appeared good news for us. Thus, patients with HAE will be provided with medications until the age of 18. And now, upon requests from doctors, the Foundation will purchase advanced medications for underage patients.

The first pathogenic long-term therapy for HAE – that is lanadelumab/Takhzyro – has joined the Circle of Good.

SPAIN

From President Sarah Smith, HAE Spain (AEDAF)

23rd AEDAF General Assembly: Because of our decision to avoid in-person events during all of 2021 and in keeping with the Association's Statutes, AEDAF held its 23rd General Assembly on Zoom on 11 November 2021. We are hoping that in 2022 we can resume face-to-face meetings and events and are planning to hold our 24th General Assembly and Annual Meeting in person on 26 March 2022.

Centers of Reference for HAE: In July 2021, Spain's Ministry of Health approved three CSUR (Reference Centers, Services or Units of the National Health System) for Hereditary Angioedema (children and adults).

These three centers, the first officially designated national centers of reference for HAE in Spain, are:

- University Hospital La Paz (Madrid): Coordinator, Dr. Teresa Caballero Molina
- University Hospital Vall d'Hebron (Barcelona): Coordinator, Dr. Mar Guilarte Clavero
- University Hospital Virgen Del Rocio (Seville): Coordinator, Dr. Stefan Cimbollek

Dr. Caballero says that it has taken a lot of time and effort to achieve the designation of these official national centers of reference. The three centers are now in the process of preparing a document to facilitate patient access to the centers and to unify criteria and coordinate among themselves in order to benefit patients and improve their healthcare.

Project "Zero Attacks": During the National Congress of the Spanish Society of Allergology and Clinical Immunology (SEAIC) in October 2021, the Spanish Study Group on Bradykinin-Induced Angioedema (GEAB) presented the project "Cero Ataques" (Zero Attacks), an initiative that aims to raise awareness of the situation of the more than 800 patients affected by HAE in Spain. This project is supported by CSL Behring and coordinated by Dr. Mar Guilarte, allergy specialist at the Vall d'Hebron Hospital in Barcelona and member of GEAB. The objectives of this project are to promote reflection and understanding of the impact of this rare disease, to increase awareness of the support needs of HAE patients and to identify future work areas in order to improve their management.

"It was practically impossible to think about a patient having zero attacks until recently", says Dr. Guilarte, "but today, for some patients, it is now almost a reality and means they no longer feel sick and can lead normal lives. Zero attacks implies total control of the disease; patients can improve their quality of life and they can make plans as they no longer have to face the unpredictability of having an angioedema attack at any time or in any place that would make them unable to carry on with their day-to-day activities."

In this sense, Dr. Guilarte points out that to improve the quality of life of patients "we must offer them therapeutic and diagnostic strategies that reduce their burden of disease. It is important that all HAE patients have access to optimal treatment, that they have a good action plan to know how to act in the event of an attack and that HAE management always be individualized for each patient, taking into account their previous experiences, their personal situation and their current burden."

Currently, HAE treatment is experiencing a "unique moment", says Dr. Guilarte: "We have new treatments for preventing life-changing attacks in patients and that, in many cases, achieve control of the disease."

Specifically, the research on HAE focuses on the study of new treatments, especially aimed at preventing attacks, and also at the identification of biomarkers for a better understanding of the pathophysiology of HAE that will help establish the best therapeutic strategy for each patient. Likewise, instruments are being developed to be able to study the control and impact of the disease, to evaluate its burden or its severity and, thus, to be able to better assess the response to the different treatments.

Finally, Dr. Guilarte says that "the current situation is not perfect. Access to these new treatments is not universal as they are limited to those patients with a high burden of the disease; as a result many patients continue to have attacks and live with the fear and uncertainty that having an episode of angioedema implies."

CANADA

From President Jacquie Badiou and COO Daphne Dumbrille, HAE Canada

This fall HAE Canada hit the ground running. Our first task of the season was to present our poster titled, "Hereditary angioedema in Canada: Changes in medication use and untreated attacks between the 2017 and 2020 surveys" at the Canadian Society of Allergy and Clinical Immunology (CSACI)'s Annual 2021 Scientific Virtual Meeting. It was a great conference, and we were proud to present at this well-respected meeting.

We are thrilled that our abstract titled "HAE with normal C1-INH: Treatment and attack frequency based on data from the Canadian 2020 national survey" has been selected for a poster presentation at the American Academy of Asthma & Immunology (AAAAI)'s Annual Meeting in February 2022. We would like to once again thank Suzanne Kelly of Red Maple Trials who did a fabulous job developing this abstract. We also need to thank the HAE specialists across Canada who contributed their expertise to this abstract, as well as the HAE Canada Advocacy Committee.

Since HAE Canada is always growing, we are grateful to have the support of our volunteers. We officially welcomed new people to the HAE Canada team: Regional Director Assistants (RDAs). When we need to contact our members individually for certain projects, or to gather updated information, helpful RDAs will lend us their support. Each province has at least one RDA and we want to thank each and every one for their commitment and assistance.

