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Global perspectives:

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96 Member countries

Global perspectives

Global Perspectives
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Cover photo
Participants from 22 countries came together for the first regional conference in the 2023 HAEi Regional Conference APAC – read more on page 16

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HAEi is a global non-profit network of member organizations dedicated to raising awareness of hereditary angioedema (HAE) and improving the lives of people with HAE.

DEAR HAEi FRIENDS,

This edition of *Global Perspectives* offers the customary comprehensive overview of all that is happening in the world of HAE with a special added feature: A detailed summary of the incredibly successful **2023 HAEi Regional Conference APAC** held 17-19 March in Bangkok, Thailand.

Before providing highlights of the magazine's exciting content, however, I am very pleased to announce promotions approved by the HAEi Board of Directors that ensure HAEi has experienced and talented leaders in place to meet the opportunities and challenges facing our global community now and in the future. Effective 1 July 2023:

- **Henrik Balle Boysen** becomes HAEi's President,
- **Fiona Wardman** assumes the role of Executive Vice President Global Advocacy and Chief Diversity Officer,
- **Jørn Schultz-Boysen** will be HAEi's Executive Vice President Global Operations and Chief Compliance Officer, and
- **Michal Rutkowski** steps in as Director, Regional Patient Advocate Program.

I will continue in my role as Chief Executive Officer and have gratefully accepted being appointed to serve as Chairman of the Board of Directors.

2023 HAEi Regional Conference APAC
Over 250 participants from 22 countries, including Key Patient Opinion Leaders (KPOL), people with HAE, caregivers, physicians/scientists, and pharmaceutical company representatives, gathered in Thailand's bustling capital to celebrate the power and flourishing influence of our united HAEi community and "Take Action" for HAE. A special sense of purpose could be felt as HAEi friends learned, interacted, and planned strategies for increasing advocacy efforts in their home countries. I encourage you to read about the highly informative lectures, presentations (by patients and physicians), and overview of HAEi's many free apps and platforms (see pages 16-35).

13th C1-INH Deficiency and Angioedema Workshop
The Co-chairs of this renowned biennial meeting of the global HAE physician and scientific community honored HAEi with their 2023 "For the Patients" award. Board member Sarah Smith Folz accepted the award on behalf of HAEi and delivered a keynote address stressing the "Spirit of Budapest", which acknowledges the foresight of the workshop organizers – Prof. Henriette Farkas and Dr. Lillian Varga – who have always encouraged and welcomed patient participation in the Workshop. Sarah also cut the first piece of a beautifully designed "ceremonial" cake provided to commemorate this prestigious award (see pages 43-45).

HAEi LEAP
As noted in past editions of *Global Perspectives*, HAEi LEAP is our new educational program that helps youngsters learn new skills, develop as individuals, and work on an advocacy project that benefits themselves and their local Member Organization. HAEi's inaugural LEAP class of twenty young people from fifteen countries started with an intensive two-day in-person seminar covering skills such as project and time management, advocacy best practices, and public speaking. I invite you to read more about the amazing program offered to our future advocacy leaders on page 50-53.

While on the subject of future HAEi Advocacy leaders, we are delighted that a member of our Youngsters Advisory Group - Isabel Brunkan - contributed two insightful and must read feature articles: "Climbing Kilimanjaro with a Rare Disease", and "Top 5 Tips for Traveling with a Rare Disease" (see pages 54-63).

Finally, the pages that follow offer additional interesting articles along with regular features that include news from our Regional Patient Advocates, member organizations, and the pharmaceutical industry. Be sure to also check out the pages that describe HAEi's totally free programs and services.

I wish you happy reading and, as always, good health.

Warm regards,

Tony

Anthony J. Castaldo
President and CEO, HAEi

IN THIS ISSUE OF GLOBAL PERSPECTIVES

NEWS FROM HAEi'S REGIONAL PATIENT ADVOCATES

We are almost at the end of the first half of 2023 – and didn't we get here fast!

Over the past few months, I had the privilege of participating in local patient meetings, including several in the Middle East. In this part of the globe (as is the case in all regions of the world), extremely motivated people with HAE are making remarkable progress in (1) building effective advocacy organizations and (2) establishing alliances and close working relationships with expert physicians. It is heartwarming to observe the progress being made on these fundamental actions, which are the key elements that create a clear path to obtaining access to and reimbursement for modern HAE medicines.

I would like to remind everyone that HAEi is ready, willing, and able to help at every step in a Member Organization's (MO) HAE advocacy journey. Our kind, compassionate, and highly experienced Regional Patient Advocate (RPA) team is always available to help MOs grow their membership and enhance the impact of advocacy efforts. We help make achieving these goals more possible by offering a variety of truly amazing tools and services. The article about the successful 2023 HAEi Regional Conference APAC (see pages 16-35) summarizes many of our free platforms and apps.

I am also delighted to welcome Yong Hao Lim from Singapore as our new RPA for Eastern Asia taking over from me effective from 1 June. Initially, Yong Hao will support Singapore, Hong Kong, Indonesia, Malaysia, China, Taiwan, and Sri Lanka.

While it is exciting to have 96 member organizations throughout the globe, there are many countries where we don't have anyone representing people with HAE. Our RPAs are continuously searching in these countries to find that one special person who is willing to invest the time and effort to be part of the global movement to improve the quality of life for people with HAE.

Fiona Wardman
Chief Regional Patient Advocate

For country specific information from the Regional Patient Advocates, please see the section "News From the HAEi Countries Around the World" (from page 64)

MICHAL RUTKOWSKI
CENTRAL EASTERN EUROPE, BENELUX, AND MIDDLE EAST

In this report, I will focus on the Middle East, as so much has been going on there in just a few months.

Indeed, the last three months have been the busiest period since I was appointed Regional Patient Advocate (RPA) for this region. At the same time, it has been an extraordinary period in which we fully reached a larger group of patients and HAE expert physicians in the Middle East. Taking this opportunity, I would like to express my gratitude to Fiona Wardman, the HAEi Chief RPA, and Mohamed Osman, the HAEi Advocacy Facilitator Middle East and North Africa, for their invaluable contribution, commitment and help in organizing HAEi Patient Meetings in Oman, Qatar, Saudi Arabia, and the United Arab Emirates, and Kuwait.

Fruitful cooperation with local Member Organizations allowed HAEi to successfully organize educational and awareness meetings:

- 14 January 2023, in Muscat, Oman
- 8 February 2023, in Doha, Qatar
- 25 February 2023, in Riyadh, Saudi Arabia
- 5 March 2023, in Abu Dhabi, United Arab Emirates
- 13 May 2023, in Kuwait City, Kuwait

A total of 125 attendees participated in the five meetings, and this achievement would not have been possible without the dedication of the local HAE patients, caregivers, and HAE expert physicians. Therefore, I would like to acknowledge this group of amazing people (in the order of the organized meetings):

Dr. Salem Al Tamemi, Dr. Iman Nasr, Dr. Latifa Al-Shekaili, Dr. Salma Al Abri, Dr. Tariq Al Farsi, Maryam Al Balushi, Dr. Mariam Ali Yousuf Al-Nesf, Dr. Hassan Mobayed, Dr. Tayseer Ibrahim, Dr. Ramzy Ali, Ameera Elawad, Dr. Hassan Alrayes, Dr. Rand Arnaout, Ahmad Aleliwi, Dr. Mohamed Abuzakouk, Dr. Ravi Gutta, Shradha Singhania, Dr. Mona Al Ahmad, and Mubarak Al Ajmi.

Images from meeting in Muscat, Oman

Images from meeting in Abu Dhabi, United Arab Emirates

Additionally, HAEi has also participated in important scientific conferences:

- The 2nd Qatar Allergy and Immunology Conference, and
- The 2nd Emirates Allergy & Clinical Immunology Conference.

Here HAEi had the opportunity to catch up with regional expert physicians and discuss the potential collaboration in different scientific projects. We are looking forward to it very much. Hopefully, we will be able to share specific details with you in the next edition of Global Perspectives.

Actually, it doesn't stop here as HAEi keeps working on more local patient meetings in the Middle East to be held in 2023. It is the responsibility of the global organization to reach all patients regardless of the region and help them to advocate for themselves.

The start of this year was also busy for all members of the HAEi team, including the RPAs, with preparing for the 2023 HAEi Regional Conference EMEA (Europe, Middle East, and Africa) that will be held 1-3 September 2023 in Munich, Germany. I have been working closely with Member Organizations in my region to help them with the travel grant application and the registration process.

Images from meeting in Doha, Qatar

I am delighted to inform you that the following countries I am responsible for will be participating in this event (in alphabetic order): Armenia, Belgium, the Czech Republic, Egypt, Estonia, Georgia, Hungary, Iran, Iraq, Jordan, Kazakhstan, Latvia, Lebanon, Lithuania, the Netherlands, Oman, Poland, Qatar, Saudi Arabia, Slovakia, Ukraine, and the United Arab Emirates.

Finally, I am happy to share with you that more and more local Member Organizations are using HAEi resources. We just finalized the HAEi Emergency Room Poster in Czech and Persian, and I have been working on a children's book translation with HAE Junior Czech Republic. Also, HAE Poland is about to release the latest edition of The Brady Club Activity Book.

This being the first issue of the Global Perspectives, I'd like to welcome you to the New Year! I wish you all that 2023 will become a year of outstanding successes and achievements in your private and professional life. But most of all, that the HAE global family will continue advocacy successes in accelerating the diagnosis process, gaining access to and reimbursement for HAE modern therapies, and delivering HAEi projects and resources to our patients' community.

Images from meeting in Riyadh, Saudi Arabia

Image from meeting in Kuwait City, Kuwait

May is always a special month with the **hae day :-)** celebrations. I would like to share with you two examples:

During the meeting in Kuwait held on 13 May, I was privileged to celebrate **hae day :-)** together with the local community. Even though it was the first such kind of meeting, it was so amazing to see the patient interactions, willingness to share personal experiences and different personal HAE journeys. So many questions were raised, and many answers were given.

On 6 May, the HAE Patient Day was organized by the HAE community in Belgium. The goal was to reconnect Belgian patients and celebrate **hae day :-)** 2023. There were 41 participants (including 11 online) to follow presentations of Belgium HAE expert physicians and patients.

NATASA ANGJELESKA
SOUTH EASTERN EUROPE

Most of the focus at the beginning of the year was on the announcement of the 2023 HAEi Regional Conference EMEA and applications for travel grants for interested participants. We have a relatively large group of participants from South Eastern Europe that have applied for and received travel grants, and we are very excited about the opportunity to meet in person again in Munich, Germany, this year.

Many of the HAEi resources are used by the Member Organizations in South Eastern Europe, but there is always another opportunity. For example, HAE Albania and HAE Croatia have translated the new booklet "Understanding HAE" into their local languages and plan to use it in their upcoming activities. HAE Turkey has translated the HAE poster as well as HAE information cards into Turkish, which they will use for their posts and communication on social media. And as for HAE TrackR, it is now available in Slovenian – just as is the case with the Emergency Room poster. Some updates regarding the use of HAEi Connect have been provided to HAE Turkey, and HAE Greece has initiated the use of this tool for their organization as well.

HAE Albania consulted with me on their plan to collaborate with the Association of Allergologists in Albania for the register for HAE patients and some joint informative sessions on HAE.

I provided support to HAE Greece for the patient meeting in the country in which I participated and presented about the HAEi network, the decentralized approach in our operations as well as the many resources and tools that are available for patient groups and organizations.

I have had meetings with HAE Bosnia and Herzegovina and discussed their initiative to register the patient organization and considered all the options and needs to start the process of registration. I had similar discussions with patient representatives in Slovenia, and I hope to be able to assist them in the registration for their patient organization as well.

I have been informed that the Kosovo expert body has accepted the plan for the treatment of rare diseases, including HAE. The physician from Kosovo expects to have approved modern therapy this year.

Furthermore, I have held meetings with several pharma representatives active in South Eastern Europe upon their request or my initiative.

FERNANDA DE OLIVEIRA MARTINS
SOUTH AMERICA AND MEXICO

First of all, I would like to welcome José Ignacio Contreras Silva as the leader of the new Member Organization in Chile. In Spanish, the name is Corporación Angioedema Hereditario Chile – globally known as HAE Chile. The new group is getting to know the HAEi tools and resources and will soon be able to implement a website as well as other support tools such as the Emergency Card. For more information, please visit https://haei.org/hae-member-countries/chile.

The Member Organizations in my region have been busy with events and activities in celebration of the global Rare Disease Day. Together, we are helping to raise awareness of HAE. Congratulations to all the Member Organizations in the region!

We are very proud to have eight participants from South America and Mexico among the 20 total young people participating in the LEAP program. They are the future of the HAE advocacy work, and we very much congratulate them for this achievement.

Furthermore, I would like to mention that the region has been represented at patient meetings of pharma companies such as Takeda and Pharvaris.

PATRICIA KARANI
SUB SAHARA AFRICA

A new HAE patient has been identified in Mozambique. We are working with doctors in the country to ensure that she receives the best care and also make sure that medications are available for her.

In Sudan, we have a new physician contact, Dr. Ahmed Seri Ibrahim, who is working in collaboration with Prof. Nahla Erwa in diagnosing patients with HAE in the country. Dr. Ahmed is a clinical immunologist specialist based at the Royal Care International Hospital in Khartoum and takes care of HAE patients in the facility.

JAVIER SANTANA
CENTRAL AMERICA AND CARIBBEAN

During recent months, many of the patient groups in the Central America and Caribbean region have worked hard to gain access to HAE drugs in their countries. Not least, patients from Costa Rica and Panama have held multiple meetings with government representatives seeking to finally achieve the acquisition of treatments.

Due to the behavior of the government leaders of various countries, a new strategy has been promoted in the Central America and Caribbean region for representatives and legislators to promote laws aimed at protecting people with HAE and guaranteeing the purchase of medicines for patients. Leaders of some patient groups have acquired laws from other countries around the world to share with representatives of their legislatures to draft and create laws in favor of HAE and direct governments to protect the right to receive medicines and fair treatment for people with HAE.

New information has emerged in the region about the distribution of medications for HAE in some countries. Representatives of many companies that distribute HAE medicines in Latin America have notified that, for the first time, efforts to bring the drugs to some of this region's countries have begun.

MARIA FERRON
THE MEDITERRANEAN, NORTH AFRICA AND THE BRITISH ISLES

2023 has started with a lot of energy around the world.

The first registration steps for the 2023 HAEi Regional Conference EMEA took place during February and March, and I have been supporting all the queries and questions raised by the Member Organizations.

Due to the recent appointment of Mohamed Osman as HAEi Advocacy Facilitator for the Middle East and North Africa region, we are performing introduction calls to all the North African countries.

JØRN SCHULTZ-BOYSEN
NORDICS, GERMANY, AUSTRIA, SWITZERLAND, AND ISRAEL

Following the 2022 HAEi Global Leadership Workshop, there has been a lot of dialogue around many of the items and offerings that were presented in Frankfurt, Germany. Not least around HAE TrackR, the app that enables patients to take control of their HAE by registering acute and prophylactic treatments, HAEi Connect, the member database that is offered to the Member Organizations, and HAE Companion, the pocket-size travel partner offered as an app. It has been fantastic to talk about these and other offerings and how they can benefit the Member Organizations as well as the patients and caregivers in the different countries.

We are still working on putting together the Regional Medical Advisory Panel. We have several participants confirmed, and they are already feeding in very valuable information and ideas. Other countries have not yet been able to appoint a member of the panel. We are looking forward to continuing the dialogue with the panel to benefit even more from the collaboration.

Similarly, feedback from the Regional Advisory Groups has also come in from many of the countries in the region. This will enable us to benefit from the experience of the local organizations and to use the ideas in the tools and services provided by HAEi.

As mentioned, HAE TrackR continues to be a great tool and is now available in 33 languages – several of which are spoken in my region (Danish, Finnish, French, German, Norwegian, and Swedish). The HAE TrackR app is easy to use – and a safe way to store your data – and it will help the patient and physician in their dialogue on current and future treatment options. I can only urge everyone to check it out – and to start using it! New functionality has recently been released, not least one to remind you to take your prophylactic treatment and an improved reporting to share your treatment data with your physician.

The HAE Companion app deserves another mention. It is available in both Apple App Store and Google Play, and truly is a great tool to use. This app will help you find local HAE treatment centers and directions hereto, as well as you will find the Emergency Cards available in more than 80 countries. You can download the Emergency Card in the local language of the country you are visiting to your smartphone, e.g., to Apple's Wallet and Android's Passbook. A great help when you are traveling to a country to have the Emergency Cards ready in the local languages. Or to have the Emergency Card in your own language available on your smartphone when being at home.

Also, we are working towards the 2023 HAEi Regional Conference EMEA taking place in Munich, Germany, 1-3 September. This conference is intended for patients and caregivers in the European, Middle Eastern, and African regions, and it will be great to gather patients and caregivers from so many countries again.

During the months of April and May, we were once again celebrating the **hae day :-)** awareness day. It has been exciting to see all the fun activities patients, caregivers, and others have carried out to track their 'steps' on haeday.org.

FIONA WARDMAN
ASIA PACIFIC AND SOUTH AFRICA

The 2023 HAEi Regional Conference APAC in Bangkok, Thailand, was a success bringing together over 250 HAE patients, family members, physicians, and pharmaceutical companies to learn more about each other and HAE, to talk about advocacy, the importance of working together and the needs for the region.

I was pleased to see so many familiar faces and to meet new people I hadn't yet had the opportunity to get together with.

The Regional Conference brought together people with a shared interest and commitment, motivation, and spirit from Bangladesh, China, Hong Kong, Indonesia, India, Japan, Taiwan, South Korea, Malaysia, Pakistan, Nepal, Thailand, Philippines, Australia, and New Zealand.

I'm excited to see how our working together in this region will improve the quality of life for HAE patients.

Nepal is not yet a member of HAEi, but I am happy to report that Dr. Dharmagat Bhattarai from the Om Hospital & Research Center in Kathmandu participated in the Bangkok conference. Indeed, Dr. Bhattarai, who is a pediatric immunologist and rheumatologist, is the first HAE-knowledgeable physician we have registered in Nepal, where there are now five diagnosed patients. They can, at this stage, only be treated with danazol or tranexamic acid. Information on the hospital can be found at https://omhospitalnepal.com.

Vietnam is another country still waiting to become a member of the HAEi family. Here we have registered the Allergy and Clinical Immunology Center of the Vinmec International Hospital Times City in Hanoi as the first HAE-knowledgeable hospital. For further information on the hospital, please see https://www.vinmec.com/en/benh-vien-da-khoa-quoc-te-vinmec-times-city-17265/hoi-suc-cap-cuu.


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HAEi REGIONAL CONFERENCE APAC BANGKOK 17-19 MAR 2023

Take Action!

HAEi's global advocacy philosophy – think globally, act regionally – was transformed into reality on 17-18 March at the 2023 HAEi Regional Conference APAC held in Bangkok, Thailand. Over 250 participants from 22 countries attended, including people with HAE, caregivers, physicians/scientists, and pharmaceutical company representatives.

Enthusiasm and motivation for "Taking Action" could be felt throughout the conference as participants learned, interacted, and made plans to ramp up advocacy efforts in their home countries. Below are highlights from the various sessions held during this highly successful meeting – the first of three HAEi Regional Conferences to be held over just 12 months.

Conference Welcome

The HAEi Leadership Team – President and Chief Executive Officer Anthony J. Castaldo, Executive Vice President and Chief Operating Officer Henrik Balle Boysen, and Chief Regional Patient Advocate Fiona Wardman – opened the conference with a warm welcome. The team invited delegates to spend the next two days meeting others in the region to share experiences, take advantage of the unique learning opportunities, and have fun!

Henrik went on to note that the conference's theme was "Take Action". He explained that the sessions were structured to inspire new and creative approaches to HAE advocacy and engagement that can be applied in everyone's home country. Tony recommended that all HAEi friends seek out fellow advocates, medical professionals, and industry attendees they don't already know.

Fiona noted that almost all the region's Member Organizations were in attendance. She encouraged representatives from Nepal and Vietnam to continue their efforts to form an HAE group and congratulated the efforts underway to identify patients and physicians in Cambodia, Laos, Papua New Guinea, and Sri Lanka.

The three leaders then took turns expressing their individual hopes that all attendees would be inspired by what they learn and take action to translate that knowledge and enthusiasm into efforts that improve the lives of HAE patients in their local communities.

Fun fact about Bangkok

The official title of Thailand's capital has 168 letters earning it a spot in Guinness Book of World Records

HAEi Regional Conference APAC Keynote Address

Dr. Philip Li from Hong Kong University delivered a highly informative talk to open the conference and addressed three main topics: The HAE Experience in Hong Kong, A Call to Arms, and The 4A's to Tackling HAE in Asia Pacific.

The HAE Experience in Hong Kong

Dr. Li began his presentation by describing the Hong Kong success story that required sustained efforts to overcome limited knowledge of HAE and the absence of support from the government and hospitals. The goal of winning access to HAE medicines resulted from the combined efforts of Dr. Li and colleagues, a group of patients who worked to form a Hong Kong HAE group, and support from HAEi. The breakthrough happened in 2019 when Queen Mary Hospital established an HAE treatment Consensus that:

- Affirmed that every patient should have access to C1 esterase inhibitor therapy,
- Established a treatment algorithm and patient management guidelines,
- Promoted physician and patient awareness/education, and
- Insisted on comprehensive family screening.