On 20 November 2021, HAE Canada hosted a Patient Information Update. We were hoping to have in-person updates in London and Sudbury, Ontario, however, COVID-19 is still preventing us from gathering. We remain grateful for the option to host virtual events, especially since this allows us to connect with members across Canada. The day stayed on task with

Daphne Dumbrille and fellow panelist Michelle Cooper, the Ontario Regional Director who kept her eyes on the questions and comments. To start, the participants enjoyed two interesting and informative presentations by HAE specialists from the London area: Dr. Harold Kim, MD, FRCPC, Allergy & Clinical Immunology, and Dr. Samira Jeimy, MD, PHD, FRCPC, Allergy & Clinical Immunology. Dr. Kim informed us about the available treatments for Ontario HAE patients, and how specifically to access these products, and Dr. Jeimy shared her presentation titled "HAE and Pregnancy: ten things I want patients to know". Next, Michelle Cooper kindly opened-up and shared her patient journey and how she became involved with HAE Canada. Jacquie Badiou followed Michelle with a presentation asking three HAEi representatives about their early patient days and how they became involved with HAEi. These representatives included President & CEO Anthony J. Castaldo, Treasurer & Chief Regional Patient Advocate Fiona Wardman, and Executive VP & COO Henrik Balle Boysen.

We also learned about Treatments on the Horizon from Anthony J. Castaldo, and the day ended with a Question & Answer session with our already mentioned guests, plus Dr. William Yang, MD, FRCPC, FAAAAI, and Dr. Sylvain Grenier, CD, B Pharm, PharmD, FFIP, FOPQ, Director, Canadian Blood Services.

All in all, it was a wonderful event, and we are extremely grateful to all our invited guests; they were fantastic. We want to thank them immensely for taking the time to help inform Canadian HAE patients.

HAE Canada will remain busy with different projects in the next few months, for instance, the Annual General Meeting in December. We are excited to examine the excellent Real-World Evidence from our Canadian membership that has been gathered in our 2020 National Report Card survey.

GUATEMALA

We are happy to inform you that the first two HAE knowledgeable physicians in Guatemala have been registered to our world map. Please see the Guatamala page for contact information: https://haei.org/hae-member-countries/guatemala.

SOUTH AFRICA

From HAE South Africa

HAE South Africa have received our approval as a non-profit company which means we are now able to actively raise funds for our organization. We have recruited two new members on to our committee, Jane Rushton, an HAE patient and attorney, as well as Sister Sheila Baker, a registered nurse who has many years' experience working alongside our HAE specialists and currently works as a locum at the UCT Lung Institute.

In August, Takeda and Professor Jonny Peter from our ACARE Centre In Cape Town, hosted the first of several planned training symposiums, with Dr. Marc Riedl and Dr. Aleena Banerji as guest speakers. The session was well attended with over 70 medical practitioners and other stakeholders in attendance. The Allergy Foundation of South Africa (AFSA) held a Masterclass in October consisting of an in-depth module focusing on angioedema, including an introduction to HAE and pathophysiology, clinical characteristics, diagnosis, and management.

Over the next year, in conjunction with Professor Mike Levin from AFSA and Professor Jonny Peter, our focus will be on physician awareness and education, to ensure that all doctors on our referral lists are up to date on diagnosis and treatment protocols and to recruit new doctors who are willing to treat HAE patients. An Angioedema Hotline has been set up and will form part of this initiative.

We are currently working on social awareness of HAE via newspaper and magazine articles, and we are in the process of upgrading our website and other social media platforms. We have implemented a couple of new initiatives to encourage more involvement amongst our patients, via a closed Facebook group as well as an "HAE Buddy System" where we are able to put patients of similar ages and circumstances in contact with other for emotional support.

In conjunction with Rare Diseases S.A. and other more advanced rare disease associations, we are exploring several new options regarding reimbursement and funding of medications.

NEWS FROM MEMBER ORGANIZATIONS AROUND THE GLOBE

TURKEY

From President Gökben Yurdakul, HAE Turkey

We are so happy to be here and share our accomplishments with you. During the COVID-19 pandemic we have held a number of online meetings with our patients and their relatives. This has been done in order to gather information about COVID-19 in-fected people's troubles and concerns. Also, we have contacted our doctors to ensure the healthy completion of those patients' treatments. Likewise, we informed our doc-tors about the complications, troubles and problems experienced due to COVID-19 vac-cinations, so that the correct procedures could be followed.

As always, we ensured that people who reached our association were diagnosed properly and provided information about their treatment. We have been working on the recognition and acceptance of the disease to a great extent, by sharing our emo-tional experiences. Thanks to our WhatsApp patient group, we have contributed great-ly to the study on the psychological and physical effects that patients experience during HAE attacks.

We have submitted our written requests to the relevant state authorities about treat-ments and demanded changes in the legislation. We expect positive results as soon as possible.

In the coming days, we will be holding a meeting with psychologists and doctors to dis-cuss the effects of the disease on small children and young patients. We would be hap-py to share the expected and obtained outcomes of this meeting with you soon.

As an association, it is crucial to us that the network we have established with doctors develops and expands every day.

What makes us happy and successful is being able to produce quick solutions to the problems experienced by the patients. We will continue to work for HAE with all our heart.

CUBA

In the capital La Habana three HAE knowledgeable physicians have been added - please see the Cuban map for contact details at https://haei.org/hae-member-countries/cuba.

AUSTRALIA & NEW ZEALAND

From CEO Fiona Wardman, HAE Australasia

Patients in Australia are thankful for our Health Minister's decision to sign off on the recommendation to fund Takhzyro (lanadelumab). As of 1 December 2021, more patients have access to this treatment, closing the gap of access for prophylaxis medications for many of our patients.

Our patients in New Zealand also received some good news via a press release that Intellia's Phase 1/2 study will be recruiting patients by the end of the year.

HAE Australasia looks forward to hosting two Patient and Carers Conferences in February 2022. The registration websites (utilizing HAEi's Event Zoo application) are now open for the Australian meeting on 5 February and the New Zealand meeting on 26 February 2022. We are excited to connect face-to-face once again to have presentations from top physicians and experts on exciting subjects and network.

The Board of HAE Australasia will convene early in the new year for a strategy meeting to work on plans and projects for 2022. We have some great ideas to discuss, and we look forward to bringing these to our patients of all ages and their family members.

HAE Australasia has seen an increase in HAE patients and their family becoming members of our organization. We welcome everyone to the group, and we look forward to meeting them in person soon.

We wish everyone a Merry Christmas and all the best for a safe, happy, and healthy 2022.

DENMARK, NORWAY, AND SWEDEN

HAE Scandinavia has appointed the Board for the next two years: Chairman Henrik Balle Boysen (Denmark), Vice Chairman Jørn Schultz-Boysen (Denmark), Treasurer Karina Langsager (Denmark), Secretary Erik Hovgaard Hansen (Denmark), Karen Jespersen-Hansen (Denmark), Youngsters responsible Nanna Maria Boysen (Denmark), Youngsters responsible Victoria Schultz-Boysen (Denmark), Camilla Eriksson (Sweden), Cecilia Grahn (Sweden), Ann Helen Hellevik (Norway), and Trine Dahl-Johansen (Norway). In addition, deputies Cecilie Harms Döscher (Norway) and Kristoffer Grahn (Sweden).

Photo:Anna Rönning

CLINICAL TRIALS

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

A Gene Therapy Study of BMN 331 in Subjects with HAE

– recruiting in the United States

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

– recruiting in Austria, France, Germany, Greece

A Study of Lanadelumab in Teenagers and Adults to Prevent Acute Attacks of Non-histaminergic Angioedema with Normal C1-Inhibitor (C1-INH)

– recruiting in Canada, Germany, Hungary, Italy, the Netherlands, Poland, Spain, the United States

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

– recruiting in Argentina

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

– recruiting in the United States

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

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

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

– recruiting in France

Biomarker for HAE Disease

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

C1 Inhibitor Registry in the Treatment of HAE Attacks –

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

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

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

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

– recruiting in the United States

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

– recruiting in Japan

CLINICAL TRIALS

Epidemiological Analysis for HAE Disease

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

Expanded Access Program with Lanadelumab for Japanese People with HAE

– recruiting in Japan

Firazyr General Drug Use-Results Survey (Japan)

– recruiting in Japan

Firazyr Patient Registry (Icatibant Outcome Survey - IOS)

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

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

– recruiting in Italy

HAE Kininogen Assay –

recruiting in Germany

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

– recruiting in France

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

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

NTLA-2002 in Adults with HAE

– recruiting in New Zealand

Pathophysiological study for autoimmune dysregulation of HAE

– recruiting in Japan

Patient Registry to Evaluate the Real-world Safety of Ruconest

– recruiting in the United States

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

– recruiting in the United States

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

– recruiting in Canada, Puerto Rico, the United States

Study to Evaluate the Real-World Long-Term Effectiveness of Lanadelumab in Participants with Hereditary Angioedema HAE

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

The influence of stress and lifestyle in HAE

– recruiting in New Zealand

The Role of the Coagulation Pathways in Recurrent Angioedema

– recruiting in France

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

– will be recruiting

A Study with Lanadelumab in Persons with HAE in Poland

– will be recruiting in Poland

Efficacy and Safety of GNR-038 vs Berinert in Patients with HAE

– will be recruiting in Russia

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

– will be recruiting

Open-label Berotralstat Access to HAE Patients Previously Enrolled in Berotralstat Studies

– will be recruiting

Read more about these and other clinical trials at:

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

MEDICAL PAPERS

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

Lanadelumab Efficacy, Safety, and Injection Interval Extension in HAE: A Real-Life Study *– by Thomas Buttgereit, Charité - Universitätsmedizin Berlin, Germany, et al.:*

Gradual extension of injection intervals of lanadelumab presented in this study can minimize the burden of therapy without losing efficacy.