Dr. Li shared the bottom line result of patient-physician collaboration and HAEi support – people with HAE in Hong Kong can now access medicines. C1-INH is now subsidized, and icatibant is available with "means-tested" financial support. Implementation of family screening has almost quadrupled the number of identified patients in Hong Kong from .16 to .6 per 100,000 of the population. Dr. Li emphasized the need

"A really nice conference – informative and with good networking. Also, nice to share stories about the HAE experience. Hopefully to inspire others and increase awareness."

– Rudy Purwono, Indonesia

"Nice to meet you, family. Thank you to the sponsors in this event, and thank you for letting me know that we are not alone."

– Nakwan Rattanamongkol, Thailand


17-19 MAR 2023


APAC
BANGKOK

for ongoing family screening because the current HAE population is approximately three times lower than the estimates cited in the literature.

A Call to Arms

Turning to the situation in Asia Pacific, Dr. Li called for continued and even enhanced international collaboration in the region to address issues such as:

- Epidemiology/prevalence of HAE among Asians,
- Unique clinical features among HAE in the Asia Pacific,
- Diagnostic delay and low physician awareness,
- Frequency of laryngeal/abdominal attacks,
- Rates of intubation/ICU admission and hospitalization,
- Genetic or genuine clinical differences vs. referral/ascertainment bias,
- Priorities for HAE diagnosis and management,
- Enhanced public and physician awareness, and
- Referral and diagnostic pathways.

A study Dr. Li co-authored entitled, *Epidemiology, Management, and Treatment Access of Hereditary Angioedema in the Asia Pacific Region: Outcomes from an International Survey*, reveals an important step in international cooperation among physicians. Published in the April edition of the prestigious Journal of Allergy and Clinical Immunology In Practice, the authors concluded that,

"Hereditary angioedema in the AP differs from that in Western countries. Hereditary angioedema-specific medications were registered in only a minority of countries and territories, but those with patient support groups or regional guidelines were more likely to have better access. Asia Pacific-specific consensus and guidelines are lacking and urgently needed."

Dr. Li emphasized that raising diagnosis rates will require a cooperative effort to make sure all countries in the region have the appropriate equipment and knowledge for testing. He stressed that most patients in the region do not have access to modern HAE medicines. On-demand treatment is only available in half of the region's countries – Australia, China, Hong Kong, Japan, South Korea, Taiwan, and Thailand. Moreover, prophylactic treatment is available only in Australia, China, Japan, and Taiwan.

The 4A's to Tackling HAE in Asia Pacific

In summarizing his message, Dr. Li pointed to four A's that will lead to further success for HAE in the Asia Pacific:

- Awareness through public and physician education,
- Access to HAE-specific medications,
- Advocacy by patient organizations,
- Alliances with HAEi and the APAACI--the Asia Pacific Association for Allergy, Asthma, and Clinical Immunology.

Dr. Li closed his presentation by challenging participants to be energized by the motivation and momentum generated at the 2023 HAEi Regional Conference APAC. He then called for all parties to work with HAEi in a concerted effort aimed at (1) organizing physicians and patient advocates and (2) marshaling the expertise and resources to win access to HAE medicines throughout the region.

He ended his presentation by reminding the audience that in APAC, "We have the biggest voice in the world, as we represent half of it."

Patient and Caregiver Track

Fiona opened the patient and caregiver panel discussion with some interesting statistics:

- Five out of the top ten most populous countries in the world are in the region, and they are: China (1.41 billion), India (1.39 billion), Indonesia (276 million), Pakistan (225 million), and Bangladesh (166 million).
- The region has another four countries that are in the world's top 20 when it comes to population: Japan (125 million), the Philippines (111 million), Vietnam (98 million), and Thailand 69 million).

If one uses the most widely cited statistic regarding HAE prevalence – 1 in 50,000 people – there could be more than 400,000 people with HAE in the Asia Pacific region.

Consistent with the conference theme of Take Action, Fiona quoted the physicist, chemist, and two-time Nobel Prize laureate Marie Curie who said,

"Life is not easy for any of us. But what of that? We must have perseverance and, above all, confidence in ourselves. We must believe that we are gifted with something and that this thing must be attained."

Panel Members then provided an overview of what is going on in their countries.

Australia & New Zealand, Olivia Worthington

We urge HAE patients to be more involved in advocating for new treatments to be funded and available. We need patient voices and lived experiences to be heard by the funding bodies. We absolutely cannot be complacent when it comes to having treatments. We must continue to work together to ensure that future generations can access the newest therapies. Also, we are working to ensure that every patient knows that there are new options – and that it is important to take part in trials because, without trials, there are no new treatments.

Hong Kong, Sandy Chan

Unfortunately, there is a taboo in Chinese culture toward family screening. However, we have built a very strong patient community, obtained our doctors' support, and achieved registration of the first acute attack medicine in 2022. We hope HAE patients will hold each other together while we wait for new medicines and that the price of medicines will get much lower very soon.

India, Shaibal Guha

Uniting HAE patients into a strong group is still the biggest challenge. We don't have a system of a national registry of patients or a system of referral from general practitioners to specialists, so it's very difficult to trace the patients. When we started in the pre-WhatsApp era, we added patients one by one into the group, and we now have about 200+ patients in the WhatsApp group called 'HAE Bravehearts'. It's a very cohesive group: Every day, you'll find members sharing their sorrows and joys, and every other person is always eager to help others. However, much work needs to be done. When you consider the country's population, there must be about 20,000 to 30,000 patients, so 200+ is just the tip of the iceberg.

Indonesia, Rudy Purwono

No doubt there is strength in numbers, so we work on creating more contacts and raising our voices together. We are learning from what others are doing to ensure no undiagnosed or misdiagnosed patients. Hopefully, we will gather more members and have many hospitals and doctors aware of HAE.

Japan, Professor Beverly Yamamoto

Setting incremental goals and taking a gradual approach to building a patient organization is important. Consistently focusing on incremental goals, in the aggregate, can result in drastic changes. Growing HAE Japan into a strong organization we have over a relatively short period significantly improved the HAE treatment environment. We are almost on par with some leaders, like the US and the European countries, regarding the number and quality of HAE treatments available. In this context, gathering data is very important when talking to the authorities. Data is almighty if it is the right data.

Pakistan, Shakeel Afridi

HAE Pakistan is working on establishing an HAE care center and a range of HAE-knowledgeable hospitals all over the country. We also want to be able to offer gene therapy testing for each patient who wants to test their children and family. In the meantime, using the HAE Emergency Card is essential, as it will help you in urgent situations.

The Philippines, Krizzia Lavone Ramos Alferez

While we are still working on establishing an official HAE group, some concerned people have communicated with us through our website. We have been able to get information about the disease to them, and we have encouraged anyone else who has experienced similar symptoms to HAE to see a specialist and get tested. There are tests available in the country for the diagnosis of HAE. In the Philippines, plasma transfusion is the only treatment for acute and major attacks, while danazol tablets are used for prophylaxis. Unfortunately, danazol is no longer available, so we must buy it from another country.

Singapore, Lim Tong Hao

Whether you have had HAE for years or have recently been diagnosed, you should share your experiences. Sharing your story can raise awareness and inspire others going through a similar journey. Together we can tackle our challenges and build a community of support and understanding. Once you have a strong patient group, it is far easier to get things done. With the help of the Rare Disease Society of Singapore, we have shared a patient story on national TV. In addition, we have teamed up with doctors to share a survey with their patients and family members so we can get to know them better and find out what challenges they are facing. Our goal is to work together to come up with solutions that will be helpful to everyone.

Taiwan, Hsin-Fang 'Frank' Tseng

Thankfully, more and more people and doctors know about HAE. However, the number of confirmed HAE families in Taiwan is much smaller than in other regions, so there must be many people who have yet to be diagnosed. Remember to pay more attention to whether people around you have similar symptoms, as your kindness can save a patient or a family.

Thailand, Suchitta Kengyanyagarn

Patients and caregivers should join HAE Thailand as givers because we are not burdened. We are strong; we are fighters; we are special. All the pain we have been through – someone lost a dream, someone lost their job, someone lost the people they loved the most. This is an excellent opportunity: We have us, we have our medical people, we have HAE partners, and we have HAEi. Together we are stronger. We can stop the pain and give a better future for our children.

Asked about their number one priority for future HAE work, the panelists mentioned:

- Bringing those patients forward who hide their faces (Pakistan),
- Finding more patients and gathering data (Singapore),
- Getting funding (Hong Kong),
- Having access to medication (Indonesia),
- Identifying the remaining patients (Japan),
- Increasing awareness among doctors as that will increase the number of patients (India and Taiwan),
- Making sure that all patients have access to treatment (the Philippines and Thailand), and
- supporting patients (Australia & New Zealand).

Participants then watched videos recorded by HAEi friends from recordings by Representatives from Afghanistan, Bangladesh, China, and South Korea.

Afghanistan

Please support us because we don't have any treatment facilities, and HAE patients are struggling. We must travel to neighboring countries for HAE tests, and that is expensive. Also, visa facilities are currently unavailable in Afghanistan, so please support and help us.

Bangladesh

We don't have facilities like diagnosis and medications, so our message to doctors, patients, and healthcare professionals in Bangladesh is this: please come forward and raise your hand to help people with HAE.

China

HAE emergency drugs and preventive drugs have been introduced to China in a short period. Now the drugs are covered by national medical insurance, and the quality of life of Chinese patients will be significantly improved. We originally had only one HAE specialist in

Beijing. Still, we have doctors working on HAE in major cities nationwide, making it more convenient for us to get medical treatment and confirm the diagnosis. In addition, we hope to have more opportunities to communicate with patient groups from different countries. This way, we aim to have more experience in HAE medication and knowledge of mental health, and we also hope to travel abroad and get help from HAE doctors overseas.

South Korea

HAE Korea has a short history but has been registered as a nonprofit foundation. In addition, the treatment environment for patients with severe symptoms has been improved by raising the prescription of icatibant from one to two at a time. We will continue to try to improve patients' treatment and psychological environments. We are delivering our voices to government agencies with the help of many people so we can get insurance benefits for the long-term preventive medicine we want. To do that, more patients must join us to raise our voices.

Fiona closed the session by reemphasizing the conference theme and challenging the audience to 'Take Action' and make things happen in their countries.

HAEi Patient Resources

Henrik and Tony took the stage to provide an overview of the numerous free resources HAEi offers its Member Organizations. Due to space limitations, we refer readers to our website, haei.org, for detailed descriptions of HAEI's incredibly useful programs and services that include:

HAE Companion – provides users with an easy way to store HAEi-designed emergency cards available in 84 countries. In addition, users can access contact information and directions to the closest ACARE Center, knowledgeable HAE physician, or hospital. The app is available on both Apple's App Store and Google Play.

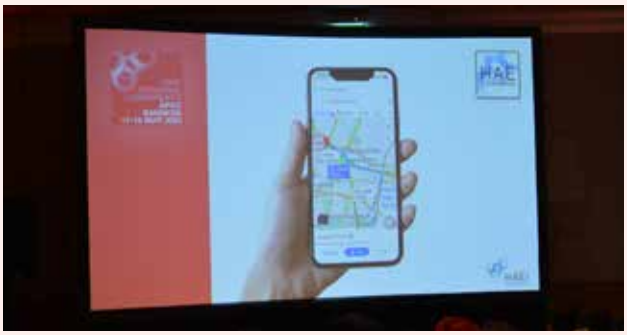
HAE TrackR – available in 35 languages (with Thai recently added), this advanced app makes it easy for patients to keep a record of their attacks, treatments, and prophylactic treatments, and it allows the patients to set reminders for their prophylactic treatments. The app is available on both Apple's App Store and Google Play.

HAEi Connect – a regulatory-compliant, sophisticated, yet user-friendly patient membership database platform that puts highly relevant information at the fingertips of Member Organizations. HAEi Connect eliminates the need for confusing and easy-to-misplace paper files and Excel spreadsheets. The platform provides a simple online process for new members to join and enables thorough and granular analysis of membership demographics through an easy-to-use graphical interface. It also allows timely delivery of newsletters, surveys, and general correspondence. HAEi Connect fully complies with EU-GDPR data protection.

HAEi Advocacy Academy – an online, cloud-based virtual training platform featuring comprehensive educational modules on disease-related information and grassroots advocacy skills. The HAEi Advocacy Academy is available to anyone who wants to sharpen their advocacy proficiency.

Emergency Room Posters and the **Understanding HAE Guide** were also mentioned as great tools to raise awareness of HAE.

All technology platforms, resources, and services provided by HAEi are carefully designed to fit the unique needs of our global community.



Raising HAE Awareness in APAC

Fiona Wardman and Rachel Annals were the next speakers and delivered a great talk on 'Raising HAE Awareness in APAC'.

Fiona and Rachel encouraged the audience to use social media to share their stories, make connections, and establish collaborative relationships. They pointed to the power of distributing flyers and posters, writing articles for the HAEi magazine Global Perspectives, attending meetings, and taking part in the annual **hae day :-)** awareness activities, and completing HAEi Advocacy Academy courses.

Rachel reminded the audience that "Knowledge is Power". Contact your government officials and keep them up to date. Keep reminding them that you are there and need them to make decisions for the benefit of people with HAE."

Fiona added, "Persistence will get you there, while consistency will keep you there. Remember to speak to the media – and use your youngsters to spread the word via the social media channels as they are often far better at it."

The Path to Success in APAC – Take Action!

Tony and Fiona then took the stage to discuss, 'The Path to Success in APAC – Take Action!' They described the study methodologies that HAEi offers to its member organizations. These studies are designed to provide scientifically collected data that will give people with HAE a "seat at the table" when government officials consider granting access to and reimbursement for HAE medicines and include HAEi's

- Heat Map Survey,
- Baseline Burden of Illness Study, and
- Pharmacoeconomic, Socioeconomic, and Quality of Life Assessment.

While individual stories are vital, government officials responsible for making healthcare budget decisions demand data to support access and reimbursement for HAE medicines.

The '**Heat Map Survey**' identifies clusters of people with chronic swelling in countries where few, if any, are diagnosed with HAE. **HAEi's Baseline Burden of Illness Survey** provides valuable data regarding the number and types of attacks people are experiencing, emergency room and hospital visits, impact on work, school, and family life, and overall quality of life. **The Pharmacoeconomic, Socioeconomic, and Quality of Life Assessment** targets countries that already reimburse HAE medications and is designed to measure the positive economic, social, and quality of life improvements that result from access to modern therapies.

Youngsters Track

For an hour on Friday night and for Saturday morning, the HAE youngsters – patients and caregivers aged 12 to 25 – broke away from the main track to concentrate on topics for their specific age group. HAEi Youngsters Community Coordinator Nevena Tsutsumanova took the participants through items such as 'This is the HAEi Youngsters Community and How to Get Involved', 'Face2Face with an HAE Expert', 'Understanding HAE', and 'Shared Story Telling'.

Please see pages 34-35 for the coverage of the Youngsters track.

Scientific Track

For an hour on Friday night and for Saturday morning, our healthcare professional and scientific community participated in a dedicated Scientific Track. This track included a poster session, case study discussion, plenary talks and oral presentations selected by our Scientific Committee from the abstracts submitted for consideration.

Please see pages 30-33 for coverage of the Scientific track.


The Latest Developments in
HAE Science and Therapies


HAE TrackR


HAEI
REGIONAL
CONFERENCE
APAC
BANGKOK
17-19 MAR 2023


Introduction to HAE
10 things patients
need to know
REGIONAL
CONFERENCE
APAC
BANGKOK

Plenary Session with All Participants

After lunch on Saturday, all conference attendees gathered for a talk by Prof. Bruce L. Zuraw, Director of the University of California San Diego, United States. Professor Zuraw addressed **Ten Important Questions Often Asked About HAE**:

1. Why me?

HAE is a genetic condition, and in most cases, one of your parents has a mutation that causes HAE. There are patients with HAE that have no family history. This group had a spontaneous gene mutation that causes HAE at conception and can pass the condition to their offspring.

2. Am I in Danger?

Untreated patients have about two attacks per month, but swelling can occur more or less frequently. Swelling affecting the airway can be fatal if not appropriately treated. Abdominal attacks are painful and debilitating. Untreated HAE has a significantly negative effect on the patients' lives, affecting school, work, and social activities. HAE can cause a significant psychological burden.

3. What about my Family?

Many HAE patients have family members who have died from laryngeal swellings. Proper diagnosis is critical for effective management. All family members should be tested for HAE.

4. What Causes Attacks?

A complex biological process in the blood that ultimately causes the production of bradykinin – a peptide that causes the capillaries to leak fluid into body tissues. Triggers include stress, physical trauma, surgical procedures, infections, medications such as a blood pressure medicine called ACE inhibitors, and estrogen used in women for birth control and hormone replacement therapy related to menopause.

5. Can I Treat Attacks?

There is a variety of effective treatments approved for treating HAE attacks, and they include C1 inhibitor IV injections (recombinant and plasma-derived) and icatibant. Attacks affecting the airway are emergencies requiring immediate medical care to provide treatment and protect the airway. It is crucial everyone knows that antihistamines, corticosteroids (such as prednisone), and epinephrine do not work and should not be used to treat HAE attacks.

6. Can I Prevent Attacks?

There are a variety of therapies to prevent HAE attacks. First-line therapies include Plasma-derived C1 inhibitor concentrate that can be injected subcutaneously or IV. Lanadelumab is a kallikrein inhibitor delivered by subcutaneous injection, and berotralstat is another kallikrein inhibitor in pill form. Second-line therapies include androgens (danazol) and antifibrinolytics (tranexamic acid). There is no formula for who should be prescribed preventative treatment. The decision must be individualized based on improving the quality of life.

7. How Do I Find a Doctor?

Very few doctors are HAE experts. You want a doctor who is willing to learn about HAE, work with an HAE expert, and develop a patient-physician partnership with you that includes shared decision-making. Every patient should have an HAE management plan that includes extensive patient education and consideration of all treatment options, coordination of care, and treatment logistics.

8. What if I get pregnant?

HAE does not affect fertility nor cause spontaneous abortion or negative pregnancy outcomes. The impact of pregnancy on HAE is highly variable – attacks may increase, decrease, or stay the same. Attacks are very rare during delivery but may increase in the weeks following delivery. Depression is not uncommon after delivery. C1 Inhibitor is the medication of choice during pregnancy.

9. Will My Life Ever Be Normal?

The goal of HAE treatment is to allow leading a normal life free from symptoms and medicine-related side effects. Reaching this goal requires a team effort between the doctor and patient that includes education and a treatment and action plan. Eight treatments are approved by regulatory authorities, and the future looks bright with nine potential therapies in various stages of clinical trials.

10. Who Can I Turn to for Help?

HAEi works every day to make sure your voice is heard. Building networks of physicians and patient organizations is key, as is the further development of clinical registries and research consortiums.

Topics Raised by APAC Member Organizations

The Scientific Committee members joining us in Bangkok each gave a presentation covering a topic raised by our community in APAC.

Before the talks began, Dr. Hiroshi Chantaphakul, Co-Chair of the Scientific Committee, presented the Scientific Track Young Researcher Award. The award is granted to an abstract authored by – either solely or as part of a team – a young investigator or researcher deemed to be of the highest quality by the conference Scientific Committee. Unfortunately, the recipient, Dr. Zeijan Zhang of China, could not attend the meeting. Dr. Zhang was announced as the award winner during the Scientific Track, and Mr. Xiaogang Qi of HAE China received the award on her behalf during the main program.

Dr. Chantaphakul then discussed laryngeal edema in HAE, its symptoms, the importance of their recognition, for example, >50% of patients report prodromal symptoms like a rash or muscle aches before this type of attack, and how it can be treated. His take-home message for all people with HAE was that these attacks should be treated regardless of location or severity.

In the next talk, Dr. Narissara Suratannon discussed access to medications, particularly androgens, and FFP, two more commonly available in the Asia Pacific region. She gave an overview of both types of medicine, how they can most effectively be used to manage and treat HAE, and some of the concerns and practicalities of using these medicines. Finally, she closed her talk with a call for more access to pathway-targeted therapies with high efficacy and good safety profiles in the Asia Pacific region.

Dr. Philip Li stressed that 'you need your doctors, but your doctors also need you' as part of his talk on the importance of doctors and patients working together. He outlined what doctors can do for patients regarding diagnosis, advice, treatment, and family planning in the context of the information provided by patients and the services and support that society offers. Dr. Li stressed the need for individuals, families, patient groups, and society to work together to improve awareness, access, advocate, and form alliances in the Asia Pacific region. In his words: "The engine of change is with you."

The next topic covered was HAE in children and the importance of family screening. In this talk, Dr. Ankur Jindal gave an overview of how HAE in children differs from adults covering diagnosis and management, emphasizing that 'Children with HAE are not small adults.' He then discussed the how and why of family screening and stressed the importance of family members of patients with HAE being screened; grandparents, parents, siblings, children, and grandchildren to improve the lives of those potentially living with undiagnosed HAE.

Dr. Hilary Longhurst closed this session by posing the question, 'What's good about taking part in research?' She then covered a compelling list of benefits that included:

- The potential to access to study medicine until regulatory authorities approve it
- Being seen by an HAE expert, and
- Helping to move science forward by getting new and better medicines approved
- Many people in clinical trials cite feeling good about giving something back and contributing to an important cause.

The Latest Developments in HAE Science and Therapies

Professor Marc Riedl from the University of California San Diego, United States, then took the stage to provide an update on developments that affect the HAEi Community.

Professor Riedl began his talk by emphasizing the need for continued efforts to raise awareness of HAE among physicians and patients. He pointed out that making the HAE diagnosis requires people to have enough knowledge to think about it when trying to figure out the cause of a chronic swelling condition.