J Allergy Clin Immunol Pract, October 2021

COVID-19 and HAE: Incidence, outcomes, and mechanistic implications *– by Camila Lopes Veronez, University of California San Diego, the United States, et al.:*

Patients with HAE have been postulated to be at increased risk for COVID-19 infection due to inherent dysregulation of the plasma kallikrein-kinin system. A total of 1162 participants who completed an online questionnaire were analyzed. Subjects with HAE-C1INH who were not taking HAE medications had a significantly higher rate of reported COVID-19 infection. Subcutaneous C1INH and icatibant use were associated with a significantly reduced rate of reported COVID-19. The results implicated potential roles for the complement cascade and tissue kallikrein-kinin pathways in the pathogenesis of COVID-19 in patients with HAE-C1INH.

Allergy Asthma Proc, November 2021

How do patients and physicians communicate about HAE in the United States? *– by Gagan Jain, Takeda Pharmaceutical Company Limited, et al.:*

Vocabulary differences suggest that the full impact of HAE is not consistently communicated by patients to physicians during clinical visits, indicating the potential for misaligned understanding of disease burden. A patient-driven, rather than physician-driven approach to the discussions may elicit valuable information that could help to optimize treatment approaches.

PLoS One, December 2021

Physicochemical and Biological Characterization of rhC1INH Expressed in CHO Cells *– by Ekaterina Zubareva, JSC "GENERIUM", Russia, et al.:*

The physicochemical and biological characterization of a novel recombinant human C1 esterase inhibitor (rhC1INH) from Chinese hamster ovary (CHO) cells for the treatment of HAE compared to Berinert and Ruconest allow us to conclude that the novel molecule could become a potential therapeutic option for patients with HAE/AAE.

Pharmaceuticals (Basel), November 2021

Pharmacological and clinical study results of Berotralstat Hydrochloride for long-term prophylactic treatment of HAE *– by Satoshi Orui, Torii Pharmaceutical Co., Ltd., et al:*

Berotralstat hydrochloride (Orladeyo capsules 150 mg) is an oral, selective plasma kallikrein inhibitor approved for the suppression of the onset of acute attacks in HAE in Japan in January 2021. Preclinical and clinical data indicate that Berotralstat is an effective treatment for long-term prophylactic treatment by suppressing the onset of acute attack in HAE patient and is considered to be a useful treatment option for patients.

Nihon Yakurigaku Zasshi, 2021

First Census of Patients with HAE in the Canary Islands *– by Alejandro Mendoza-Alvarez, Universidad de La Laguna, Spain, et al.:*

Forty-one patients (33 F, 8 M) and nine healthy relatives belonging to 29 families were recruited for this study. Positive family history of HAE was reported in 13 patients, and a mean diagnosis delay of 7.9 years was estimated. Cutaneous edema was the most common symptom. Prophylactic treatment was indicated for 23 patients, while 14 also require on-demand rescue treatment. We estimate a minimum prevalence of 1.25:100,000 for HAE due to C1-INH deficiency or dysfunction in the Canary Islands, which is higher than the estimates for mainland Spanish populations.

J Clin Med, October 2021

Case report: HAE in pregnancy *– by Adam D. Jakes, St. Thomas' Hospital, the United Kingdom, et al.:*

Intravenous C1INH is the first-line therapy in pregnancy and breastfeeding. It should be given if any obstetric intervention is planned. Routine prophylactic administration may be appropriate if symptoms recur frequently during the third trimester. Pregnant women with C1INH-HAE should deliver in a hospital with C1INH replacement, fiberoptic intubation and front-of-neck access equipment readily available. A documented treatment plan should be developed within a multi-disciplinary team to pre-empt complications.

Obstet Med, September 2021

Optimization of care for patients with HAE living in rural areas *– by Marc A. Riedl, University of California San Diego, the United States, et al.:*

Ways to improve HAE patient care in rural areas include health care provider recognition of the undiagnosed HAE patient, development of individualized management plans, expansion of telemedicine, effective care at the local level, appropriate access to HAE medication, and increased awareness of patient support and advocacy groups.

Ann Allergy Asthma Immunol, October 2021

Measurement of C1-Inhibitor function alone is sufficient for diagnosis of HAE – *by Sorena Kiani-Alikhan, Barts Health NHS Trust, the United Kingdom, et al.:*

Analyzing six months' worth of data generated in our laboratory which is a specialist regional immunology service and also provides laboratory service for the Barts Health immunology department, we found that an efficient and sensitive approach for laboratory diagnosis of HAE is to only test the C1-inhibitor function. This approach had a sensitivity of 100% and reduced the cost of laboratory investigations for HAE diagnosis by 45%.

J Clin Pathol, October 2021

Consensus on treatment goals in HAE: A global Delphi initiative *– by Marcus Maurer, Charité - Universitätsmedizin Berlin, Germany, et al.:*

The ultimate goal for HAE treatment is to achieve no angioedema attacks. The availability of improved treatments and disease management over the last decade now makes complete control of HAE a realistic possibility for most patients.

J Allergy Clin Immunol, December 2021

Clinical profile of HAE from a tertiary care center in India *– by Susmitha Perumalla, Christian Medical College, India, et al.:*

Many cases of HAE may be going undetected in India. There is a need for clinical awareness and laboratory means to accurately identify and administer appropriate treatment.

Indian J Med Microbiol, October-December 2021

PubMed

NEWS FROM THE INDUSTRY

30 September 2021

Cycle Pharmaceuticals launces Sajazir (icatibant) Injection, a new treatment option for patients affected by HAE approved by the US Food and Drug Administration (FDA). Sajazir is a bradykinin B2 receptor antagonist indicated for treatment of acute attacks of HAE in adults 18 years of age and older.

Sajazir is supplied in a prefilled syringe delivering 30 mg icatibant. Patients may self-administer Sajazir subcutaneously upon recognition of symptoms of a HAE attack after training under the guidance of a Healthcare Professional or a Registered Nurse from Cycle Vita.

"The launch of Sajazir gives the HAE community an exciting new treatment option. Cycle understands the importance of providing product support to complement the impact of therapeutic products. Sajazir patients can take advantage of our newly launched product support hub, Cycle Vita." says Zac Bohlen, Cycle's VP of US Sales.

(Source: Cycle Pharmaceuticals)

30 September 2021

CAMP4 Therapeutics presents preclinical data demonstrating the utility of its RNA Actuating Platform (RAP) and the therapeutic potential of oligonucleotide-mediated gene upregulation targeting a new class of RNA known as regulatory RNAs ("regRNAs").

The data describe this novel treatment approach for two genetically defined diseases, one being HAE.

"These data demonstrate that by using oligonucleotides to target regRNA, we can directly upregulate endogenous gene expression at the transcriptional level and achieve a therapeutically relevant result," says David Bumcrot, Ph.D., Chief Scientific Officer of CAMP4. "With the results of these studies, we have the early proof points that our novel approach to harness the power of regRNA for gene upregulation works across multiple genes, fueling our conviction as we advance the development of precise, potent, programmable and durable therapeutics for genetic diseases that lack disease-modifying therapies."

RegRNAs act as gene-specific rheostats that can finely modulate gene expression upstream of mRNA transcription, but not to excessive levels that might generate toxicity. CAMP4 leverages its extensive set of proprietary genomic data to efficiently and systematically identify gene-specific regRNA targets and generate precise oligonucleotide drug candidates, or RNA ActuatorsTM, to drug them. This approach is applicable to any genetic disease whereby a small increase in gene output can lead to meaningful therapeutic outcomes.

In primary mouse hepatocytes, RNA Actuators increased Serping1 expression by 2-to-3-fold with minimal impact on neighboring genes. The RNA Actuators also normalized the levels of Serping1 in a HAE mimic in vitro model and led to an increase in Serping1 protein in mice.

(Source: CAMP4 Therapeutics)

6 October 2021

Intellia Therapeutics, Inc.'s Clinical Trial Application (CTA) has been authorized by the New Zealand Medicines and Medical Devices Safety Authority (MEDSAFE) to initiate a Phase 1/2 study evaluating NTLA-2002 for the treatment of adults with HAE. NTLA-2002 is a systemically administered single-dose CRISPR/Cas9-based therapeutic candidate designed to inactivate the target gene Kallikrein B1 (KLKB1) to permanently reduce plasma kallikrein activity and thus prevent HAE attacks.

"We look forward to initiating this year our first-in-human study of NTLA-2002 for people living with HAE", says Intellia President and CEO John Leonard, M.D.: "We believe NTLA-2002 has the potential to be a curative therapy for patients with HAE by providing continuous suppression of plasma kallikrein activity following a single dose and eliminating the significant treatment burden associated with currently available HAE therapies. This study of NTLA-2002 leverages early insights from our ATTR amyloidosis program, where we established proof-of-concept for our modular in vivogenome editing platform with interim Phase 1 data earlier this year. The NTLA-2002 program represents the second systemic in vivo CRISPR genome editing therapy candidate to enter human clinical trials."

The Phase 1/2 study will evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2002 in adults with Type I or Type II HAE. This includes the measurement of kallikrein protein levels and activity as determined by HAE attack rate measures. The Phase 1 portion of the study is an open-label, single-ascending dose design used to identify up to two dose levels of NTLA-2002 that will be further evaluated in the randomized, placebo-controlled Phase 2 portion of the study. This Phase 1/2 study will identify the dose of NTLA-2002 for use in future studies.

Intellia is submitting additional regulatory applications in other countries as part of its ongoing, multi-national development approach for NTLA-2002.

(Source: Intellia)

9 October 2021

Plasma helps your body fight diseases, and it deserves greater recognition. Ask people who have certain rare and chronic complex diseases – they will tell you that therapies made from donated plasma help them manage conditions such as immunodeficiency disorders, hemophilia, and HAE.