Moving on to describe new treatments on the horizon that are at various stages of clinical development, Professor Riedl discussed details regarding:

- Four medicines for HAE prophylaxis delivered by subcutaneous injection
  - CSL Behring's Garadacimab, phase 3,
  - Ionis Pharmaceuticals' Donidalorsen, phase 3
  - Astria Therapeutic's Star 0215, phase 1B/2, and
  - ADARx Pharmaceuticals' ADX 324, phase 1.
- Three orally administered medicines
  - Kalvista, sebetralstat for on-demand treatment, phase 3
  - Pharvaris
- PHVS 416 for both on-demand and prophylaxis, Phase 2
- PHVS719, an extended-release tablet for prophylaxis, Phase 1
- Two gene therapy treatments
  - Intellia Therapeutics' NTLA 2002, phase 1/2
  - BioMarin Pharmaceuticals' BMN 331, phase 1/2.

Prof. Riedl stressed the need for continued clinical development efforts and answered the fundamental question of "Why Does it Matter" by sharing a quote from the HAE Patient-Focused Drug Development meeting held at the FDA several years ago:

"The unpredictability of the disease is stressful, and it limits educational and employment opportunities as well as disrupts social activities, and has a negative impact on family relationships. A higher frequency of attacks is associated with a higher burden of disease, just as there can be an impact on the patient's quality of life in between episodes. Despite advances, the burden of disease remains high."

Dr. Riedl closed his talk by addressing what he would like to see as a model for patient/physician interactions. He believes HAE management plans should be based on an open discussion with the treating physician. In addition, they should be designed around an understanding of how HAE affects a patient's emotions, work, school, relationships, travel, exercise, hobbies, and family planning. Professor Riedl added that management plans should be dynamic and updated as life circumstances change.

Q&A Expert Panel Discussion

The next session featured an Expert Panel that answered questions posed by conference delegates. The panel included Scientific Committee Co-Chairs Dr. Hilary Longhurst (New Zealand) and Dr. Hiroshi Chantaphakul (Thailand). Dr. Ankur Jindal (India), Dr. Philip Li (Hong Kong), and Dr. Narissara Suratannon (Thailand) also participated as panel members.

Space permits mentioning only a few of the items addressed during the session.

Can newborns be tested for HAE, and is the test reliable?

The answer was that it is possible to test the C1 inhibitor levels of a newborn, but the results might not be reliable. That is because a newborn's immune system may not be mature enough to yield valid results.

Are modern prophylaxis medicines safe?

The response pointed to the remarkable safety record of currently available modern preventive medicines. Doctors noted nothing in life is 100 percent guaranteed but expressed confidence in the safety of prophylaxis medicines currently being prescribed.

What is the best way to understand the side effects of HAE medicines?

In response, one of the doctors said, "Please talk to your doctor, don't Google it."

Do gene therapies being tested alter DNA to the extent that a patient's future offspring would not be at risk for HAE?

The response was "no." The gene therapies currently in clinical trials do not affect the mutations that cause HAE. Children of people with HAE would still have a 50-50 chance of inheriting the condition.

Closing Remarks

Tony, Henrik, and Fiona closed the conference by (1) celebrating the warm fellowship achieved over the weekend and (2) asking delegates to transform the knowledge gained during the HAEI Regional Conference APAC by Taking Action when they return to their home countries.

"I met so many patients and physicians from all through APAC. The conference was a good chance to learn more about what's happening in other countries and their HAE journey. Let's all participate in achieving a better quality of life for HAE patients! Thank you HAEi, for making this conference possible!"

– Sandy Chan, Hong Kong

"Thank you for letting me know we are not alone."

– Sidra Akhtar, Pakistan

Supporters

The global HAEi family is grateful for the pharmaceutical companies that supported the 2023 HAEi Regional Conference APAC:

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2023 HAEi Regional Conference APAC Scientific Track

By Deborah Corcoran, Chief, Special Projects and Research

The 2023 HAEi Regional Conference APAC track for healthcare professionals was planned by the Co-Chairs, Dr. Hilary Longhurst from Auckland City Hospital, Auckland, New Zealand, and Dr. Hiroshi Chantaphakul from Bumrungrad International Hospital, Bangkok, Thailand.

Friday 17 March 2023

Following the Conference opening, welcome and Dr. Lis's presentation in the main room, all healthcare professionals and researchers left the main auditorium for the Scientific Poster Session, which was open to all research conducted in the Asia Pacific region on the topic of HAE (summary of posters on page 33).

Saturday 18 March 2023

The second day commenced with a welcome to attendees given by the Regional Conference Co-Chairs, Dr. Hilary Longhurst of Auckland City Hospital in New Zealand, and Dr. Hiroshi Chantaphakul from Bumrungrad International Hospital, Thailand.

As the recipient was unfortunately unable to attend the Regional Conference in person, Mr. Xiaogang Qi of HAE China received the award on behalf of Dr. Zeijan Zhang.

Following the Co-Chairs' introduction, a plenary talk was given by Dr. Sira Nanthapisal of Thammasat University, Thailand. Dr. Nanthapisal gave an update on the progress made in how HAE is managed in Thailand by outlining the strategic plan being followed, and key initiatives undertaken, including developing Thai HAE Guidelines and a social media campaign to improve public and healthcare professional awareness of the disease.

The Co-Chairs then presented a series of fictitious clinical cases for discussion. Four cases were shown, which followed patients of different ages and gender over a number of years. Delegates were invited to vote on the best management course at key points, such as an increase in attacks, switching of prophylaxis, and patients attending the emergency room. The cases promoted much discussion and were well received by delegates.

After a short coffee break, delegates returned to a further plenary talk delivered by Dr. Ankur Jindal of the Post Graduate Institute of Medical Education and Research, Chandigarh, India. Dr. Jindal spoke on progress with HAE management in India. Key achievements, in collaboration with the HAE Society of India (HAESI), included the increased availability of facilities for diagnosis and genetic testing, a dedicated society for healthcare professionals, and the availability of plasma-derived C1-INH. Dr. Jindal concluded that while awareness had increased, more could be done; and that a national registry and further dedicated care centers for patients with HAE are expected soon.

At this point, delegates heard from oral presenters of selected abstracts.

The first abstract ('N-glycome signatures are potential biomarkers for hereditary angioedema diagnosis and stratification') was delivered by Dr. Zeijan Zhang, winner of the Young Researcher/Investigator Award, via a pre-recorded video presentation. Dr. Zhang's research focused on discovering new biomarkers of HAE to improve options for diagnosis, especially in people with HAE with normal C1-INH. Dr. Zhang indicated that her research showed the full plasma N-glycomic signature of HAE for the first time and that changes in N-glycosylation that are specific to HAE could be used for diagnosis, prediction of disease severity, and monitoring.

Dr. Sanghamitra Macchua of the Postgraduate Institute of Medical Education and Research, Chandigarh, India, delivered the next oral presentation. The research, entitled 'Transmission patterns in C1-INH deficiency hereditary angioedema favors a wild-type male offspring: our experience at Chandigarh, India', looked at the risk of transmission of SERPING 1 gene mutation (which causes deficiency of C1-INH protein) from either father or mother to children. The researchers found no statistical significance between the transmission rates between fathers to female children or mothers to either male or female children. Dr. Macchua concluded that the transmission patterns indicated that normal genes were slightly more likely to come from the father and that further research is needed to explain why this is so.

Professor Marc Riedl of the US HAEA Angioedema Center in San Diego, United States, spoke next. He presented data from a study entitled 'Efficacy And Safety Of Bradykinin B2 Receptor Inhibition With Oral PHVS416 In Treating Hereditary Angioedema Attacks: Results Of RAPIDe-1 Phase 2 Trial'. The research investigated a new bradykinin B2 receptor antagonist under development to treat and prevent HAE attacks. Prof. Riedl indicated that this study is of an investigational oral, soft-gel capsule formulation of the medicine called PHVS416 for use in treating attacks in people with HAE due to C1-INH deficiency. The presented data demonstrated a significant reduction in attack symptoms in patients taking the trial medicine compared to those taking a dummy pill or placebo. In those taking the investigational medication, there were three treatment-related adverse events. In the placebo group, one treatment-related adverse event was recorded. Prof. Riedl concluded that results from this research provided evidence to support the efficacy and safety of PHVS416 in treating HAE attacks and as a potential on-demand therapy.

The final oral presentation ('Genetic profile of patients with hereditary angioedema at a tertiary care referral hospital in North India') was given by Ms. Sanchi Chawla of the Postgraduate Institute of Medical Education and Research in Chandigarh, India. Ms. Chawla told delegates that the objective of her research was studying the genetic landscape of HAE within a tertiary referral hospital in India, as there is a lack of literature on the genetics of HAE in the country. The research conducted genetic studies of patients suspected to have HAE. The results led Ms. Chawla to conclude that the genetic profile of people with HAE in India may be different from that seen in other countries, as the majority of genetic variants were observed on the later parts of the SERPING1 gene. Ms. Chawla suggested that these mutations may influence the presentation of the disease.

The morning session ended with questions from assembled delegates, with responses from the Scientific Committee and other participants.

Scientific Poster Session

A summary of the posters available during the session:

Drug Allergy Mislabelling In Hereditary Angioedema Patients: Prevalence And Impact *– by Jane Chi Yan Wong et al., Division of Rheumatology and Clinical Immunology, The University of Hong Kong*

The researchers reviewed the medical records of all HAE patients in Hong Kong to conclude that drug allergy is a common misdiagnosis among HAE patients, leading to negative clinical outcomes and delayed HAE diagnosis. Dr. Noel Wang, who presented the poster during the session, suggested that the research should lead immunologists/allergists to review all suspicious drug allergy diagnoses, especially among HAE patients.

Delay In Diagnosis Is The Commonest Proximate Reason for Mortality in Hereditary Angioedema: Our Experience At Chandigarh, India *– by Prabal Barman et al., Pediatric Allergy Immunology Unit and Venerology and Leprology, Post Graduate Institute of Medical Education and Research, Chandigarh, India*

The authors examined the causes of death in patients with HAE in India. Their research was conducted amongst Indian families who reported the death of at least one family member due to laryngeal edema, but only 13 out of 65 families had a diagnosis of HAE. The authors suggest that delay in diagnosis may be a common reason for death and that awareness and appropriate emergency care need to be prioritized.

Start And Success Of Long-Term Prophylaxis In Hereditary Angioedema In Hong Kong *– by Jane Chi Yan Wong et al., Division of Rheumatology and Clinical Immunology, The University of Hong Kong*

This paper focused on the use and efficacy of long-term prophylaxis in Asia. The authors, represented by Jane Chi Yan Wong during the poster session, trialed LTP in a group of adult patients with HAE and found that the number and duration of attacks significantly reduced following treatment, and the quality of life scores significantly improved. Jane C.Y. Yong concluded that long-term prophylaxis is a safe and efficacious preventative treatment option and encouraged the introduction of long-term prophylaxis into Asia.

Triggers and Prodromes Identified in Patients with Hereditary Angioedema in a Single Centre Cohort from North India *– by Suprit Basu et al., Postgraduate Institute of Medical Education and Research, Chandigarh, India*

This paper considers the unpredictability of HAE and the existence of triggers and prodromes (early symptoms indicating the onset of illness). The authors report on evidence from clinical records of 180 people with HAE in a single center in India. They identified that 37.2% of people reported prodromal symptoms, with these symptoms occurring more commonly in women. Just over half (57.8%) of people reported triggers for their attacks; most commonly, this was trauma (65%). Where possible, the authors suggest that the avoidance of known triggers may be useful, especially in resource-constrained settings due to the lack of access to HAE treatments and care.

Profile of Hereditary Angioedema From Nepal – A Speck of Imprint On Everest *– by Dharmagat Bhattarai et al., Advanced Centre for Immunology and Rheumatology, Kathmandu, Nepal*

The authors investigated how HAE is diagnosed and managed in Nepal. By reviewing recurrent angioedema patient records, five people with HAE were identified. The authors conclude that this is the first Nepalese cohort of proven HAE cases. Speaking to the poster at the session, Dr. Bhattarai suggested that a lack of awareness and diagnostic facilities had hampered diagnosis, leading to inappropriate treatment and poor outcomes for people with HAE in resource-limited settings like Nepal.

APAC's First Youngsters Track!

By Nevena Tsutsumanova, Youngsters' Community Coordinator

What a weekend in Bangkok, Thailand!

Young people from the Asia Pacific region joined the Youngsters Track at the 2023 HAEi Regional Conference APAC. The youngsters spend the morning, learning about the HAEi Youngsters Community, storytelling, and how to get more involved in the global HAE community.

Dr. Narissara Suratannon stopped by to talk to our youngsters about understanding HAE, how HAE changes from adolescence to adulthood and the importance of having an HAE management plan.

The morning continued with a session about how storytelling can empower a youngster's personal advocacy journey. We are all storytellers and it is important that young advocates recognize that words have power and stories can change the world.

After the morning activities concluded, youngsters spent some time networking before rejoining the main Patient Track program.


Welcome to Bangkok!


3 Things in Common


HAEI LEAP Class of 2023 is meeting
in Dubai on 31 March and 1 April
2023!

ENHANCING HAEI'S ABILITY TO GROW AND SUCCEED NOW AND IN THE FUTURE

The HAEi team works hard to provide our community with programs, services, and activities that help member organizations achieve their advocacy goals. We now have a global advocacy network of member organizations in 96 countries and expect that number to grow significantly in the coming years. Recognizing the need to keep pace with rapidly evolving opportunities and challenges facing people with HAE, HAEi's Board of Directors approved organizational changes with an eye toward the future. These changes will be implemented on 1 July 2023.

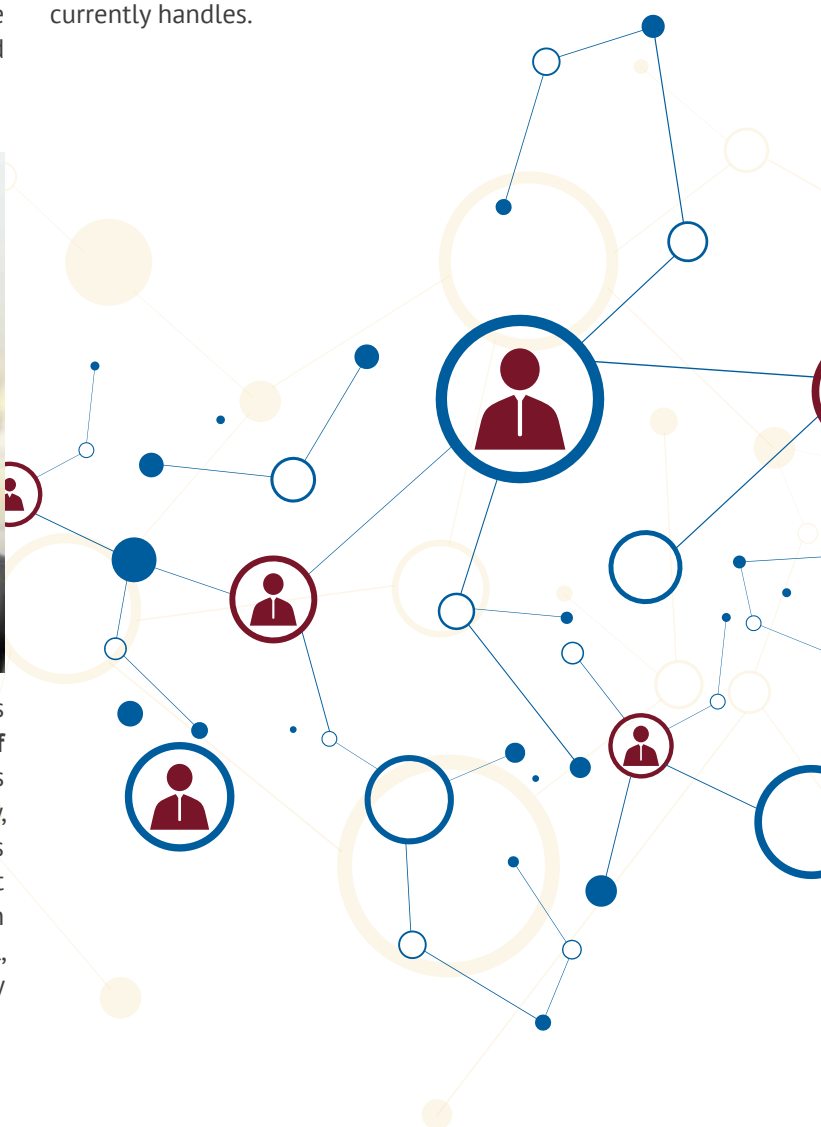
Tony Castaldo, who has led HAEi since the organization's inception in 2004, will continue serving as **Chief Executive Officer** and has also been appointed **Chairman of the Board**. He will continue leading the entire HAEi enterprise and work with the new executive team to establish HAEi's long- and short-term strategic and operational direction and plans.

Henrik Balle Boysen has been appointed as HAEi's **President**. Currently serving as Executive Vice President and Chief Operating Officer, Henrik has been the driving force behind our remarkable growth and the architect of the technology-based platforms and apps. His efforts are the reason that HAEi has the distinction of being considered one of the world's leading rare disease global umbrella organizations. As President, Henrik will be responsible for strategic and operational planning and guiding the leadership team's implementation of HAEi's programs, services, and activities. In addition, Henrik has been elected to the Board of Directors.

Fiona Wardman, our Chief Regional Patient Advocate (CRPA) and RPA for Asia Pacific, moves up to become **Executive Vice President Global Advocacy and Chief Diversity Officer**. In her capacity as CRPA, Fiona has provided effective leadership that helped our highly talented Regional Patient Advocates achieve the goals set out for the various HAEi regions. She has led a very successful effort to establish new member organizations in the Asia Pacific Region. Her new role expands her responsibilities to include leading and overseeing all of HAEi's advocacy activities.

Michal Rutkowski has been appointed as **Director, Regional Patient Advocate Program**. Michal moves up from his position as RPA for Central Eastern Europe, Benelux, and The Middle East. His many successes include helping existing member organizations expand their capabilities and nurturing the formation of many patient groups throughout the huge region that he serves. He will continue as the RPA for the region he currently handles.

Jørn Schultz-Boysen has been selected to serve as **Executive Vice President Global Operations and Chief Compliance Officer**. Jørn currently serves as HAEi's Executive Project Manager and RPA for Nordics, Germany, Austria, Switzerland, and Israel. He has a deep business background, having served in executive positions at various companies with international operations. Jørn will take over the day-to-day operational, managerial, and financial responsibilities formerly handled by Henrik. He will also continue serving as an RPA.

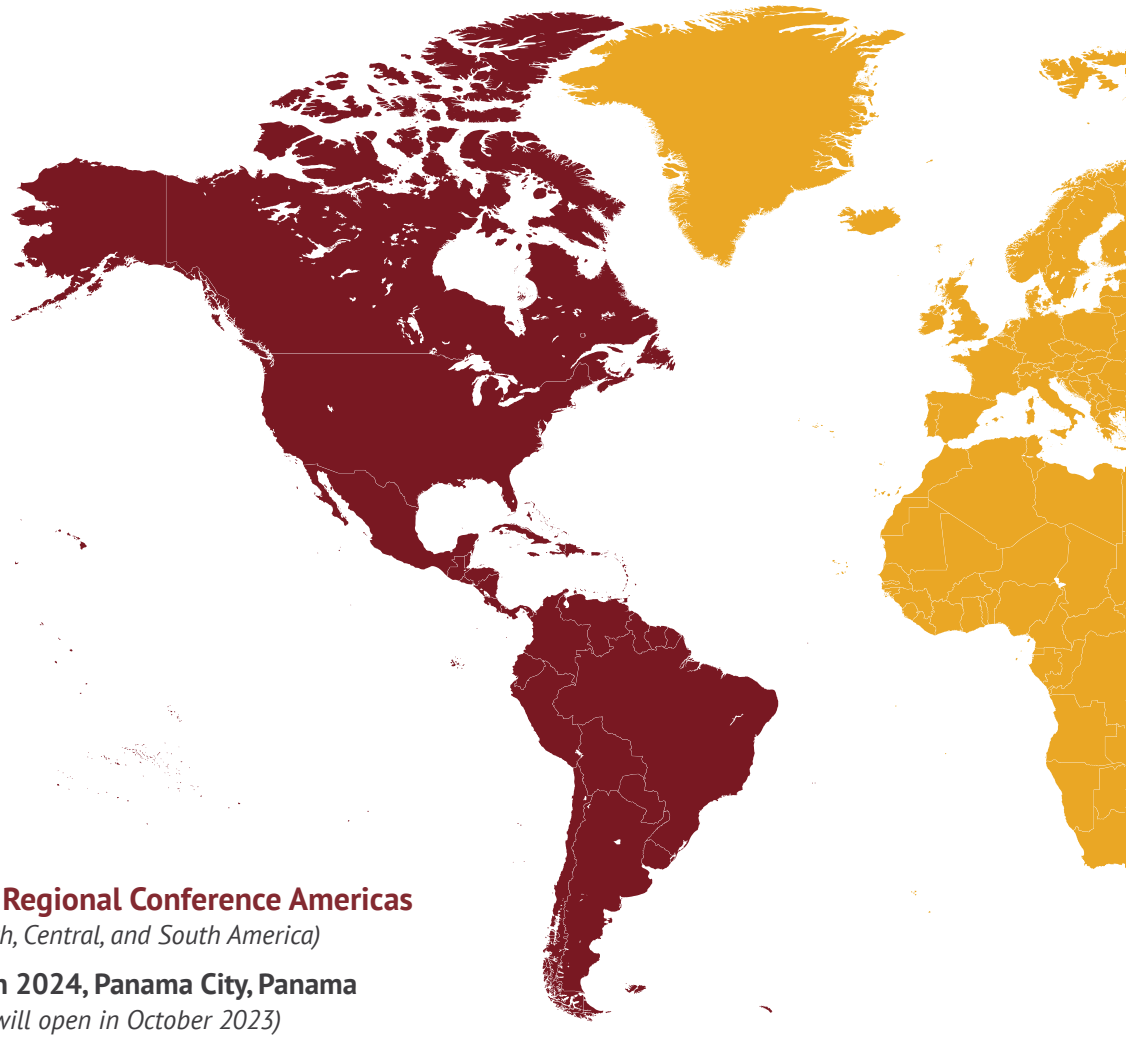


HAEi'S FUTURE REGIONAL CONFENCES AND GLOBAL LEADERSHIP WORKSHOPS

HAEi has chosen to change from the well-known single Global Conference format every two years, to one Global Leadership Workshop and three Regional Conferences to take place over a two-year period.

Following the highly successful 2022 HAEi Global Leadership Workshop and the first regional conference, the 2023 HAEi Regional Conference APAC, HAEi will follow up with continuous series of Regional Conferences and Global Leadership Workshops in the coming years.

"We look forward to welcoming patients and caregivers, youngsters, and physicians to the highly focused Regional Conferences as we know that in-person gatherings offer inspiring and motivating opportunities to learn from fellow patients and caregivers as well as medical experts. And as always, we will do our very best to offer attendance at a very low price and will also work hard to secure travel grants for as many patients and caregivers as possible", says Executive Vice President and COO, Henrik Balle Boysen.



HAEi REGIONAL CONFERENCE AMERICAS PANAMA CITY 15-17 MAR 2024

2024 HAEi Regional Conference Americas
(covering North, Central, and South America)

15-17 March 2024, Panama City, Panama
(Registration will open in October 2023)

MARK YOUR CALENDARS AND PLAN TO ATTEND THE EXCITING HAEI EVENT THAT WILL BE HELD IN YOUR PART OF THE WORLD!

HAEi's Global Leadership Workshops are for Patient Advocacy Leaders of HAEi member organizations, HAE Physicians/Scientists, HAEi Youngsters Advisory Group, and industry sponsors (read more on page 42).

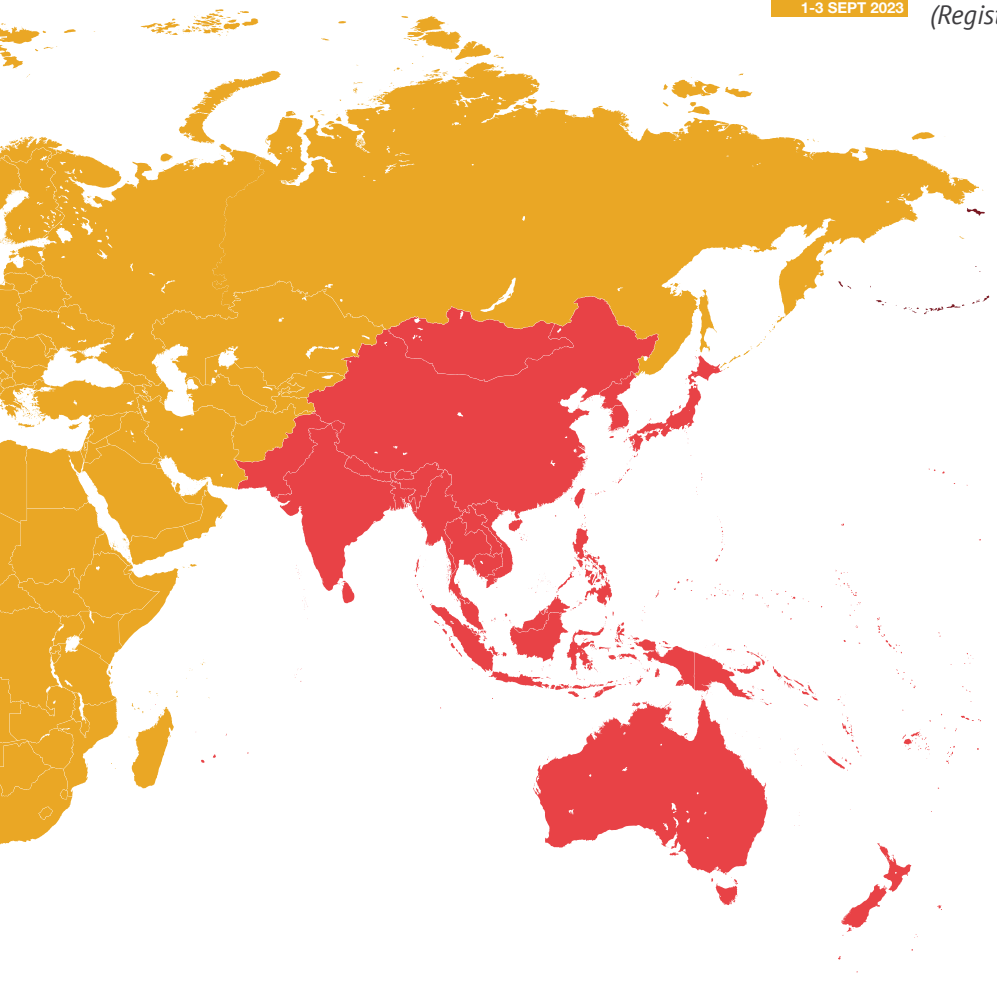
HAEi's Regional Conferences are for HAE Patients and Caregivers, Youngsters, HAE Physicians/ Scientists, and industry sponsors of the region.

2023 HAEi Regional Conference EMEA

(covering Europe, Middle East, and Africa)

1-3 September 2023, Munich, Germany

(Registration will open in April 2023)



2025 HAEi Regional Conference APAC

(covering Asia Pacific)

1st half 2025

HAEi
REGIONAL
CONFERENCE
EMEA
MUNICH
1-3 SEPT 2023

TAKE ACTION

Supporters

We are delighted to have support from numerous leading pharmaceutical companies in the field of HAE. We thank our supporters for their contribution to this conference, which is greatly appreciated.

Diamond Supporters

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CSL Behring

Pharming

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astria THERAPEUTICS

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KalVista Pharmaceuticals

PHARVARIS

Welcome to the 2023 HAEi Regional Conference EMEA

HAEi continues to plan for the upcoming 2023 HAEi Regional Conference EMEA, which takes place in Munich, Germany, from 1 to 3 September 2023 and covers the European, Middle Eastern, and African region.

"Although our perspective is global, we recognize and celebrate the diversity among the regions of the world that we serve. That is why we are organizing the 2023 HAEi Regional Conference EMEA with the theme "Take Action". We expect to welcome around 500 HAEi friends (including patients, caregivers, HAE physicians/scientists, and industry supporters) to share experiences, meet others in the region, have fun, and learn how to improve quality of life for people with HAE.", says HAEi President and CEO, Anthony J. Castaldo.

Designed to fulfill the needs of the entire HAE community, the conference features a Patient and Caregiver track, a Youngsters track (12-25 years old), and a Scientific track. We are finalizing the individual track programs, so please check the conference website at emea.haei.org for updates.

We look forward to welcoming you to the 2023 HAEi Regional Conference EMEA in Munich.

Register now!

Registration for the 2023 HAEi Regional Conference EMEA is on a first-come, first-serve basis. We offer extremely attractive registration rates and conditions, so we advise you to register as soon as you can!

Please register at emea.haei.org/registration

Wordly – Interpretation options

We will offer translation into 20+ languages during our 2023 HAEi Regional Conference EMEA. Languages currently supported by our translation partner "Wordly" include:

Arabic, Bengali, Chinese (Simplified), Chinese (Traditional), Czech, Dutch, English (AU+UK+US), French (CA+FR), German, Hebrew, Hindi, Indonesian (Bahasa), Italian, Japanese, Korean, Polish, Portuguese (BR+PT), Romanian, Russian, Spanish (ES+MX), Swedish, Tagalog, Tamil, Thai, Turkish, and Vietnamese.

SAVE THE DATE!

Following the success of the first ever HAEi Global Leadership Workshop in Frankfurt, Germany, in October 2022, HAEi is thrilled to announce the date for the next workshop:

2024 HAEi Global Leadership Workshop

(covering all HAEi member countries)

3-6 October 2024 in Copenhagen, Denmark

Almost 500 participants representing +75 countries participated in the 2022 HAEi Global Leadership Workshop, which featured almost 1,000 minutes of talks, presentations, and interactive sessions across the Member Organization Lead and Scientific Programs.

HAEi looks forward to welcoming Patient Advocacy Leaders of HAEi Member Organizations, HAE Physicians/Scientists, HAEi Youngsters' Advisory Group, and industry sponsors to the upcoming 2024 HAEi Global Leadership Workshop and recommend you save the date for this event.

13th C1-INH Deficiency and Angioedema Workshop

Diagnostic and Therapeutic Applications of Genetic Research Results

The 13th C1-INH Deficiency and Angioedema Workshop took place in Budapest from 4-7 May 2023. Nearly 400 participants arrived in the Hungarian capital this year from 42 countries. The Workshop is dedicated to the C1-inhibitor deficient and other bradykinin-mediated angioedema disorders considered rare diseases.

This scientific conference series has been organized every second year since 1999, and Hungary has been the host since the beginning. The conference was brought to life by the desire for knowledge. The professionals treating Hungarian patients, led by Henriette Farkas, wanted to learn about the experiences of other professionals but to do this, they would have to travel to many foreign clinics as the number of patients with rare diseases is low at a single location.

On the initiative of Henriette Farkas and Lilian Varga, the decision was made in 1998 that the European professionals dealing with the disease should gather and hold a consultation to define the guidelines for diagnosis and therapy. The first workshop took place in a restful place, the Citadel of King Matthias in Visegrád, Hungary. Later, the event moved to Budapest.

Even at the first workshop, clinicians, researchers, and laboratory specialists were invited, as well as drug developers and patient representatives, some of whom later became the founders of HAEi.

This unique composition continued to be very fruitful later as well because problems related to rare angioedematous diseases occurred from several perspectives, and solving the problems was facilitated by the exchange of views and collaboration of conference attendees from different backgrounds. The scientific breakthrough was soon demonstrated in the development of diagnostic methods; more and more patients were registered, and more regions established specialized centers to treat angioedema patients.

(continues on the next pages ...)

Top: HAEi's President & CEO, Anthony J. Castaldo, delivers the keynote address at the Gala Dinner.

Right: Henriette Farkas and Lilian Varga, founders and hosts of the biannual C1-INH deficiency and angioedema workshops.

At the workshops held every two years in Budapest, researchers reported newer results about the more precise details of the pathomechanism of the disease, which provided a basis for therapeutic developments to take off. In the 21st century, there is hardly any other rare disease studied in so many clinical trials to develop new and more modern medications with fundamentally different mechanisms of action. It became apparent that the range of angioedemas based on the effect of bradykinin is wider, meaning that besides C1-inhibitor deficient patients, other patients with normal C1-inhibitor levels can also benefit from the developed therapies.

Patient organization representatives have been equivalent, active participants of the workshops from the start. In 1999, some European countries already had patient organizations, which benefitted other regions; in 2001, representatives (Anthony J. Castaldo and Henrik Balle Boysen, among others) arrived from 15 countries. Soon the number of patient organizations and the number of their members increased, and during the regular meetings, the cooperation increased with national organizations. The need to establish an international patient organization also developed.

HAEi was established in 2004 after the 3rd C1-INH Deficiency and Angioedema Workshop held in 2003. At this year's workshop, the president of HAEi, Anthony J. Castaldo, talked about the role of the workshops in establishing the international organization – he simply called the impact, the workshops held every two years in Budapest, has on people with HAE and other angioedema patients, the 'Budapest Spirit'. Not only did the number of patients diagnosed and receiving treatment multiply, but the therapy became more modern, and therefore the patients' quality of life increased significantly.

Primarily the workshop is a scientific forum and the only one in the area of angioedema, of which the program is based on the presentation of new results. This year, the scientific committee accepted 100 abstracts, which were presented by the authors partly orally and partly in poster form. Apart from presenting the primary results, the invited speakers at the conference, Vladimir Leksa, Konrad Bork, and Despina Sanoudou, gave summary presentations on the more and more important areas. This year, the focus was on diagnostic and therapeutic applications of genetic research results. In addition, significant progress has been made in understanding the pathogenesis of hereditary and non-hereditary angioedema diseases and their therapeutic possibilities.

At this year's conference, there were an outstanding number of presentations on clinical research results; the new developments are very promising. In addition, we could also get to know the recent experiences with the already marketed medicines. The group of angioedema diseases expanded with additional types, so it became necessary to renew the classification of

angioedemas, as we could learn about this in Avner Reshef's presentation.

The conference also provides an opportunity for professionals worldwide to create professional recommendations and conventions directly. At this year's conference, the guideline based on the international consensus about the role of genetics in the diagnosis and therapy was updated due to the many types of HAE moderated by Anastasios Germenis. The renewal of the international convention on pregnancy, led by Teresa Caballero, was also discussed. Modern therapy for rare diseases is possible in specialized comprehensive centers. In a separate section, the operation of specific reference and excellence centers and the activities of ACARE, the international network created for the coordinated, interactive cooperation of the centers, was presented by Marcus Maurer.

The workshop is more than a scientific forum. Even though the number of people increased to nearly 400, the atmosphere was still friendly, almost family-like. The participants who return every two years greeted each other warmly, as they were happy to meet again in person. Many of them were in contact during the intervening period. The new participants easily and gladly integrated into this intimate community.

HAEi receives the 'for HAE Patients' award

The tradition that, since 2003, one person is selected at the workshops based on the vote of the 19-member Scientific Committee representing the community, receives the 'for HAE Patients' award is also a unifying force. This year, in addition to Anete S. Grumach, Sarah Smith Foltz, one of the founding members of the HAEi, also received the certificate and the trophy, the 'Gömböc' artifact, on behalf of HAEi as a recognition of the organization's work. The celebrants personally cut and offered the conference participants the celebratory cakes, one of which was decorated with the photo of award winner Anete S. Grumach and the other with the HAEi logo.

At the end of the conference, four authors under age 35 received the 'Grant for Young Investigator' certificate and the accompanying monetary reward, whose work was deemed best by the jury led by Stephen Betschel.

You can find the program and abstract book of the C1-INH Deficiency and Angioedema Workshop' at: https://haei.org/c1-inh-2023/

Photographer: Tamás Thaler

Thank You for Being #active4HAE and Celebrating our Community!

By Deborah Corcoran, Chief, Special Projects and Research

Throughout April and May 2023, our global community organized an incredible number of HAE events and activities with **hae day :-)** – May 16 – as a focus. Member Organizations arranged patient days, family days, walking and hiking events, virtual patient days, educational events for doctors, and much more.

"Our voices are one of the most powerful advocacy tools we have," says Henrik Balle Boysen, Executive Vice President, and Chief Operating Officer, HAEi. "It is wonderful to see so many of our community sharing their HAE stories on social media, in magazines, and in television interviews for **hae day :-)**".

Participants in our annual activity challenge added their time spent on physical and well-being activities to our **hae day :-**) website. Between 1 April and 31 May, the steps generated took us around the world a record 3.5 times! Well done, everyone!

"**hae day :-**) gives us a focus for advocacy activity and an opportunity to celebrate our global community. We are continually inspired by the positive difference our community makes for people with HAE – it is advocacy in action!" says Anthony J Castaldo, President, and Chief Executive Officer, HAEi.

2023 ACTIVITY CHALLENGE IN NUMBERS

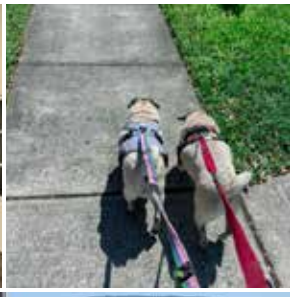
174,733,777
steps taken in total

11,339 activities

38 countries

351 photos

Head to haeday.org to see all the results

"Over 10 years ago, back in 2012 **hae day :-)** was the day when the story of HAE patients in our country started, and therefore it means a lot to HAE patients from Macedonia. It was a day that helped shape our actions, it became clear to us what we were supposed to do to make medications available in Macedonia and put us on our paths for a better future."

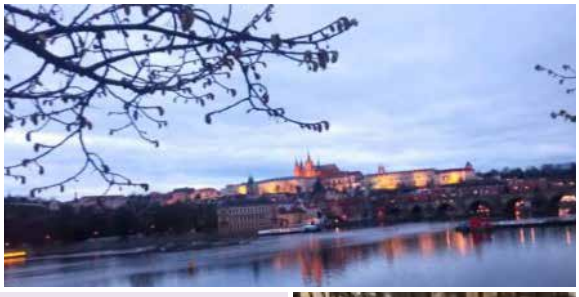
HAE Macedonia




"**hae day :-)** is a great occasion for patients, caregivers and physicians to share experience and feel as a big family! Having a dedicated day is very helpful as we can share the news in our social pages and also organized dedicated events in our specialized Angioedema centers where patients but also physicians from other specialties have the opportunity to learn what's new in HAE's world."

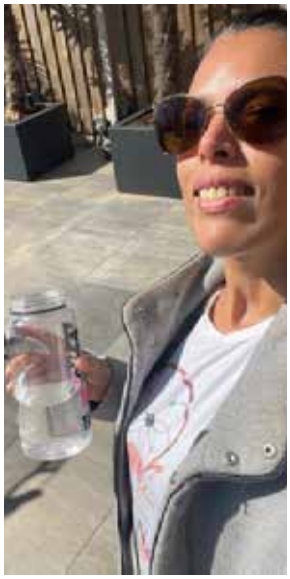
HAE Italy (AAEE)






"**hae day :-)** is a symbol of hope and solidarity, reminding us that we are not alone in our journey. It serves as a powerful platform to foster a sense of community, encouraging individuals with HAE to share their experiences, challenges, and triumphs. **hae day :-)** serves as a rallying point for advocacy efforts, enabling us to call for change and improvements in the lives of those affected by HAE."

HAE Portugal (ADAH)





See more images and quotes on page 91

Meet the New Members of the Youngsters' Advisory Group

By Nevena Tsutsumanova, Operations Manager and Youngsters' Community Coordinator

We are very excited to welcome two new members to our fantastic HAEi Youngsters' Advisory Group. We want to say a warm welcome to Kamila from HAE Peru and Jess from HAE Australasia!

We asked Kamila and Jess to tell us a little bit more about themselves, their countries, and their involvement with HAE advocacy. If you want to read their full stories, head over to the HAEi Youngsters' Community website at youngsters.haei.org.

Jess

I am so excited to further my involvement in this wonderful community that has given me so much comfort and love and helped me grow in ways I never thought imaginable.

Kamila

I can't wait to work together so more patients can experience a pacefull life and just as I enjoy sharing my days with my brother, they can enjoy their lives with those they love the most!

Exciting new Hangout with lots of resources

HAEi Youngsters: Let's Hang Out!

The HAEi Youngsters' Hangout is a collection of short videos and blogs featuring interesting and valuable content for all of our HAEi Youngsters, no matter where you are in your HAE journey.

You can find presentations from international HAE experts, stories from youngsters, caregivers, and parents, and last but not least, tools developed by HAEi to help you manage HAE in your daily life.

More content is added to the Hangout all the time, and you can help expand the Hangout with fresh material by sharing your story or asking a question.

We invite you to Hang Out with us on our website at youngsters.haei.org/hangout.

Your HAEi Youngsters' Advisory Group

Still haven't joined the HAEi Youngsters' Community?

The community is free and open to youngsters aged between 12-25 who are members of their local Member Organization! Head over to our website: youngsters.haei.org, and click the "Join us" button – it is green and right at the top.

First HAEi LEAP Class: An Inspiring Advocacy Journey Begins

By Nevena Tsutsumanova, HAEi Operations Manager and Youngsters' Community Coordinator

HAEi LEAP is a new educational program that aims to train and motivate future HAEi advocacy leaders. It is designed to provide youngsters with new skills that will help them develop as individuals and HAE advocates.

LEAP participants will work directly with their Member Organizations on an advocacy project that will support the local HAE community.

HAEi LEAP's two-day in-person seminar took place on 31 March and 1 April 2023 in Dubai, United Arab Emirates.

Twenty young people from fifteen countries traveled to Dubai for the official start of the LEAP education program and to meet their classmates. The in-person seminar covered various topics to support our LEAP students with skills to help them both in life and to develop their projects before heading to deliver their projects with their Member Organizations.

The LEAP Class of 2023 started with HAEi Leadership welcoming our students, sharing HAEi's story, and highlighting the power of advocacy as a force to change the world.


HAEI LEAP
Kick-off seminar
LEARN
EXPERIENCE
ADVOCATE
PAVE THE WAY

HAEi LEAP Youngsters

Deborah Corcoran, Chief, Special Projects and Research, and I delivered a training program filled with learning sessions, group work, networking, and fun. In her words:

"We had two very intense learning days. We took our LEAP students on a journey through project and time management, advocacy best practices, public speaking, presentation skills, and writing for advocacy. But, we made sure to factor in time for collaboration and sharing experiences to build the feeling of a class environment."

The LEAP students also had opportunities to exchange ideas about their projects and draw inspiration from each other.