Plasma is a core substance within our blood and carries important cells, proteins, antibodies, hormones, and oxygen to help our bodies fight infection and prevent blood clots. Plasma collected from healthy donors is processed into life-changing therapies that replace missing or deficient proteins for people who generally require regular infusions or injections of these therapies for the duration of their lives. Plasma is also used in a wide variety of emergency and critical-care settings, further adding to its therapeutic importance and increased need throughout the world.

Because plasma cannot be produced in a lab, it is a rare and precious resource. That's one of the reasons why it's important to highlight the versatility and power of plasma, help people understand how plasma is used to treat disease, and to remind everyone of the urgent need for plasma donations. There's also a growing global demand for medicine developed from plasma which, is exactly why **Takeda** is continuing its pursuit of broadening access to plasma therapies for those in need around the world.

"BioLife celebrates the generosity of plasma donors for the role they play in producing vital, life-sustaining treatments for people in need – and encourages others to consider donating too," says Hema Tallman, Senior Vice President, Global Head of BioLife, part of Takeda. "Often referred to as 'liquid gold,' plasma is a source of hope for thousands of people living with rare and chronic, complex diseases. BioLife is honored to be one of the largest and most innovative plasma donation networks in the world, enabling the production of Takeda's plasma-based therapies."

Between 130 to 1,200 plasma donations are needed to treat just one patient for a single year. With plasma donations lower than usual due to the COVID-19 pandemic, BioLife Plasma Services is expanding to help meet the urgent need for plasma with almost 200 state-of-the-art plasma donations centers around the world.

In October, Takeda and the Plasma Protein Therapeutics Association (PPTA) are recognizing International Plasma Awareness Week (IPAW). Dedicated to raising global awareness around the urgent need for plasma donations, IPAW celebrates the contributions of those who donate and helps increase understanding about the life-saving role of medicine developed from plasma.

(Source: Takeda)

9 October 2021

Adalvo is pleased to announce the successful closure on the DCP procedure for our Icatibant development, a complex injectable peptide product, forming part of our high-value product portfolio offering to our partners.

Icatibant is an equivalent and more affordable version of Firazyr that will now be made more accessible to patients world-wide. The product is used to treat acute attacks of HAE. The development of this product was done in close collaboration with our strategic partner AmbioPharm, a global peptide manufacturer with one of the largest worldwide capacities.

Icatibant is truly a landmark product and this DCP registration procedure, which was submitted within almost all the EU region, proves our ability to bring complex high-value products to the market. With this achievement, we are among the first companies to get approval in all our major markets.

(Source: Adalvo)

28 October 2021

At the presentation of the **Pharming Group N.V.** presentation of the preliminary (unaudited) financial report for the first nine months ended 30 September 2021, CEO Sijmen de Vries comments:

"Supported by the strength of the underlying business, we are continuing to invest in future growth in line with our strategy to develop and expand our pipeline through leverage of our in-house expertise. This investment includes licensing of OTL-105, an investigational gene therapy for the potentially curative treatment of HAE, from Orchard Therapeutics in July 2021."

For the remainder of 2021, we expect:

Continued quarter on quarter increase in revenues from Ruconest sales due to normalizing pharmaceutical markets following the impact of COVID-19

Continued investment in ongoing clinical trials for rhC1INH and other development activities, including OTL-105.

(Source: Pharming)

3 November 2021

Announcing the financial results for the third quarter ended 30 September 2021, **BioCryst Pharmaceuticals, Inc.** President and CEO Jon Stonehouse says:

"With the significant revenue we expect to generate with Orladeyo – our oral, once-daily treatment for prevention of HAE attacks – in its first year of launch, BioCryst plans to repeat our clinical and commercial success with Orladeyo again and again as we bring much-needed oral medicines to patients waiting for them."

Regarding the U.S. launch of Orladeyo Charlie Gayer, Chief Commercial Officer of BioCryst, says:

"Almost a year into the launch of Orladeyo, we continue to see strong, consistent demand from new patients switching to Orladeyo from their existing injectable prophylactic and acute therapies, and it is exciting to see the positive impact Orladeyo is having on their lives. With the excellent start to the launch, and the excitement we hear from physicians and patients, Orladeyo is now on a trajectory to become the market leader in HAE prophylaxis."

The number of new physicians prescribing Orladeyo grew by another 25 percent in the third quarter and the Orladeyo prescriber base has now increased to include nearly half of the top 500 HAE-treating physicians in the United States. Orladeyo has been very well received by payors and is now covered by nearly all national and regional pharmacy benefit managers.

(Source: BioCryst)

8 November 2021

At the American College of Allergy, Asthma & Immunology (ACAAI) Annual Scientific Meeting, **KalVista Pharmaceuticals, Inc.** presents data on Phase 2 for KVD900, KalVista's lead program for oral on-demand treatment of HAE attacks.