When planning the program, it was essential for us that all training sessions involved lectures and practical exercises. We want our students to learn from trying, and we are delighted to say everyone was open-minded and joined us on every challenge.

Currently, our students are enjoying the world of HAEi Advocacy Academy, the online component of our HAEi LEAP program, where a new course is released on a weekly basis. All courses are designed to propel our students toward their LEAP learning objectives by covering subjects that can enhance their final projects and empower them to thrive in life, whether at school or in the competitive work market.

Each course comprises a blend of learning on our students' own schedule and activities and homework assignments, allowing the LEAP students to reflect and then cement their knowledge through exercises.. As we like to say in our team: "It's not just about learning new things; it's about putting them into practice."

As we head towards the final milestone of the LEAP online education in mid-June, we feel very excited. Picture this: A week where our students will present their project ideas in proposal format they learned about in Dubai, and can enhance with activities and ideas they learned in the courses. All before they head out to collaborate with their Member Organizations to turn their proposals into reality. We cannot wait!

We are grateful for the driven, open-minded, and creative youngsters, who were part of this first LEAP class.

Our Motto: Prepare to be inspired. Prepare to be taken on this remarkable LEAP into a brighter future!

Here is a glimpse at the courses LEAP students are undertaking:

Join the HAEi LEAP Class of 2023 on Their Journey!

We have created a page on the youngsters' website so everyone can follow along with the class and have a look at some of their experiences as they go through the HAEi LEAP program.

You can scan this QR code or visit our website youngster.haei.org/leap-class-2023

Climbing Kilimanjaro with a Rare Disease

By Isabel Brunkan, HAEi Youngsters' Advisory Group Member

I am an HAE patient. At the beginning of 2023, I had the opportunity to summit Mount Kilimanjaro (5,895 meters/19,341 feet) as part of Osmosis and Elsevier's Year of the Zebra initiative! This was an incredibly serendipitous trip. The Year of the Zebra honors the Orphan Drug Act's 40th anniversary and rare diseases – the zebras of medicine. I am one of those zebras, as I have HAE. My life, just as many others, has been saved countless times by medicines enabled through relentless efforts of HAE advocates who early on promoted the Orphan Drug Act's formidable benefits to attract pharmaceutical company interest in developing HAE medicines.

As a patient with HAE, there can be times when one day, I'm climbing a mountain, and the next, I'm bedridden. Luckily, with modern HAE medicine, I can travel, explore, and exercise safely. As part of the HAEi Youngsters' Advisory Group, I hope to inspire other youngsters with HAE to see that having HAE can be a source of positive motivation to live life to the fullest and maximize the moments that we're well.

Join me as I take you with me on this amazing journey!

Before setting off

I had a long talk with my HAE doctor before deciding to do Kilimanjaro. We made a management plan for my trip and discussed the best approach based on my individual treatment. As discussed with my HAE doctor, I did a preventive treatment in the morning before setting off because the climb and altitude would be a physical strain on my body.

Day 1

Londorosi Gate: 2,260 meters

We began the journey at Londorosi Gate with a quick lunch while the porters loaded up the gear. The porters were the true most valuable players of the trip carrying (maximum) 20 kilograms each and all of the cooking supplies, camp equipment, tents, and the rest of the gear we would need on our seven-day trek.

Morum Picnic Site: 3,407 meters

We began hiking at Morum Picnic Site and hiked across the moorland to Shira Camp 1. While we didn't have any altitude gain during this hike, the altitude itself was a change! The mantra of the guides was "polé polé", Swahili for "slowly slowly". This hike was as much a journey to the first camp as it was a practice at walking slowly.

Shira 1 Camp: 3,500 meters

We arrived at Shira Camp 1 for dinner – the temperatures dropped quickly overnight as this camp was on a plateau. Everything was covered by frost in the morning, but the sky was so clear we could see some of the most beautiful stars I've ever seen.

Day 2

Shira 2 Camp: 3,850 meters

On day two, we trekked through the moorland from Shira 1 Camp to Shira 2 Camp, which has an altitude of 3,850 meters. We're all taking Diamox, an altitude sickness pill, so we have been spared severe altitude effects. At about the halfway mark, we have a tea break. The camp is shrouded in a misty fog as we hike in.

Altitude Training Hike: ~4,000 meters

After a quick break, we keep climbing up to 4,000 meters as an altitude training hike – "climb high, sleep low" is the mantra – to get our bodies used to being at high altitudes. Our expedition guides sing a song about Kilimanjaro in Swahili, and we begin to try to learn it.

Day 3

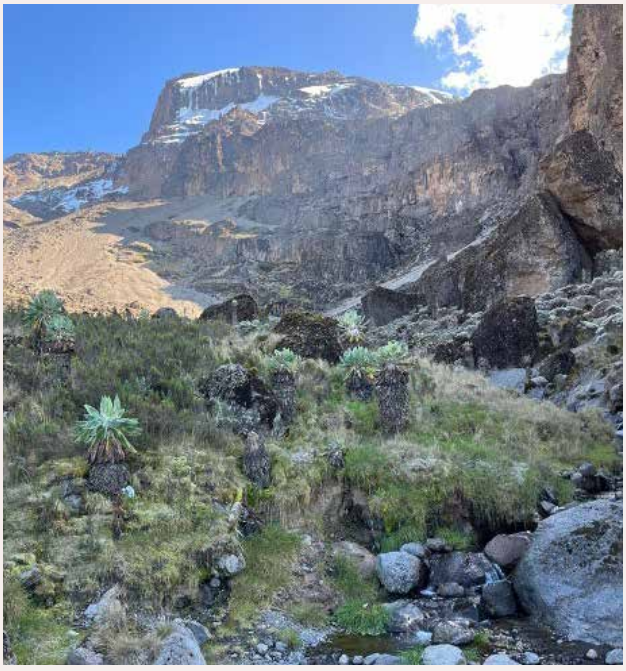
Lava Tower Camp: 4,600 meters

Today we set out from Shira 2 Camp to reach the Lava Tower Camp, our highest elevation point so far at 4,600 meters. We've moved from moorland to alpine desert, and there are more ups and downs on this hike than on previous ones. As we set off in the morning, the other tallest mountain nearby, Mount Meru, was rising up behind us, but eventually, we climbed higher than its peak! At Lava Tower, we broke for a long lunch, designed to get us even more accustomed to high altitude.

Mount Meru in the background

Baranco Camp: 3,900 meters

After lunch, we begin our descent to Baranco camp, where we'll spend the night. The peak of Kilimanjaro is now clearly within view and towers over Baranco camp.



View of Kilimanjaro from Baranco

Day 4

Scaling Baranco Wall

In the morning, we set out from Baranco Camp to scale the Baranco Wall, a massive cliff face. It was amazing to see the porters scramble nimbly up with up to 20 kg on their heads! The altitude definitely affects us, with every step being extremely slow and needing to catch our breath frequently. After climbing the wall and reaching our highest point of the day, we began a descent into a valley which is very welcome until we have to climb back up the other side of the valley to reach the camp!

Altitude Hike: 4,100 meters

After reaching Karanga Camp, we took a quick altitude hike up to around 4,100 meters so that our bodies would keep getting accustomed to the altitude. Mount Kilimanjaro seems within reach! At our turning back point, a light snow begins to fall!

Day 5

Barafu Camp: 4,673 meters

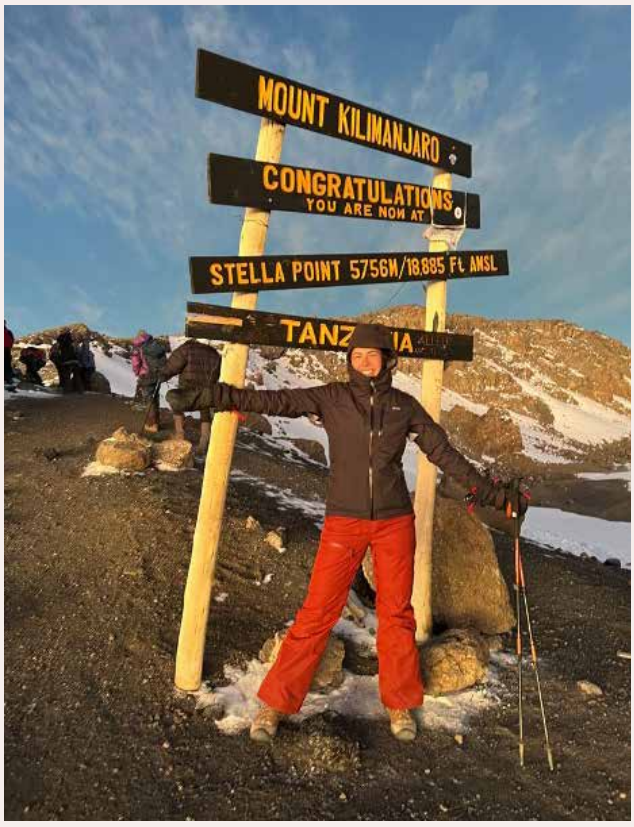
We reached base camp today! There's a big push with almost 600 meters of elevation gain to reach it. In the tents, each night, I'm starting to feel the altitude – packing and repacking our duffle bags leaves me out of breath if I move quickly. But we listen to music and dance our way up the final ascent to base camp!

Altitude Hike: 4,800 meters

Before we can rest, we do another altitude hike up to around 4,800 meters. This is following the path that we'll climb to the summit in just a few hours! There's some tricky rock scrambling up for a few hundred meters which serves the purpose of letting us familiarize ourselves with the trail before we do it in the dark. Everyone heads to be around 2 pm because we'll wake up at 10 pm for dinner before we set out for the summit, climbing overnight!

As discussed with my HAE doctor, I do another infusion at lunch before we do the summit. I'm already feeling a little bit of an attack, possibly because of the altitude, so I hope that the medicine can curb any more leaking.

Day 6

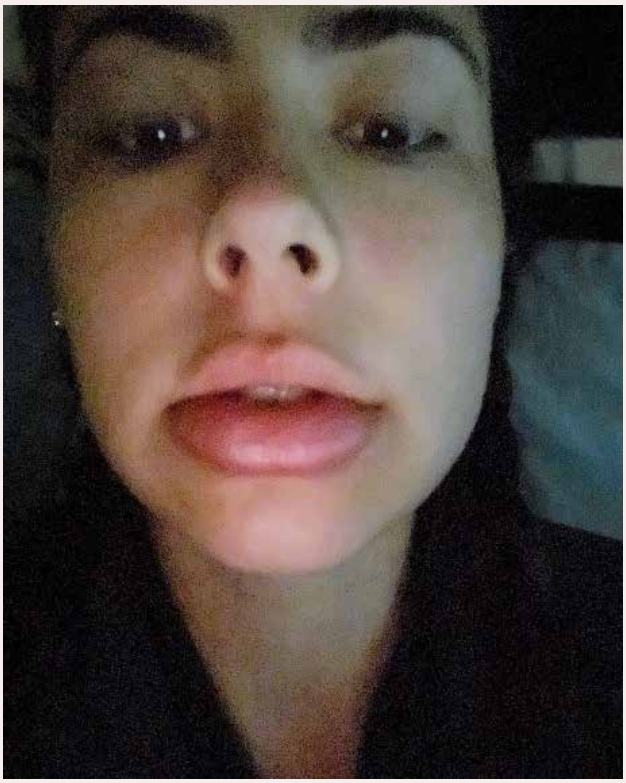


Push to Stella Point: 5,756 meters

We wake up at 10 pm, and I can feel that my lip is quite swollen. However, because I've already used my medicine, I know it won't progress further, and it's contained to my lip and not severely affecting my body in any way, so I push ahead with the climb. It was one of the most physically challenging things I've ever done. With the altitude, we were going about one step a minute in the dark of the night.

The sky was crystal clear with stars shining brightly, and it was almost a full moon, so I didn't have to use my headlamp. We climb for seven hours, and some of us start to feel the effects of the altitude. The expedition guides have kept us going singing the Kilimanjaro song in Swahili, plying us with hot tea with glucose packets and cookies. The final push up to the crest of the mountain is in negative temperatures, with the wind blasting us as we climb vertically through gravel and sand.

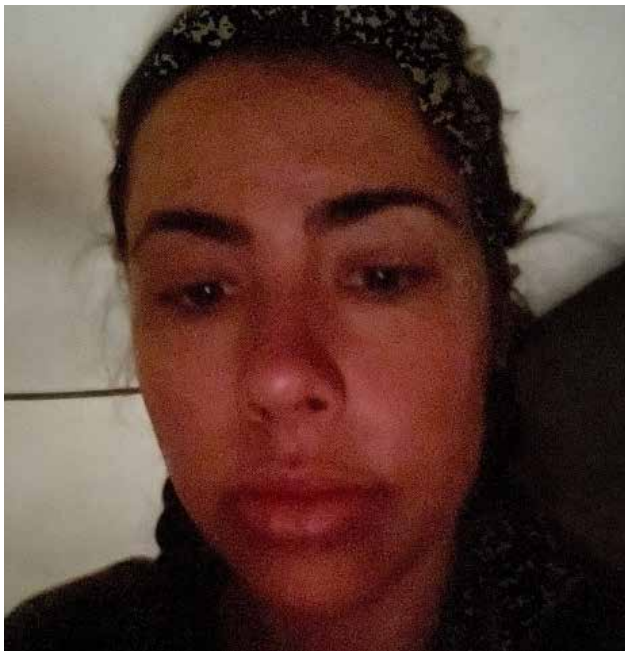
The beginning of the sunrise gives us more energy for the final push, with us reaching Stella Point, at the top of the crest of Kilimanjaro, just after 6 am.



Lip swollen when waking up at 10 pm.

Summit: 5,895 meters

After another round of tea and cookies, we begin the final leg of the summit, climbing a gentle slope up the ridge of the mountain to reach the highest point of Kilimanjaro. There's jubilation at the summit, with other climbers waiting in line to take photos with the summit sign. It's freezing at the top, so we begin our descent after the photos. What took us seven hours on the way up takes only three on the way down, with some of us almost skiing through the loose rock, gravel, and sand. We get a couple of hours to recover and rest, having lunch before continuing our descent to the next camp. My lip has unswollen a little bit, but I'm constantly reapplying Chapstick to try to prevent my lip from splitting.



Lip starting to un-swell

Mweka Camp: 3,100 meters

Our final destination for the night is Mweka Camp at 3,100 meters, meaning we've descended over 2,500 meters in altitude after climbing up 1,200 meters to reach the summit. On this descent, we go through the various landscapes, from the alpine desert filled with barren, sandy gravel, to beginning to see trees and bushes and finally ending the day with the camp located in a lush, tropical-looking moorland.

Day 7: The morning of the last hike!

We have a final breakfast, with all of our porters and expedition guides gathering to sing songs before we begin the final descent to Mweka Gate, descending almost 1,500 meters in three hours. We catch glimpses of Kilimanjaro through the trees and see monkeys as we approach the gate! My lip is also deflating, so Kilimanjaro has been a success!

I feel very grateful to all of the guides, porters, and people in my group who trekked alongside me to raise awareness for rare diseases as part of Osmosis' Year of the Zebra campaign. While summiting Kilimanjaro required a lot of introspection and pulling extra strength from deep within, the camaraderie from the group I was climbing with was a large part of why I was able to summit and not only summit but enjoy the experience.

Get Your HAE under Control with the HAE TrackR App

Features of HAEi's HAE TrackR App

- ✔ Easy-to-use electronic diary
- ✔ Safe and secure – all data is the sole property of the user
- ✔ Store and share data about your HAE with your physician
- ✔ Product and company neutral with no commercial interests
- ✔ Endorsed by the ACARE network
- ✔ Accessible from anywhere at any time and in many languages

New Features added in Version 2:

- ✔ Smart reminder functionality for prophylactic treatments
- ✔ Improved reporting for easy sharing of data with physician
- ✔ Option to only list preferred/used treatment(s)
- ✔ Option to add clinical trial medication if needed
- ✔ Upload function for photo(s) of batch/LOT number for documentation

Download on the App Store bit.ly/haetrackr-appstore

GET IT ON Google Play bit.ly/haetrackr-googleplay

Start using **HAE TrackR** today – download from **App Store** or **Google Play**!

Top 5 Tips for Traveling with a Rare Disease

By Isabel Brunkan, HAEi Youngsters' Advisory Group Member

Packing for any trip requires thought, but as someone traveling with a rare disease, there are always a few extra steps that go into the process. These are the main things I've found can help make traveling with a rare disease more manageable.

1 Carry your medicine with you at all times

- Always keep your medicine in your carry-on luggage. Apart from not losing your medicine if your luggage is lost or needing to treat in an emergency, the checked luggage compartment might not be temperature regulated, which most medicines need to be.
- If you have two pieces of carry-on luggage and, depending on how long you're traveling for, keep the majority of your medicine in your larger item that goes overhead (I usually put it in a roller bag to not have to carry it!) but keep a couple of rescue doses in your backpack or purse in case you need to treat during the flight and can't easily access your other bag.
- Don't forget about your supplies: make sure you have all the supplies needed to administer the medicine in your carry-on. I usually stash alcohol prep pads in many different pockets, so they're always handy.
- You're allowed to bring ice! Even though there are liquid restrictions, ice doesn't count, so if you need to keep your medicine at a specific temperature range, you can bring an ice pack.
- For most airlines, you can bring medicine onboard, and it won't count towards your carry-on luggage restrictions. Having a dedicated bag for your medicine can be one way to keep it and the supplies all in the same place and help bypass airline bag restrictions.

2 Carry any important items you might need in case your baggage is delayed or lost

- Aside from medicine, it can be a good idea to bring a spare change of clothes, toiletries, snacks, and other necessities. As someone with HAE, I'm always looking for ways to mitigate stress, so knowing I have the necessities in my bag just in case my checked bag is lost can help with that.
- When I was traveling to Kilimanjaro, my flight was canceled, so I had to reroute and take three additional flights. I had packed my hiking boots, a pair of leggings, my down jacket, and basic toiletries in my carry-on bag, so I could start trekking even if I lost my suitcase. A lot of people were also headed to Kilimanjaro and rerouted as I did, and some had all their hiking gear in their checked luggage. We

had a very tight connection time, so there was (and always is) a chance the luggage might not make it onboard. If you're traveling for a specific reason and need specific outfits or gear, wearing it onboard (such as wearing your hiking boots!) or packing it in your carry-on helps ensure that even if your travel plans are disrupted, you can minimize the impact.

3 Bring a doctor's letter and prescriptions for all of your medications

- I get stopped about every fifth time at security for having medicine. Most of the time, the security guards wave me by once they've seen it, but a couple of times, I've had to pull out my doctor's letter that says it's medically necessary that I travel with the medicine on me before the guards would let me pass.

4 As HAE can be triggered by stress, figure out small hacks that work for you to help minimize stress

- I always travel with earplugs and an eye mask to try to be as well-rested as I can when I land. This is also helpful if you're going to be staying in hostels or traveling long distances no matter what type – by car, bus, train, or plane!
- Download a book or some episodes of your favorite song, podcast, or show to listen to to relax on the journey or while you're waiting in lines.
- Make sure you have snacks! Keep your energy up, and don't stress your body any more than travel already will.
- Bring an empty water bottle and fill it up after you get through security.

5 Don't be embarrassed to use the disability line at immigration

- If your HAE is triggered by fatigue, standing too long, or you're not feeling great, use the disabled lines at immigration to get to your destination sooner. It's not worth standing in the main line, triggering a swell, and needing to use your medicine, if you're embarrassed about looking fine and using the line.

And an extra tip:

If you haven't already, make sure to download the HAE Companion app.

- HAE Companion will provide you with an easy way to access and store HAEi's Emergency Card in many of the languages of the HAEi member countries.
- It also offers geofencing: the app will send you push messages when you are on the move in a new country.
- And last but not least, it provides you with a list of ACARE Centers and HAE-knowledgeable hospitals and physicians, and using GoogleMaps or Apple Maps, HAE Companion also indicates directions and distance to the nearest place.

apple.co/33Qn4ZK

Download on the App Store

bit.ly/3osxkzm

GET IT ON Google Play

NEWS FROM HAEi COUNTRIES AROUND THE GLOBE

In this edition of Global Perspectives, we present an adaptation so that it is both the Member Organizations, the Regional Patient Advocates, and HAEi that contribute news from the currently 96 member countries worldwide. For clarity, information from the Member Organizations is marked with 💬, while news from Regional Patient Advocates (RPAs) is marked with 🔖. No mark means the information is from HAEi.

UKRAINE

HAEi recognizes the horrific situation in Ukraine. HAEi members stand in support and solidarity with our fellow HAE brothers and sisters in Ukraine. HAEi understands that some Ukrainians are fleeing to neighboring countries for safety. HAEi advises those arriving in a country to reach out to the HAE Member Organization for advice on doctors and treatment centers for HAE assistance – please see https://haei.org/about-haei/globally.

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

AFGHANISTAN

🔖 *From RPA Fiona Wardman:*

We have welcomed HAE Afghanistan to our family in the last few months. As we all know, HAE is a burdensome disease, and in most of our countries, we have access to an orderly "state of the nation"; however, our HAE family in Afghanistan has many more hurdles than just HAE. I'll be working with the national contacts to improve the awareness and education of HAE, so there can be proper emergency care for Afghan people with HAE in the short term.

Afghanistan is country no. 96 to join the global HAE family. The national contacts are Khatera Naimi and Mohammad Ramin Naeemi. You can read more about Afghanistan at haei.org/hae-member-countries/afghanistan and follow the organization at facebook.com/profile.php?id=100089699169289.

UNITED KINGDOM

💬 *From Executive Officer Rachel Annals, HAE UK:*

We have had a busy few months, including arranging our next patient day. We have had a busy few months including arranging our next patient day; Saturday 20 May. Patients and their families as well as HAE professionals will join us to hear the latest news relevant to the UK, to meet with the team and other HAE friends.

The Rt Hon Sir Iain Duncan Smith MP and CEO Angela Metcalfe, HAE UK

We have also recently been working hard to raise awareness of HAE, not least by engaging with Members of the UK Parliament. In 2020 the UK Rare Disease Framework was published, setting out a coherent, national vision of how the UK will improve the lives of those living with rare diseases.

On Rare Disease Day 28 February 2023, the UK Government published its Rare Disease Action Plan on how the Framework is progressing. Angela Metcalfe, CEO of HAE UK, was delighted to meet the Rt Hon Sir Iain Duncan Smith MP to discuss how we are working to raise awareness of this rare disease, how we are ensuring equity of care across the country and devolved nations, and are putting together an action plan to educate and train emergency medicine practitioners about the condition.

In addition, the latest issue of "Revolution Magazine" was published, which was entirely focused on HAE. Many very interesting articles from patients and healthcare professionals were included, and we encourage you to have a read: https://bit.ly/RDD2023-HAE.

On 9 March 2023, Angela Metcalfe attended a Debate in Westminster Hall at the UK Parliament, which was led by Jim Shannon, Member of Parliament for Strangford in Northern Ireland. The 90-minute debate entitled "Patients with Rare Diseases" was attended by Liz Twist MP, Deidre Brock MP, Feryal Clark MP, and the Minister of State for Social Care, Helen Whately MP. It was excellent to have the opportunity for Jim Shannon to talk about HAE and other rare diseases and for the minister to then update and answer questions.

You can read the whole debate in the daily journal of Parliament "Hansard" at https://bit.ly/hansard2023.

On 20 May we held our first in-person patient day for 3 years, due to the COVID-19 pandemic, in central London. The event was well attended by patients and caregivers, and we had some fantastic presentation from some of our amazing HAE clinicians. We have received great feedback from attendees, especially highlighting how great it was to be back meeting their HAE "family" again. During our lunch break we took part in a beautiful sunny walk to celebrate HAE day on 16 May, around Russel Square. Everyone wore special HAE t-shirts to raise awareness and shoe togetherness. We are so thankful to everyone who joined us for the day and we very much look forward to our next event!

CHILE

We welcome the new Member Organization in Chile, Corporación Angioedema Hereditario Chile. The President is José Ignacio Contreras Silva, and he can be contacted via corporacion.aeh.chile@gmail.com as well as +56963373694. Also, you can find HAE Chile on both Instagram at https://www.instagram.com/corporacion_aeh_chile and Twitter at https://twitter.com/AehChile.

CORPORACIÓN
ANGIOEDEMA
HEREDITARIO

SWITZERLAND

From President Helene Saam, HAE Switzerland:

We would like to thank Mediaplanet and BioCryst for the production of a short video for Rare Disease Day 2023. You can watch the video here: qrco.de/bdonis.

Also, we have produced a film explaining HAE to patients as well as anyone else interested. The film explains in non-medical language what triggers the disease, how the processes in the body work and what can be done about it. The film – with English and German subtitles – can be seen at https://youtube.com/playlist?list=PLH2WqEquIjX7vleSR7H1UbcYPAlcLt7Kl.

Let us spread knowledge about HAE via social media –

please follow us on Instagram, link to us on Facebook, and chat with us on WhatsApp. See our social media platforms here: https://www.hae-vereinigung.ch/news/schweizer-hae-vereinigung-goes-social-media/

(Source: https://www.sbbhistoric.ch)

On 29 April 2023 we were able to welcome 52 people to our patient meeting in Olten.

Among them were again numerous doctors, representatives of the various pharmaceutical companies. We had a varied program with interesting topics about the film "HAE - Simply Explained", "What medication is available to HAE sufferers in Switzerland?", "For adults, children and adolescents", "State of Switzerland HAE Cohort Database", "The route of new medicines", and information from the Board of Directors.

We fortified ourselves with a fine lunch buffet before the afternoon program. A bus took us to the museum of old locomotives and wagons of the Swiss Railways, and at the end, we had a final aperitif before the journey home.

SPAIN

From RPA Maria Ferron:

On 20 February 2023, the 1st HAE patient workshop organized by CSUR (Reference Centers, Services or Units of the National Health System) took place at La Paz Hospital in Madrid. Dr. Teresa Caballero was the coordinator of the course, and I had the pleasure of introducing HAEi to the attendees.

From President Sarah Smith, HAE Spain (AEDAF):

25th General Assembly & Annual Meeting: The 25th General Assembly and Annual Meeting of AEDAF took place on Saturday 22 April 2023 in La Paz Hospital, Madrid. For this very special milestone for AEDAF, we presented the online course "Expert Patient in HAE", which was launched in May to coincide with **hae day :-)**, and we will pay tribute to Dr. Teresa Caballero for her long professional career dedicated to HAE.

AEDAF Camino Walk 2023: Once again, AEDAF had organized an **hae day :-)** event on the Camino de Santiago, which took place from 13 to 17 May 2023.

The aim of **hae day :-)** on 16 May every year is to raise awareness of HAE among the general public and medical community in order to create an environment in which there is better care, earlier and more accurate diagnosis, and recognition that people with HAE can lead a healthy life. One of the main reasons for walking the Camino is the publicity we can generate as an **hae**

AUSTRALIA & NEW ZEALAND

From Director Fiona Wardman, HAE Australasia

The first significant project for HAE Australasia has closed off this year is the HAE pharmaco and socioeconomic/quality of life survey. We look forward to receiving the data results, which will be used to advocate our ministries of health and pharmaceutical funding bodies about the importance of HAE patients' access to prophylactic therapies and the cost savings versus burden when the treatments are available.

HAE Australasia is about to embark on a Wellness Pilot Program across New Zealand and Australia for HAE patients. We look forward to recruiting patients and watching how the program will benefit patients by assisting them in managing their stress levels which may lead to lower attack numbers.

What a turnout we had from Australia and New Zealand at the 2023 HAEi Regional Conference APAC in Bangkok, Thailand. It was great to have 30 Australians and 10 New Zealanders come to Bangkok to learn more about HAE, network, and make new HAE friends from 13 other countries in the region. Thank you to everyone who took part and participated :)

day :-) event. The Camino Walk served as a statement that people with HAE, many of them frequently incapacitated by their attacks, are overcoming the obstacles to leading normal and fulfilling lives and can now feel free to undertake a journey of this nature.

This time we walked on the Portuguese route of the Camino de Santiago, an extensive network of pilgrimage routes leading to Santiago de Compostela in Galicia, in the northwestern part of Spain. We were walking an average of 15 km per day for three days and had a short walk on the fourth day to the shrine of the Apostle Santiago (St. James) in the Cathedral of Santiago de Compostela. We were welcomed at an institutional reception in Hotel Monumento San Francisco in Santiago on **hae day :-)** on 16 May.

AEDAF were delighted to welcome more than 30 pilgrims to the Camino Walk 2023.

DENMARK, NORWAY, AND SWEDEN

From Jørn Schultz-Boysen, Vice President, HAE Scandinavia

On 10 December 2022, HAE Scandinavia gathered 34 HAE patients and their family members in Norway to offer knowledge and information on various topics. In the city of Bergen, we had a very good Saturday with mostly people from the western region of Norway. The meeting was held in collaboration with the dermatology department at Haukeland University Hospital. Dermatologist Dr. Lene F. Sandvik gave information on their plan regarding the follow-up for HAE patients and how they are building a team with nurses to be a part of the health care for this patient group.

The national volleyball player, Kristian Morken Bjelland, shared his patient journey with HAE. Two years ago, the 30-year-old athlete was diagnosed with HAE after many years of swellings and stomach troubles – without any logical explanations. Then his mother and one of his two brothers were also diagnosed with HAE. His story resonated with many, who could relate to his struggles, fears, and hopes regarding living with this rare disease.

In this patient meeting, we had a big section regarding young patients. Our own youngsters, Victoria Schultz-Boysen and Nanna Maria Boysen, shared how young people suffering from HAE and their siblings are building a young community across borders. They hope more Scandinavian youngsters will join and benefit from having a young support system they can reach out to when needed.

HAE Scandinavia is working on several projects targeting young people. Our daily manager, Trine B. Boysen, could reveal we are making a podcast series with five episodes containing these topics: Community in a young HAE network, Education abroad, Travels abroad, Information about HAE to friends/colleagues/family etc., and "Youngsters" in the future.

She also revealed that one of our youngsters had gotten the opportunity to be a part of the LEAP project and will be working on how to get the youngsters included on our website.

HAE Scandinavia is also planning on publishing a children's book about HAE, which will be translated into Norwegian, Danish, and Swedish. In addition, we are translating the booklet "Understanding HAE" to all our languages to provide good and understandable information about HAE, which our members also can use in their dialog with the people around them.

We were also very fortunate to get nurse Siri Grønhaug from the National Competence Service for Rare Diseases to make a presentation. She has worked for many years preparing young people and their parents for a life with intravenous and subcutaneous medication. She shared tips and tricks on how to prepare a child and how to find good strategies for collaborating with healthcare personnel.

HAE Scandinavia's President, Henrik B. Boysen, presented a summary of the results of our pharmaco- and socioeconomic study. It highlights the burden of living with this disease from an economic perspective, but also the burden on the life of HAE patients and their

surroundings. Yes, it costs a great sum of money to treat HAE, but if all seizures could be avoided, society would be able to save money. New treatment options results in an 84 to 86% reduction in the number of seizures. This gives a significant improvement in the patient's quality of life. With the new treatment possibilities, we have come much closer to the medical vision of a seizure-free life for patients with HAE.

Another important part of the program was the treatment options available in Norway. Board Member Trine Dahl-Johansen guided the participants through the new rules and system regarding HAE medication in Norway. In April 2022, the Norwegian health administration for all national hospitals introduced price tender and rules for which products should be provided for this patient group. Even though the patients, for now, are allowed to stay on their current medication, the new system will require many to switch to a cheaper version in the future. We fear that it will be based on economics rather than a medical switch. And right now, there is officially only one prophylactic treatment available through the new tender system, even though our other member countries, Denmark and Sweden, have several options. This is an injustice that HAE Scandinavia is highlighting in our work targeting the health authorities.

We also looked into the crystal ball and talked about exciting new trials and studies which might lead to new treatment options in the near future.

Last fall HAE Scandinavia also held two successful meetings in Sweden, one in Malmö and one in Stockholm. These meetings gathered nearly 50 HAE patients, caregivers, and healthcare professionals from all over Sweden and featured informative lectures from Linda Sundler Björkman, a leading expert in HAE from the university hospital in Lund.

The first meeting was held in Malmö, a city in southern Sweden known for its beautiful architecture and vibrant culture. The event was held at a conference center in the heart of the city and attracted both healthcare professionals, patients, and caregivers. Attendees got the chance to network and acquire lots of knowledge and information. Linda Sundler Björkman who presented her research on HAE and told us about new medications and upcoming treatments, while Henrik Balle Boysen and Trine Balle Boysen gave useful information about HAE Scandinavia and Youngsters.

The second meeting was held in Stockholm, the proud capital of Sweden. The event was held at a conference center just outside the city center and attracted a similar audience as the Malmö meeting. Attendees had the opportunity to learn about stress management and MediYoga from Beatrice Casselholm de la Salles, who is a naprapath and mediyogatherapist. Also, one of our own Youngsters, Nanna Maria Boysen, shared information about Youngsters, and we were very fortunate to get Linda Sundler Björkman to make her presentation in Stockholm as well.

Both meetings were highly appreciated, providing attendees with valuable networking opportunities, practical knowledge, and new ideas for improving patient care. Now we look forward to autumn and the upcoming Scandinavian conference in Malmö, Sweden on 10-12 November 2023.

DOMINICAN REPUBLIC

From RPA Javier Santana:

A group has been formed to prepare an HAE conference. There have been conversations with me as well as with government officials and representatives of the medical school in Santo Domingo to coordinate the event.

EL SALVADOR

From RPA Javier Santana:

Raquel Fuentes, National contact of HAE El Salvador, continues to make efforts to educate about the existence of HAE and the treatments needed. She has visited hospitals and medical offices to talk about HAE as well as the existence of HAEi supporting patient groups globally.

UNITED ARAB EMIRATES

From RPA Michal Rutkowski:

There is also great news from the United Arab Emirates regarding access to modern HAE therapies: Takeda has reached an agreement, and as a result, lanadelumab can be available to all patients with a copayment liability on insurance. The local HAE expert physician must initiate this support patient program.

TUNISIA

From RPA Maria Ferron:

The 1st General Assembly of the HAE Tunisia (ANAOH) was held on Sunday 12 March 2023. Because the greater number of HAE patients are located in the north of the country, the city Beja was chosen for the meeting. Thirty-six patients attended the meeting, and they are now planning another patient meeting in the near future in the south of the country to make it more accessible to the patients from that region.

During the meeting, the main roles of the association members were officially allocated, and a patient identification card was issued to the patients who attended the meeting.

FINLAND

From RPA Jørn Schultz-Boysen:

In late March, I had the pleasure of presenting at the yearly Finnish patient meeting. It was the first in-person meeting in Finland after the COVID-19 outbreak.

UNITED STATES

From Director of Engagement & Communications Ianice Viel, US HAEA:

We are dedicated to providing our 8,000 members with programs, services, and activities that engage and unite the community in a common goal focused on improving quality of life for people with HAE.

HAEA Round Tables: Because HAE is so rare, people can feel isolated when dealing with the everyday challenges of learning how to live with this chronic illness. When we come together as a community and talk about our struggles, however, we realize that we are not alone in our efforts to live a normal life.

That is why US HAEA has developed the HAEA Round Table. This platform connects members of our community with their peers on the issues that currently affect them, including:

- HAE and Relationships
- Aging and HAE
- Caregivers for HAE

The HAEA Round Table will be posted every other month on our official Facebook page Live. Round Table recordings can be accessed at https://vimeo.com/user/115781635/folder/8930101.

HAEA Community Blog: The HAEA Community Blog is a platform that allows people with HAE to share their unique stories on a wide variety of topics ranging from emotional health to treatment.

Featured Blog Articles:

"Running was something that I always loved to do, so I was very grateful to be able to use something that I loved to work towards making a difference."

Read **The Caregiver Journey: How I Ran for a Change** at https://www.haea.org/pages/bp/Blog12_Ava

"Despite my HAE attacks increasing in frequency during pregnancy, I was determined to be proactive in my care and treatment to ensure that my HAE was well managed."

Read **A First Time Mom's Experience Managing Her HAE While Pregnant: Lisa's Story** at https://www.haea.org/pages/bp/Blog15_Lisa

Advances in Research:

Updates in HAE Care from the US HAEA: We are pleased to announce a new, free CME Program for Medical Professionals "Updates in Hereditary Angioedema Care from the HAEA". This continuing education activity brings together several expert HAE physicians who will provide highlights from the US HAEA Medical Advisory Board 2020 Guidelines for the Management of HAE, as well as discuss emerging prophylactic and therapeutic agents, and practical approaches to patient-centered care. The CME Program is available at www.haea.org.

HAEA Study on the Number of People with HAE in the United States: The prevalence of HAE has been estimated to be anywhere between 1 in 10,000 to 1 in 100,000. In 2022, we began pilot testing an approach that could potentially provide a more accurate estimate. Our methodology has two basic steps. First, we analyzed insurance claims to identify subjects who had HAE-related tests performed and medicines prescribed. Second, a panel of expert physicians reviewed the group identified in the first step and reached a consensus on whether or not the data pattern observed pointed to HAE as the diagnosis. The initial results from the pilot test will be available in the Summer of 2023.

An HAE-Specific Instrument to Measure Quality of Life: The US HAEA is working on a unique, ground-breaking research study that seeks to illustrate how HAE affects overall quality of life (QoL). Ultimately, the objective is to develop and validate a broad-based HAE QoL instrument that accurately depicts the burden of living with the disease. This research will help us publish a QoL questionnaire that truly captures the way HAE affects the everyday life of people with HAE. The QoL instrument has been validated through surveys that included 410 participants. A manuscript is being prepared for publication.

Shared Decision-Making Tool: We have designed and field-tested a Shared Decision-Making tool that can now be accessed at www.haea.org. The tool has been designed to provide an overview of your HAE before meeting with your physician to discuss a treatment plan. The HAE Shared Decision-Making Tool will provide an overview of your HAE journey to date and form the basis for collaboration between you and your treating physician. The questions in the tool are designed to better understand your current experience with HAE while capturing your goals for the future. Your answers will empower a joint decision-making process to enable the creation of your personalized treatment plan.

KENYA

From President Patricia Karani, HAE Kenya:

A new HAE-knowledgeable physician – Dr. Anne Barasa – has joined our team of HAE doctors in Kenya. She is an immunopathologist based in the largest referral hospital in Nairobi, the Kenyatta National Hospital. She is also a lecturer at the Immunology unit under the Department of Human Pathology at the University of Nairobi. Dr. Batasa has written numerous publications on various conditions and has expressed her interest in taking care of HAE patients in the country.

A new HAE family has been identified and properly diagnosed by the lead HAE doctor in Nairobi, Dr. Priya Bowry, based at The Allergy Clinic. Dr. Bowry is an allergy immunologist who has continuously shown her dedication and interest in taking care of patients with HAE in Kenya.

Around Rare Disease Day, HAE Kenya sought to reach out to a wider audience and have a louder voice via the local radio station, Radio Citizen, on 25 February 2023.

PHILIPPINES

One of the most recent countries to launch a website under HAEi's wings is the Philippines.

Have a look at haephilippines.haei.org.

IRELAND

From RPA Maria Ferron:

Since the beginning of 2023, we have had a new Member Organization Lead in Ireland, Bettina Carty. She is a patient herself and a caregiver – and is starting in her duties from the beginning, but she is really enthusiastic and willing to improve the situation in the country.

Contact Bettina Carty at bettinancj@gmail.com.

HAE Ireland
Patient support group

BRAZIL

From President Raquel de Oliveira Martins, HAE Brazil (ABRANGHE):

By 31 December 2022, there were 1,841 people with HAE registered in Brazil. During the year, ABGRANGHE assisted more than 300 new patients, of whom 58 were confirmed with HAE, 78 were waiting for confirmation, and 169 were not confirmed.

ITALY

From HAE Italy (A.A.E.E.):

Joint assembly: The joint assembly of ITACA and A.A.E.E members took place on 15 April 2023 at the university hospital of Tor Vergata, in Rome. The physicians of ITACA's 23 centers of excellence, the board of the patient association, HAEi's Regional Patient Advocate Maria Ferron, the representatives of the pharmaceutical companies and a large number of patients were present.

After the greetings of the authorities, Marco Mattei (Head of the Technical Secretariat of the Ministry of Health) and Andrea Magrini (Medical Director of Tor Vergata), Dr. Mauro Cancian, President of ITACA, gave a brief excursus on what is going on such as regards angioedema in Italy. He underlined that three new ITACA centers will be activated and that by the end of March, the Registry was back available. He also reminded the attendants of the importance of working with HAEi to achieve greater results and the recognition as an ACARE center of excellence.

Dr. Montinaro continued by presenting the currently available therapies and the studies in progress, highlighting that six new experimental drugs have been added in the last ten years. The new drugs can reduce attacks by 90%, and subcutaneous or oral administration significantly improve the quality of life of patients.

Dr. Zanichelli underlined that new treatments and prophylaxis therapy could better control the disease, and therefore ITACA will carry out a study on the quality of life, and an AE-Qol questionnaire will be used within the Registry to verify improvements or worsening of the disease.

Dr. Paola Triggianese concluded the scientific reports, presenting the PDTA (Diagnostic Assistance Pathway) as an essential tool for having an accurate diagnosis. The PDTA is made up of various specialists: the gastroenterologist, the neurologist, the ophthalmologist and the gynecologist.

Dr. Francesco Arcoleo managed the question-time patients/doctors where patients had the opportunity to ask both general and personal questions to clarify doubts and have certainties about new therapies that represent a great opportunity for the present and for the future.

Then followed a presentation of the organization and activities of HAEi by Maria Ferron and Nilla Ciairano,

Vice President of the patient association, inviting patients to greater participation in the regional conferences managed by HAEi, which provide three paths: one for patients and caregivers, one for young people (12-15 years) and a scientific path.

Carlotta Cicardi, who manages the secretariat with Martina Perera, presented the activities carried out in 2022 and the future activities of 2023:

- registration campaign of 2022, which provided the association with a 32% increase
- our first joint assembly in 2021 in Padua
- management of social pages and website
- collaboration with external companies (as workshop focused on QoL in collaboration with ATRAST)

The Assembly was concluded by President Pietro Mantovano, who asked for 2022 report approval and then presented:

- relations with external organizations (Telethon etc.)
- relations with ITACA and the various centers of excellence
- relations with the representatives of the pharmaceutical companies
- ITACA Academy Project (Todi 2022) to raise new specialists in angioedema; senior physicians tutor junior physicians in order to optimize clinical disease management and improve patients' quality of life.

Awareness day: On **hae day :-)** 2023, the "Angioedema Day - yesterday - today – tomorrow" conference of the doctors of ITACA in Rome was held at the Press Room of the Chamber of Deputies at the Italian Parliament, which was attended by representatives of the institutions, clinicians, and patients. We had the opportunity to present HAE to the press.