"Current guidelines recommend effective on-demand therapy for every patient with HAE to reduce symptom severity and attack duration," says Jonathan Bernstein, FAAAAI, FACAAI, FACP, M.D., University of Cincinnati College of Medicine and Bernstein Clinical Research Center, LLC. "Treatment of HAE attacks with KVD900 achieved rapid plasma exposure which was associated with faster improvements in initial symptom relief compared with placebo. As the first oral on-demand treatment to demonstrate this early therapeutic effect for patients, KVD900 may represent a remarkable advancement for management of the disease."

Oral Presentation: On-Demand Oral Treatment with KVD900 for HAE Attacks Achieves Rapid Exposures and Improves Patient Outcomes:

KVD900 was rapidly absorbed, with measurable concentrations detected within 15 minutes

Plasma levels reached peak concentration within 1 hour of administration

Median time to symptom improvement was significantly shorter with KVD900 than with placebo (1.6 vs 9.0 hours, $p<0.0001$), as indicated by the Patient Global Impression of Change (PGI-C) scale

A significantly higher percentage of patients also rated their HAE attack symptoms as improved within 12 and 24 hours with KVD900 compared with placebo

Poster Title: Relationship Between PGI-C Scale and Other Patient Reported Outcomes (PROs) in KVD900 Trial in HAE:

In a Phase 2 trial, several PROs were collected to capture the patient experience

60 patients completed treatment for at least one attack (n=113 attacks). PGI-C scoring of "a little better" or higher at two consecutive timepoints had 97% sensitivity for composite visual analogue scale (VAS) and Patient Global Impression of Severity (PGI-S) improvement

Moderate to substantial agreement between PGI-C and the other measures suggests that improvement on PGI-C was clinically significant from the patients' perspective.

(Source: KalVista)

10 November 2021

At the American College of Asthma, Allergy & Immunology (ACAAI) Annual Scientific Meeting, **Ionis Pharmaceuticals, Inc.** presents positive results from the Phase 2 study of its investigational antisense medicine, donidalorsen (formerly IONIS-PKK-LRx). The Phase 2 study results support the clinical profile of donidalorsen as a potential, best-in-class prophylactic treatment for patients with HAE, and underscore Ionis' commitment to advancing antisense technology to target the root cause of diseases.

Topline results of the Phase 2 study show that donidalorsen meets its primary and all secondary endpoints, achieving significant reductions in the number of attacks suffered by patients with HAE compared to placebo. These data support advancing donidalorsen into Phase 3 development, which Ionis plans to initiate this year.

(Source: Ionis)

10 November 2021

KalVista Pharmaceuticals, Inc. provides an update on the clinical trial progress for KVD900 in development for oral on-demand treatment of HAE.

"We had a productive End-of-Phase 2 meeting with the FDA and recently received meeting minutes which confirmed that our Phase 3 trial design, similar to our recent successful Phase 2 trial, is expected to be appropriate to support an NDA submission," says Andrew Crockett, CEO of KalVista. "Our development team is finalizing the Phase 3 trial protocol and preparing for study initiation, and we anticipate patients will be dosed during the first quarter of 2022. KalVista is

well-capitalized, with funding until at least early 2024, which we expect takes us beyond data from both this Phase 3 trial and the ongoing Phase 2 trial of KVD824."

The Phase 3 clinical trial of KVD900 is a crossover design evaluating dose levels of 300 mg and 600 mg KVD900 against placebo. The primary endpoint of this Phase 3 trial is time to beginning of symptom relief. The trial is expected to be conducted at more than 50 sites worldwide and recruit approximately 100 patients, consistent with late stage trials of approved on-demand treatments for HAE. The trial is intended to evaluate all HAE attacks, including laryngeal attacks and breakthrough attacks for patients using prophylaxis. Similar to the Phase 2 trial for which positive data was announced earlier in 2021, patients will administer treatment as soon as they recognize the onset of an attack.

(Source: KalVista)

11 November 2021

Reporting the financial results for the third quarter ended 30 September 2021, **Pharvaris** co-founder and CEO Berndt Modig says:

"This quarter we continued to execute on our robust clinical development strategy as we seek to advance novel treatments for HAE patients that offer efficacy without compromising on convenience. We continue enrolling patients in RAPIDe-1, our Phase 2 on-demand study of PHVS416, and have begun recruiting in CHAPTER-1, our Phase 2 prophylactic study of PHVS416 for the prevention of HAE attacks. We expect to report top-line data, including efficacy and safety, for both studies in 2022. This month, in the PHVS719 program for HAE prophylaxis we also expect to initiate dosing in a Phase 1 pharmacokinetic study designed to assess the bioavailability of extended-release formulation."