At the moment, the disease is underestimated by the population and sometimes also by medical personnel; therefore, more information is needed, and the title of the awareness day was: "Knowledge is not rare". Doctors had the opportunity to illustrate the disease, how it manifests itself, how it is treated, and the objectives that science sets intend to achieve for early diagnosis and how to improve the quality of life of patients.

The patient association has invited the institutions to allow the use of the new drugs throughout the country, avoiding differences from region to region.

During the event, the initiatives to be held on 20 May 2023 for the Angioedema Day promoted by ITACA were

presented, in particular the "Patient Card", a new IT tool with all the patient's personal clinical data. Through a QR code, general practitioners and emergency room personnel can access a section of the ITACA web portal and have all the correct information on how to intervene in the event of an acute attack of this rare pathology.

On www.angioedemaitaca.org there are videos and press releases from dozens of newspapers.

Angioedema Day: The Angioedema Day held on 20 May 2023 aimed to raise awareness and create attention towards our disease. Angioedema is managed by different specialists including above all allergists, immunologists, and internists. During the day, patients could go to the specialized health centers of the ITACA network for a check-up or for a first contact with the specialists.

The main objective of this day is to facilitate access to the nearest ITACA center, improve disease management and quality of life.

BELGIUM

From Chairwoman Vinciane Berckmans, HAE Belgium:

On 6 May 2023, an event for Belgian HAE patients with the participation of experts was held at the Faculty Club in Leuven. Attendance was possible both in person and via Zoom.

SOUTH AFRICA

From RPA Fiona Wardman:

HAE South Africa is making fantastic progress on all fronts, with awareness and education of HAE in the community and acute therapy now registered!

From Chairman Janice Strydom, HAE South Africa

We are pleased to announce the launch of the Sinovuyo South African Virtual Angioedema Center, the first of its kind in Africa. The center is the virtual arm of the UCT Lung Institute, Allergy & Immunology Unit, under the leadership of Prof. Jonny Peter and his expert team of angioedema specialists. The center is named after Sinovuyo Nkelenjane, a seven-year-old girl who tragically lost her life during an angioedema attack. You'll find the virtual center at https://aiu.haei.org.

We embarked on a social media campaign during February 2023, where various media articles and radio interviews were conducted to raise awareness and introduce the new concept to medical professionals and the South African public. We have already had a number of inquiries and appointments made via this new virtual concept.

The HAE TrackR App is now available to patients in two additional South African languages, Afrikaans and Zulu.

We are also thrilled to announce that we have finally received approval from the South African Health Products Regulatory Authority for icatibant, the first acute therapy to be approved for our patients.

For **hae day :-)** 2023, we encouraged patients, caregivers, and our doctors to join in the fun and add their steps for the HAEi Activity Challenge. Reminders were regularly sent on our WhatsApp group and shared via our social media pages. Rare Diseases South Africa supported our #activeforHAE challenge by sharing our media posts on their "Rare Aware" media pages. From 1 May 2023, in the run-up to the awareness day, we shared a series of patient stories as well as introduced our partners and colleagues from the medical and rare disease industry who contribute a big part towards the diagnosis and treatment of our patients as well as providing support and guidance for our organization.

COSTA RICA

From RPA Javier Santana:

The situation regarding HAE medications continues to develop drop by drop. After a meeting held last year between the group of patients, rare disease patient associations from Costa Rica, the Minister of Health, the Medical Directors of the country's main hospital, Government representatives, and myself, the entry of Berinert and icatibant was authorized for patients with HAE. Due to the meeting, the Government finally gave one of the medicines to a patient who was hospitalized for many weeks after an HAE attack. Until that point, medical specialists had refused to give her medicines for HAE attacks despite the request of specialist doctors from Costa Rica, physicians from other countries, international patient groups, and the HAEi Board of Directors. However, despite the entry and purchase of medicines for HAE patients being authorized, the problem continues as entry is not allowed for the number of patients with HAE attacks in the country.

HAE Costa Rica has decided to create a larger group of leaders and professionals to achieve greater results.

Jairo Gonzalez has taken over as President, while Jesus Gonzalez is new Vice President. Please see the contact information at https://haei.org/hae-member-countries/costa-rica/

PERU

From RPA Fernanda Oliveira de Martins:

I was invited to participate in a meeting organized by HAE Peru 27 February 2023. The main topic of the meeting was HAE in school children. I congratulate the organizers and invite everyone to watch to the recording og the meeting (in Spanish) at https://fb.watch/iZR2LLwQ_G/.

From Directora General Carla M. Goachet Boulanger, HAE Peru:

As the main activity for **hae day :-)** 2023, we organized an HAE Peru Family Day. We meet with patients, family and friends who are part of HAE Peru to commemorate the awareness day, among other things by sharing lunch, having integration games, and watching an artistic show for the entire HAE Peru family.

RUSSIA

From President Elena Bezbozhnaya, HAE Russia:

In recent months, HAE Russia has expanded to include new members. Over the seven years of its existence, we have already united more than 300 participants. We try to do our best so that our patients with HAE are not left alone with their disease and related problems. We provide them with legal, counseling, and psychological support. We pay special attention to families with children diagnosed with HAE.

In the fall of 2022, we offered our members training in creating video content for social media. At the end of the course, participants were asked to make short video stories based on the personal experiences of patients with HAE. We wanted the participants who completed the course to benefit from the practical application of their skills. In addition, these video stories would inform more people about the existence of such a rare disease and highlight the difficulties experienced by patients with HAE. Both parents of children with HAE and the children themselves – schoolchildren and teenagers – created the video stories. The videos turned out to be very sincere and really touching. We timed the final video story marathon to coincide with Rare Disease Day, celebrated around the world on 28 February.

At the end of 2022, HAE Russia published an almanac, presenting current information with answers to the questions that most often arise for patients with HAE and treating physicians – causes and symptoms of the disease, classification, epidemiology, and updates on diagnosing and treating the disease. Besides, the almanac includes current legal information and psychological advice.

In January 2023, we launched a new series of informative webinars, useful and interesting both for newcomers and regular participants of our events from different regions of Russia. For these online meetings, we invite the best experts in a variety of fields – doctors, lawyers, psychologists, and scientists, who introduce patients to all the changes in the legal, medical, and pharmaceutical areas concerning the provision of medicines, HAE diagnosis, and therapy. The first webinar of the series was held on 21 January 2023. We addressed the most relevant issue for HAE patients: a step-by-step algorithm to obtain advanced medicines. On 24 February, patients with HAE participated in the second online meeting of the series, "Counseling Hour". This time we covered not only legal and medical problems but also the possibilities of psychological rehabilitation. I invited members to join the free diagnostic programs for children and relatives of patients with HAE, which are now being implemented in Russia. All webinar participants were given an opportunity to ask questions and get individual expert advice.

In February, we invited children diagnosed with HAE to another online event held within our "Call a Friend" project. Analytical psychologist and art therapist Yulia Faikova and her co-host, project administrator Daria Bezbozhnaya held a "color therapy" lesson for children and trained the participants to express their emotions, feelings, and experiences. At such meetings, children learn to communicate and cope with stress, which is very important for young patients with HAE.

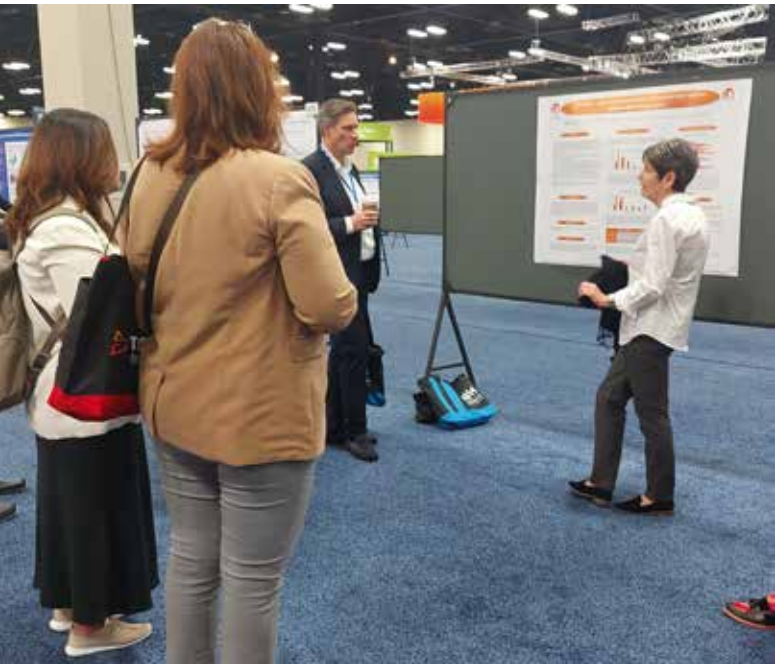
At the end of 2022, HAE Russia signed a cooperation agreement with the Circle of Kindness Charity Foundation. The Foundation supports and provides medications to children and adolescents with orphan diseases. The Foundation's wards include 20 children with severe HAE. The Circle of Kindness Foundation supply all of them with the long-term therapy lanadelumab. Recently, a very important decision was approved to extend support for children with rare diseases until the age of 19; until 2023, the foundation supported only patients under the age of 18.

The starting partnership project of HAE Russia and the Circle of Kindness Charity Foundation was to organize patronage schools in different Russian cities for families raising children diagnosed with HAE. The first patronage school opened in Kazan city on 17 March 2023, based at the Children's Republican Clinical Hospital. The meeting was held in a hybrid face-to-face and online format. The school participants included HAE patients, parents of children with HAE, and physicians, that is, pediatricians, therapists, allergists-immunologists, and other profile specialists. More than 150 people attended the event. The experts presented a clinical picture of the disease and spoke about the types of edemas and methods of diagnosing and treating the disease. The speakers highlighted a multidisciplinary approach involving specialized physicians – dentists, surgeons, gynecologists, and other specialists – together with allergists and immunologists in treating concomitant diseases of HAE patients. Our representatives informed the participants about HAE patient routing, developed by HAE Russia, and outlined our social and educational projects.

CANADA

From HAE Canada:

The first event of the year was the 2023 American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting in San Antonio, Texas, United States. Thank you to Suzanne Kelly of Red Maple Trials, who presented the HAE Canada poster on our behalf, titled "Emergency room visits by patients with HAE based on data from the Canadian 2020 national survey". As one of the authors, she did an amazing job.



We have learned that the event was a great success, and we were excited knowing there were many posters showcasing the latest HAE research. As always, we want to extend our thanks to the co-authors, as well as our Advocacy Committee, for their collaboration and support on the abstract and poster.

You can have a look at the poster here: https://haecanada.org/posters-abstracts/.

We are thrilled to share that the Canadian Agency for Drugs and Technologies in Heath (CADTH) recently announced that they are recommending the oral treatment Orladeyo (berotralstat) for reimbursement. This is a significant accomplishment, as Canadian patients are now one step closer to accessing this oral treatment.

As mentioned in an earlier issue of Global Perspectives, HAE Canada provided the patient perspective through CADTH's patient submission process. At first, CADTH decided not to recommend reimbursement. However, this decision was reversed after further advocacy work and an additional submission from HAE Canada.

Overturning a CADTH decision and getting a funding recommendation changed is a landmark event. We would not have achieved this in Canada without the extraordinary effort, expertise, and time invested by Jacquie Badiou, HAE Canada's Past President & Advocacy Committee Chair, with the assistance of Anthony J. Castaldo and Henrik Balle-Boysen of HAEi. We want to extend a huge thank you to Jacquie and also to the team at HAEi and the Advocacy Committee, who assisted her with this amazing accomplishment. Thank you also to COO Daphne Dumbrille, and Kim Speiss, Regional Director Central, who helped ensure HAE Canada was given a seat at the table at the reconsideration meeting with CADTH.

To celebrate Rare Disease Day, HAE Canada's President, Michelle Cooper, attended a Breakfast Reception in Toronto, Ontario, that was organized and hosted by the Canadian Organization for Rare Disorders (CORD). There were many attendees and a wide variety of speakers, including Durhane Wong-Rieger (CEO of CORD), multiple Ontario Members of Provincial Parliament (MPPs), Rute Fernandes (General Manager of Takeda Canada), a patient advocate representative, and a physician from Toronto's Sick Kids hospital. The speakers discussed how the Ontario government and health sector stakeholders need to collaborate to

develop a rare disease strategy that allows patients to equitably access new therapies.

The Toronto Rare Disease Day event set the stage for the March 22 announcement from the Canadian federal government: "up to $1.5 billion over three years will be provided to implement the Rare Disease Drug Strategy". Working with patient advocacy groups across Canada, CORD consulted with multiple key stakeholders to develop a strategy that will meet the patient's needs while remaining fiscally responsible in Canada's public healthcare system. Over her years as President, Jacquie Badiou, while collaborating with Anthony J. Castaldo and Daphne Dumbrille, provided insight and input to CORD in a variety of ways, from participating on a panel to filling out a survey to help ensure this strategy will benefit rare disease patients in Canada. Thanks to this advocacy work from Jacquie, Daphne, and others in the CORD family,

The strategy not only aims to provide better access to therapies but will invest in infrastructure to facilitate faster diagnosis and ongoing patient monitoring. HAE Canada is proud to be part of CORD and grateful to finally have a strategy that will help patients in Canada with a rare disease.

Michelle Cooper was lucky to spend 27 March 2023 attending CORD's Action Day on Parliament Hill, where she, along with other patient advocacy group representatives, met with Members of Parliament, Senators, and other government officials. They discussed how rare diseases impact Canadian families and communities, and what the federal government can do to provide much-needed support. Following the day on the Hill, Michelle and Daphne attended CORD's spring conference in Ottawa (while Jacquie participated virtually) titled "Delivering on Canada's Rare Disease Investment". Experts from across Canada, including physicians, patient group representatives, and government and pharmaceutical representatives, presented throughout the two-day conference discussing how to optimize the newly announced Rare Disease Drug Strategy in Canada. By the end of the conference, people were feeling hopeful and energized. We are proud to have a long-standing relationship with CORD, participating in Action Days and many conferences and webinars with current and previous board members.

To honor Rare Disease Day 2023, Kim Speiss shared her patient journey in Patient Voice, an online publication that helps amplify the patient voice to help decrease the stigma many patients with a rare disease face. HAE Canada is proud to have an HAE patient featured in Canada's Rare Voices 2023. Thank you, Kim, for generously sharing your story. You can read Kim's story here: https://www.patientvoice.io/rarevoices/kim?fbclid=IwAR0s4g0TUt7fFlBnJmSgqgpdlVdi286bagY5W41_ZzHO4FCACSmPVOfarj0.

HAE Canada started celebrating **hae day :-)** slightly early by hosting a hybrid Patient Information Update on 29 April 2023 in Edmonton, Alberta. This was our first in-person event since the start of COVID-19, and it goes without saying that we were absolutely thrilled to bring people together. Pacific Regional Director Kerstyn Lane expertly organized this event that brought in members from the area to hear about the latest news from the HAE community. Attendees enjoyed a variety of presentations, specifically from:

- HAEi's Anthony J. Castaldo, who discussed HAEi's role internationally,
- Jacquie Badiou, who introduced Michelle Cooper as the new President,
- Michelle Cooper, who provided an update on the latest HAE Canada events and accomplishments,
- Kerstyn Lane who kept everyone's full attention while she generously shared her incredible patient story,
- Dr. Bruce Ritchie, who kindly joined us remotely from his holiday in Spain, discussed HAE patient care in Edmonton and treatment options, and
- Dr. Adil Adatia, who presented on how HAE causes swelling, how to effectively treat attacks, the role of genetic testing and current and upcoming treatments.

Daphne Dumbrille moderated the Q&A session at the end while Heather Dow worked behind the scenes on Zoom to allow members from across the country to join the meeting virtually. We were very pleased

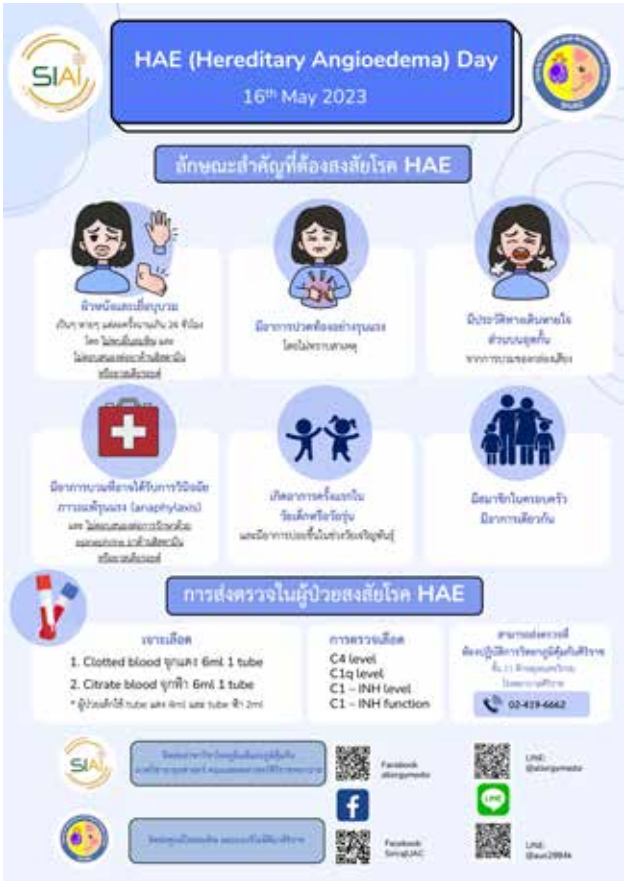
to have many in attendance on a Saturday afternoon. Thank you to our speakers for taking time out of their weekends to spend it with us. We are very lucky to have such dedicated physicians in Canada who volunteer their time to ensure patients are well-informed. At the end of the event, we encouraged everyone, both in Edmonton and across Canada, to engage in an activity and add their "steps" to the Global Activity Challenge.

Michelle, Jacquie, Kerstyn, Kim, and Daphne had the pleasure of spending 16 May 2023 with Anthony J. Casteldo and Henrik Balle-Boysen in Ottawa. All were in Ottawa to attend the Canadian Agency for Drugs and Technologies in Health (CADTH) Symposium to learn about important advocacy topics; from the importance of collecting real-world evidence (RWE) to how to accelerate access to new health technologies. It was wonderful to spend **hae day :-)** with Tony and Henrik – we all added our steps to earn the designated **hae day :-)** badge.

THAILAND

From HAE Thailand:

For **hae day :-)** 2023, Siriraj Urticaria and Angioedema Center organized and disseminated a poster and video on the topic "Hereditary angioedema (HAE) knowledge for physicians". These informative materials aimed to educate physicians about essential aspects of HAE, including its signs and symptoms, diagnostic investigations, and treatment. The distribution of these resources encompassed various channels, including the hospital itself, its official Facebook pages, and the LINE messaging platform. As a result, many physicians have shown a keen interest in these materials. This opportunity has increased awareness and understanding of HAE among physicians.



CROATIA

From President Mihaela Šogorić, HAE Croatia:

On 13 May 2023, an electoral assembly was held in Tuheljske Toplice where the Board of Directors was elected. With Ante Čobanov as Vice-President and Saša Pavlić as Secretary of HAE Croatia, I was elected President for another term.

After the assembly, doctors dealing with HAE arranged a lecture for us patients and our family members. Prof. Jasminka Milas Ahić from Clinical Hospital Centre Osijek spoke on "Genetics of HAE?", Primarius Marko Barešić, MD, PhD from Clinical Hospital Centre Zagreb gave a talk on "Short-term and long-term prophylaxis of HAE", and Boris Karanović, MD, from Clinical Hospital Centre Zagreb spoke about "Pregnancy and HAE". Furthermore, Marin Petrić, MD, from Clinical Hospital Centre Split addressed the topic "HAE patient-physician communication", while Primarius Ljerka Čulav, MD, PhD from General Hospital Šibenik spoke about "Upcoming drugs for the treatment of HAE". Also, there was a presentation by Jelena Vukić, med. tech. from General Hospital Šibenik on "Education on self-administration of medicine".

After the lectures, the administration of Tuheljske Toplice, in support of **hae day :-)** 2023, lit up the Mihanović Castle in purple. We thank them very much for that.

The meeting continued on 14 May 2023, with the psychological workshop of Maja Batista, PhD, clinical psychologist from Clinical Hospital Center Sestre Milosrdnice. The workshop was attended by all patients, family members and all nurses.

On **hae day :-)** 2023, the city of Osijek provided support to patients and lit the Osijek Pedestrian Bridge in purple. At 8:00 p.m., a few citizens, patients, nurses, and doctors from the Osijek Clinical Hospital Center gathered at the bridge. The event was also covered by the media.

We would like to thank everyone who, through their engagement, tries to bring this rare disease closer to the public and who are always with us in our small HAE community.

SOUTH KOREA

From Chairman Soojin Min, HAE Korea:

I congratulate HAEday2023 #active4HAE on an impressive achievement in Korea! We are pleased that the number of steps for **hae day :-)** reached 647,966, with over 280 people participating. By coming together and participating in this event, we have not only contributed to our own welfare but also developed a sense of unity and support within the community.

We shared HAE events on our social media platform with a larger audience to upload HAE events on HAE day #active4HAE. By doing so, we could encourage others to participate in physical activities and promote the importance of awareness of the disease. Social media has become a powerful tool to spread positive messages and encourage others. Congratulations once again on the successful event, and I hope that HAEi's support and SNS uploads will inspire many participants and more people to participate in future activities.

Thank you for the participation of many countries around the world, and HAE Korea will also take the lead in promoting HAE with more activities in the future.