Recent Pipeline and Business Highlights and Upcoming Milestones

- Phase 2 on-demand study (RAPIDe-1) of PHVS416 proceeding toward data readout in 2022. In February 2021, Pharvaris announced that dosing had commenced in its Phase 2 clinical study of PHVS416 for the on-demand treatment of HAE attacks. The company reaffirms guidance for reporting topline efficacy and safety data from this study in 2022. Pharvaris is conducting RAPIDe-1 at 33 sites in Canada, Europe, Israel, the UK, and the US.
- Phase 2 prophylactic study (HAE CHAPTER-1) of PHVS416 recruiting. In addition to developing PHVS416 for the on-demand treatment of HAE attacks, the company plans to investigate the therapeutic potential of the PHVS416 formulation of PHA121 for the prophylactic prevention of HAE attacks. In April 2021, Pharvaris announced that an IND was in effect in the US. Patient recruitment has begun and the study is expanding to Canada, Europe, Israel, and the UK. Pharvaris anticipates reporting topline safety and efficacy data from this study in 2022.
- Phase 1 pharmacokinetics study of PHVS719 initiating shortly. PHVS719 is under development as an extended-release formulation of PHA121 intended for use in the prophylactic treatment of HAE. Dosing of a Phase 1 pharmacokinetics study to assess the bioavailability of the extended-release formulation is expected to begin this month.

(Source: Pharvaris)

19 November 2021

Ionis Pharmaceuticals, Inc. initiates OASIS-HAE, the registrational study in the donidalorsen (formerly IONIS-PKK-LRx) Phase 3 clinical program. Donidalorsen is an investigational antisense medicine designed to reduce the production of prekallikrein, which plays a key role in the activation of inflammatory mediators associated with acute attacks of HAE. Donidalorsen uses Ionis' LIgand-Conjugated Antisense, or LICA, technology.

"Initiating the Phase 3 program for donidalorsen moves us one step closer to bringing a potential best-in-class prophylactic treatment to market for people with HAE globally experiencing recurrent painful and severe HAE attacks," says Kenneth Newman, M.D., M.B.A., Ionis' Vice President of Clinical Development and leader of the immunology and pulmonology franchise. "Advancing this program underscores our commitment to the HAE patient community to deliver transformative treatments."

OASIS-HAE is a double-blind, randomized, placebo-controlled registrational study in up to 84 patients with hereditary angioedema, Types 1 and 2. Patients will be randomized to receive monthly or bi-monthly subcutaneous donidalorsen for 25 weeks. Following the placebo-controlled portion of the study, patients may enter the 52-week open-label extension study.

New Phase 2 data recently presented at ACAAI highlighted an overall reduction in moderate to severe attacks, and a reduction in these attacks starting with the second dose. For the final month of the study, all donidalorsen treated patients were attack-free. In this study, donidalorsen was safe and well tolerated.

(Source: Ionis)

23 November 2021

BioCryst Pharmaceuticals, Inc. announces transactions totaling 350 million USD in new funding, among other things supporting additional investment in the global launch of Orladeyo (berotralstat), which is on a trajectory to become the market-leading prophylactic HAE therapy.

"The focused execution of our plan this year, with the successful launch of Orladeyo, has led to further investment from exceptional and committed partners. The infusion of 350 million USD on top of our growing revenue base from Orladeyo enables us to invest now to maximize the value of among other products Orladeyo. We appreciate the confidence our partners are demonstrating in BioCryst with this financing as we continue to bring oral medicines to patients with rare diseases," says Jon Stonehouse, CEO of BioCryst.

(Source: BioCryst)

10 December 2021

KalVista Pharmaceuticals, Inc. provides an operational update and releases financial results for the second fiscal quarter ended 31 October 2021.

"This quarter we made great strides in advancing the two distinct compounds in our oral HAE franchise into later stage trials. We are very pleased with the Phase 3 trial design for KVD900, our candidate for on-demand HAE therapy, where we believe the primary endpoint is both meaningful to patients and was successful in our Phase 2 trial. The KVD824 KOMPLETE Phase 2 protocol for prophylactic treatment of HAE has regulatory approvals in 12 of the 13 countries where the trial will be conducted," says Andrew Crockett, CEO of KalVista. "Importantly, we are funded into at least early 2024, beyond both the KVD900 Phase 3 and KVD824 Phase 2 clinical trial data sets."

(Source: KalVista)

15 December 2021

The first patient has been dosed with NTLA-2002, **Intellia Therapeutics, Inc.**'s in vivo CRISPR/Cas9 genome editing candidate being developed as a single-dose therapy to prevent attacks in people living with HAE. NTLA-2002 is a systemically administered therapy designed to inactivate the target gene kallikrein B1 (KLKB1) to reduce plasma kallikrein activity and thus prevent HAE attacks.

"With the progress of our first-in-human clinical study evaluating NTLA-2002 for people living with HAE, we look forward to beginning clinical testing as we aim to develop a single-dose treatment for these patients", says Intellia President and CEO John Leonard, M.D.

Intellia's multi-national Phase 1/2 study will evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2002 in adults with Type I or Type II HAE. This includes the measurement of kallikrein protein levels and activity as determined by HAE attack rate measures. The Phase 1 portion of the study is an open-label, single-ascending dose design used to identify up to two dose levels of NTLA-2002 that will be further evaluated in the randomized, placebo-controlled Phase 2 portion of the study. This Phase 1/2 study will identify the dose of NTLA-2002 for use in future studies.

(Source: Intellia)

HAEi AROUND THE WORLD

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

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