LITHUANIA

From RPA Michal Rutkowski:

Great news from Lithuania regarding access to modern HAE therapies: As of 1 January 2023, icatibant is reimbursed for Lithuanian HAE patients, and as of 1 March 2023, lanadelumab is also reimbursed for people in Lithuania suffering from HAE.

PANAMA

From RPA Javier Santana:

Since 2022 the group of patients and HAE specialist doctors have held multiple meetings with government officials to discuss the shortage of HAE medicines. Despite the constant promises to resolve the situation of drug shortages, the Panamanian government still evades its responsibility to provide patients with HAE with medication and guarantee them a quality of life.

NORTH MACEDONIA

From Natasha Jovanovska Popovska, HAE Macedonia:

HAE Macedonia – association of patients and families with HAE – celebrated **hae day :-)** by organizing a visit for HAE patients and their families to the Lesnovo Monastery and the nearby caves in Macedonia.

The event raised great interest among patients with HAE and their families and happened in an informal, friendly atmosphere of exchanging experiences on dealing with HAE. The walk was pleasant, the landscape and nature surrounding the Monastery were serene and calming, and the entire experience was quite enjoyable.

The celebration of this important day for over a decade has significantly helped in raising awareness of HAE, which resulted in available medications in many countries of the world. In addition to raising awareness, the day has created a platform for bonding of patients and their families, which is also important for better processing the hardships of having HAE.

The motto of the **hae day :-)** "Many faces, one family" signifies the importance of support and care for all people suffering from HAE throughout the world, who are united by a common thread: hereditary angioedema. The motto embraces the possibility of belonging to a close-knit community – HAEi – that provides support, lends a hand and comfort and gives inspiration and motivation to fight together as a global family for our rights to medications, education, employment, and social engagement.

MEDICAL PAPERS

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

A comprehensive management approach in pediatric and adolescent patients with HAE – *by Raffi Tachdjian, UCLA School of Medicine, the United States, et al.:*

HAE management plans are critical to optimize outcomes and should address on-demand treatment for acute attacks and plans to prevent potentially fatal laryngeal attacks. The plan should also comprise a holistic approach to address nonclinical aspects of HAE, including quality of life and psychological issues.

(Clin Pediatr (Phila), March 2023)

A multicriteria decision analysis (MCDA) applied to three long-term prophylactic treatments for HAE in Spain – *by Néboa Zozaya, Weber, Spain, et al.:*

A multidisciplinary committee of 10 experts assessed the value of lanadelumab (subcutaneous), C1-inhibitor (intravenous), and danazol (orally), using a placebo as a comparator. Lanadelumab was assessed as a high-value intervention, better than C1-INH and substantially better than danazol for long-term prophylactic treatment of HAE.

(Glob Reg Health Technol Assess, December 2022)

An investigational oral plasma kallikrein inhibitor for on-demand treatment of HAE: a two-part, randomized, double-blind, placebo-controlled, crossover phase 2 trial – *by Emel Aygören-Pürsün, University Hospital Frankfurt, Germany, et al.:*

Oral administration of sebetralstat was well tolerated and led to rapid suppression of plasma kallikrein activity, resulting in increased time to use of conventional attack treatment and faster symptom relief versus placebo. Based on these results, a phase 3 trial to evaluate the efficacy and safety of two dose levels of sebetralstat in adolescent and adult participants with HAE has been initiated.

(Lancet, February 2023)

A review of berotralstat for the treatment of HAE – *by Henriette Farkas, Semmelweis University, Hungary, et al.:*

The availability of the first targeted oral prophylactic drug, the kallikrein inhibitor berotralstat, in 2021, is a milestone in the treatment of patients with HAE.

(Expert Rev Clin Immunol, February 2023)

Burden of illness seen in HAE in Japanese patients: Results from a patient-reported outcome survey – *by Beverley Yamamoto, Osaka University, Japan, et al.:*

HAE is associated with considerable physical, social, economic, and psycho-social burdens even after diagnosis, and higher attack frequency is associated with a heavy disease burden for patients in Japan.

(Intractable Rare Dis Res, February 2023)

Consensus on diagnosis and management of HAE in the Middle East: A Delphi initiative – *by Marcus Maurer, Charité - Universitätsmedizin Berlin, Germany, et al.:*

The global World Allergy Organization/European Academy of Allergy and Clinical Immunology International guideline for HAE management is comprehensive, but the implementation of this guideline may require regional adaptation considering the diversity in disease awareness, type of medical care systems, and access to diagnostics and treatment. The aim of this Delphi initiative was to build on the global guideline and provide regional adaptation to address the concerns and specific needs in the Middle East. The Consensus panel comprised 13 experts from the Middle East (3 from the United Arab Emirates, 3 from Saudi Arabia, 2 from Lebanon, 2 from Kuwait, 2 from Oman, and 1 from Qatar) who have more than two decades of experience in allergy and immunology and are actively involved in managing HAE patients. A consensus was reached based on a 70% agreement between the participants. The key highlights include:

HAE experts in the Middle East emphasized the importance of a positive family history for arriving at a diagnosis of HAE.

The number of episodes per month or per 6-month period and severity should be used, together with other markers, to determine the need for prophylaxis.

Disease status should be monitored by periodic visits and the use of patient-reported outcome measures such as the angioedema activity score and the angioedema control test.

Attenuated androgens and tranexamic acid may be considered for long-term prophylaxis, if lanadelumab, C1-Inhibitor, or berotralstat are not available.

(World Allergy Organ J, December 2022)

CU06-1004 alleviates vascular hyperpermeability in a murine model of HAE by protecting the endothelium – *by Sunghye Lee, Yonsei University, South Korea, et al.:*

Our study shows that oral administration of the endothelial dysfunction blocker CU06-1004 significantly reduced vascular hyperpermeability in the HAE murine model by protecting the endothelial barrier function against bradykinin stimulation. Therefore, protecting endothelium against bradykinin with CU06-1004 could serve as a potential prophylactic/therapeutic approach for HAE patients.

(Allergy, February 2023)

Efficacy, pharmacokinetics, and safety of subcutaneous C1-esterase inhibitor as prophylaxis in Japanese patients with HAE: Results of a Phase 3 study – *by Tomoo Fukuda, Saitama Medical University, Japan, et al.:*

Subcutaneous C1-INH (60 IU/kg twice weekly) was efficacious and well tolerated as prophylaxis against HAE attacks in Japanese patients with HAE types I or II, which was supported by the increased and maintained C1-INH functional activity.

(Allergol Int, February 2023)

Epidemiology, management, and treatment access of HAE in the Asia Pacific region: Outcomes from an international survey – *by Philip H. Li, University of Hong Kong, et al.:*

HAE in the Asia Pacific Region differs from that in Western countries. HAE-specific medications were registered in only a minority of countries and territories, but those with patient support groups or regional guidelines were more likely to have better access. Asia Pacific-specific consensus and guidelines are lacking and urgently needed.

(J Allergy Clin Immunol Pract, April 2023)

Gene mutations linked to HAE in solitary angioedema patients with normal C1 inhibitor

– by Konrad Bork, Johannes Gutenberg University, Germany, et al.:

A search for normal C1-INH-linked mutations in patients with solitary chronic recurrent angioedema without wheals may lead to the detection of patients and families with normal C1-INH. This is important because family members can be identified who are at risk for developing potentially life-threatening angioedema, although they were previously asymptomatic. Without genetic investigation, the risk for a normal C1-INH would have remained undetected in these patients and asymptomatic relatives.

(J Allergy Clin Immunol Pract, February 2023)

Geriatric pharmacotherapy case series: Recurrent angioedema following discontinuation of ACE inhibitor therapy

– by Bryton Perman, Creighton University School of Medicine, the United States, et al.:

Angiotensin-converting enzyme inhibitors (ACEIs) are the most common cause of drug-induced angioedema in the United States. While health professionals recognize the risk for angioedema with active ACEI use, it is not well known that the risk of angioedema may occur for months following cessation of ACEI therapy. Increased awareness of delayed ACEI-induced angioedema following ACEI discontinuation is important for both providers and pharmacists to provide appropriate diagnosis and monitoring. Improved awareness would also allow patients with a history of ACEI-induced angioedema to be cognizant of the potential for recurrence following drug discontinuation.

(Sr Care Pharm, January 2023)

HAE: Impact of COVID-19 pandemic stress upon disease-related morbidity and well-being

– by Sandra C. Christiansen, University of California San Diego, the United States, et al.:

The results of online questionnaires implicate a deleterious impact of stress in the aftermath of COVID-19 awareness on HAE morbidity. The female subjects were universally more severely affected than the male subjects. Overall well-being and/or quality of life and optimism for the future deteriorated after awareness of the COVID-19 pandemic for the subjects with HAE and non-HAE household controls.

(Allergy Asthma Proc, March 2023)

HAE: 24 years of experience in a Portuguese Reference Center

– by C. Varandas, Centro Hospitalar Universitário Lisboa Norte, Portugal, et al.:

An observational, descriptive, retrospective, and cross-sectional study was performed that included a cohort of 126 patients followed in a single Portuguese Center. We observed a high prevalence of HAE-C1-INH type II (45.2% of patients). Most HAE patients (67.4%) presented the initial manifestations of the disease before adulthood, at a mean age of 12.6 ± 8.4 years. However, we found a long delay in HAE diagnosis, especially in those without a family history (mean 20.7 ± 17.3 years). Stress was the most common trigger, followed by trauma and infection. Symptoms involving different systems were increasingly reported with increased disease duration. Cutaneous symptoms (95.0%) were more frequent, followed by gastrointestinal (80.7%), and respiratory symptoms (50.4%). HAE symptoms led to abdominal surgery in 22 (17.5%) patients and induced laryngeal edema requiring intubation/tracheostomy in 8 (6.3%) patients. Most patients were under long-term prophylaxis, mainly with attenuated androgens (62.7%).

(Eur Ann Allergy Clin Immunol, December 2022)

High digit ratio (2D:4D) is associated with attack frequency and severity in HAE patients

– by Recep Evcen, Necmettin Erbakan University, Turkey, et al.:

Data from the evaluation of 35 HAE patients suggest that intrauterine sex hormone exposure, which affects the 2D:4D ratio, is significantly associated with HEA attack frequency and severity and laryngeal edema.

(Early Hum Dev, March 2023)

Long-term lanadelumab treatment improves health-related quality of life in patients with HAE – *by William R. Lumry, Allergy and Asthma Research Associates, the United States, et al.*:

Clinically meaningful improvement in health-related quality of life was demonstrated with long-term lanadelumab treatment, supporting the benefit of lanadelumab therapy associated with attack prevention.

(Ann Allergy Asthma Immunol, April 2023)

National survey on clinical and genetic characteristics of patients with HAE in Latvia – *by Adine Kanepa, Riga Stradiņš University, Latvia, et al.:*

Current data shows a significant delay and clear underdiagnosis of HAE in Latvia. Higher awareness and better information and communication between doctors would improve the diagnosis and management of HAE, as would screening of family members, patients with recurrent angioedema unresponsive to antihistamines and glucocorticoids, and patients with recurrent episodes of severe, unexplained abdominal pain.

(Allergy Asthma Clin Immunol, April 2023)

Prevention of recurrent attacks of HAE: Berotralstat and its oral bioavailability – *by Maximiliano Diaz-Menindez, Mayo Clinic, the United States, et al.:*

Berotralstat is a unique option for oral administration for routine prophylaxis. Open-label studies have demonstrated the effectiveness of a single daily dose of berotralstat 150 mg in preventing HAE attacks.

(Ther Clin Risk Manag, March 2023)

3D facial analysis for rare disease diagnosis and treatment monitoring: Proof-Of-Concept plan for HAE – *by Saumya Jamuar, KK Women's and Children's Hospital, Singapore, et al.:*

It is hypothesized that 3D facial analysis with advanced imaging and algorithmic association can create an ideal diagnostic peer to the clinician while assimilating signs and symptoms in the hospital. The facial features are captured at a granular level in the utmost finer detail. A validated and proven algorithm-powered software provides recommendations in real time. Thus, paving the way for quick and early diagnosis to well-trained or less-trained clinicians in different settings around the globe. This may have far-reaching consequences beyond disease diagnosis to benefit all the stakeholders in the healthcare arena, including research and new drug development.

(PLOS Digit Health, March 2023)

Safety of medications for HAE during pregnancy and lactation – *by Andrew Yeich, Penn State College of Medicine, the United States, et al.:*

Treatment of HAE in the past has been mainly provided by experts; however, with more medications and an increasing number of patients, knowledge of how to care for HAE patients during pregnancy and lactation is important to review. Despite the approval of additional medications in many countries, plasma-derived C1-inhibitor remain the drug of first choice for treatment in this unique population. Additional research is needed to increase safe access to other therapy options.

(Expert Opin Drug Saf, January 2023)

Trends in treatments with disease-specific and interfering drugs in patients with HAE in Sweden – *by Linda Sundler Björkman, Lund University, Sweden, et al.:*

Despite concerns regarding side effects, approximately 10% of patients with HAE received attenuated androgens for long-term prophylaxis. The common use of emergency medication also suggests poorly controlled disease in many patients, highlighting the need for increased focus on prophylactic treatment.

(J Allergy Clin Immunol Pract, February 2023)

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 or will be recruiting shortly:

A gene therapy study of BMN 331 in subjects with HAE

– recruiting in the United States

An extension phase 2/3 study to test the safety of long-term administration 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, Poland, Spain, the United Kingdom, the United States

An open-label, long term safety and efficacy study of donidalorsen in the prophylactic treatment of HAE

– recruiting in Belgium, Bulgaria, Canada, Denmark, France, Germany, Israel, Italy, the Netherlands, Poland, Spain, Turkey, the United Kingdom, the United States

A phase III, crossover trial evaluating the efficacy and safety of KVD900 for on-demand treatment of angioedema attacks in adolescent and adult patients with HAE

– recruiting in Australia, Bulgaria, Canada, France, Greece, Hungary, Israel, Italy, the Netherlands, New Zealand, North Macedonia, Poland, Puerto Rico, Spain, the United Kingdom, the United States

A phase 3, multicenter, randomized, single-blind, dose-ranging, crossover study to evaluate the safety and efficacy of intravenous administration of Cinryze® (C1 esterase inhibitor [human]) for the prevention of angioedema attacks in children 6 to 11 years of age with HAE

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

A randomized, placebo-controlled, double-blind Phase III study of the efficacy and safety of recombinant human C1 inhibitor for the treatment of acute attacks in patients with HAE

– recruiting in Italy

A safety and pharmacokinetic study of oral berotralstat for HAE attacks in pediatric patients

– recruiting in Austria, Canada, France, Germany, Hungary, Israel, Italy, North Macedonia, Poland, Romania, Spain, the United Kingdom

Assessment of the state of health, quality of life and expectations of patients with HAE

– recruiting in France

A study in adults with HAE who currently receive icatibant at home

–recruiting in the United Kingdom

A study of lanadelumab (SHP643) in Chinese participants with HAE

– recruiting in China

A study of lanadelumab in teenagers and adults with HAE

– will be recruiting in the United Kingdom

A study of lanadelumab in teenagers and adults with HAE in Argentina

– recruiting in Argentina

A study of STAR-0215 in healthy adult participants

– recruiting in the United States

A study to a) evaluate the tolerability and blood levels of KVD900 when given as a single dose to patients and b) to assess whether KVD900 is effective in treating attacks of swelling in patients with the genetic disease HAE

– recruiting in Austria, Germany, Hungary, the Netherlands, North Macedonia, the United Kingdom, the United States

A study to assess the long-term safety and efficacy of donidalorsen in the prophylactic treatment of HAE

– recruiting in Bulgaria, Canada, Italy, the Netherlands, Spain, the United States

A study to assess whether different doses of KVD824 are effective in preventing attacks of HAE Type I or Type II

– recruiting in Australia, Bulgaria, Canada, Czech Republic, France, Germany, Hungary, Italy, New Zealand, North Macedonia, Romania, the United Kingdom, the United States

A study to evaluate if different doses of KVD900 are safe and effective in treating attacks in patients with HAE

– recruiting in Australia, Bulgaria, Canada, France, Germany, Greece, Hungary, Israel, Italy, Japan, the Netherlands, New Zealand, Poland, Portugal, Romania, Spain, the United Kingdom, the United States

A study to evaluate NTLA-2002 in adults with HAE

– recruiting in Australia, France, Germany, the Netherlands, New Zealand, the United Kingdom, the United States

A study to review the treatment and outcomes of teenagers and adults with non-histaminergic angioedema with Normal C1 inhibitor in Canada

– will be recruiting in Canada

A study with lanadelumab in persons with HAE in Poland

– recruiting in Poland

A survey of icatibant in pediatric participants with HAE

– recruiting in Japan

A survey of lanadelumab in participants with HAE

– recruiting in Japan

An open-label extension trial to evaluate the long-term safety of KVD900 for on-demand treatment of angioedema attacks in adolescent and adult patients with HAE

– recruiting in France, the Netherlands, the United States

Berotralstat treatment in children with HAE

– recruiting in Austria, Canada, France, Germany, Israel, Italy, Poland, Romania, Spain, the United Kingdom

Characterization of rhythmicity profiles of bradykinin-mediated angioedema attacks using a tracking smartphone application

– will be recruiting

Cloud-R HAE registry

– recruiting in France

Dose-ranging study of oral PHA-022121 for prophylaxis against angioedema attacks in patients with HAE type I or type II

– recruiting in Bulgaria, Canada, Germany, Israel, Poland, Spain, the United Kingdom, the United States

Extension study of oral PHA-022121 for acute treatment of angioedema attacks in patients with HAE

– recruiting in Spain, the United States

Firazyr general drug use-results survey (Japan)

– recruiting in Japan

Firazyr® patient registry (icatibant outcome survey - IOS)

– recruiting in Australia, Austria, Brazil, 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 multi-national survey study

– recruiting in Argentina, Brazil, Colombia, Croatia, Denmark, Germany, Hungary, Ireland, Norway, Poland, Portugal, Romania, Sweden

Involvement of monocytic B1 and B2 receptors in inflammation and chronic vascular disease in patients with hereditary bradykinetic angioedema

– recruiting in France

Lanadelumab tested in patients suffering from hereditary angioedema with normal C1-inhibitor

– recruiting in Germany

Long-term access to berotralstat for HAE subjects from previous clinical trials

– recruiting in Czech Republic, France, North Macedonia, Slovakia, South Africa, South Korea

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, Italy, Japan, the Netherlands, New Zealand, Russia, Spain, Taiwan, the United Kingdom, the United States

NTLA-2002 in Adults with HAE

– recruiting in the Netherlands, New Zealand, the United Kingdom

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

– recruiting in Belgium, Bulgaria, Canada, Denmark, France, Germany, Israel, Italy, Netherlands, Spain, Turkey, the United Kingdom, the United States

Pathophysiological study for autoimmune dysregulation of HAE

– recruiting in Japan

Pharmacokinetics and safety of human pasteurised C1-inhibitor concentrate (Berinert/CE1145) in subjects with congenital C1-INH deficiency

– recruiting in Italy

Phase 1/2 study to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics of NTLA-2002 in adults with HAE

– recruiting in Denmark, France, the Netherlands

PK subtrial in adolescent patients with HAE type I or II participating in the KVD900-302 trial

– recruiting in France, the United States

Safety, tolerability, PK, PD of ADX-324 in healthy volunteers and HAE patients

– recruiting in Australia

Status of dental care practices in patients with HAE

– recruiting in France

Stopping androgen treatment in patients with HAE - characterization of reasons and protocols and development of advice for patients and physicians

– recruiting in France, Germany, Hungary

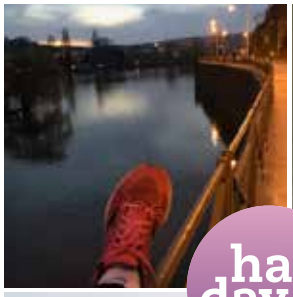
The role of the coagulation pathways in recurrent angioedema

– recruiting in France

Read more about these and other clinical trials at:

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




"**hae day :-)** is a day that unites the entire HAE community worldwide, to publicize the HAE and allows us to have greater visibility in society. **hae day :-)** reminds us that we are part of a community and motivates patients and families to continue in search of a better quality of life."

HAE Peru




"**hae day :-**) is a day for HAE community to come together, share experiences and raise awareness. This is a way for us to understand that we are not alone and that we can live a completely normal life."

HAE Spain (AEDAF)




"**hae day :-)** means renewing plans to spread awareness, thinking more about how we can reach potential patients with information and uniting more with already diagnosed patients to talk and exchange our experiences and know that we are not alone and that we have associations that are working for the best quality of life for all patients."

HAE Brazil (ABRANGHE)





"**hae day :-)** to us as an organization means raising awareness and sharing information about HAE. It also means celebrating how far we have come on our journey and the fantastic HAE friends we have met along the way. Whilst having HAE may bring difficulties to many sufferers, we have advanced so much in the past 10 years and the future is bright!"

HAE UK

8 December 2022

Pharvaris announces positive top-line data from the RAPIDe-1 Phase 2 clinical study, demonstrating statistically significant results of PHVS416 as an oral on-demand treatment for HAE attacks.

RAPIDe-1 Clinical Study Design and Results
RAPIDe-1 is a Phase 2, double-blind, placebo-controlled, randomized, crossover, dose-ranging study of PHVS416 softgel capsule for the acute treatment of angioedema attacks in patients with Type I or II HAE. Seventy-four patients were enrolled across 13 countries and were randomized into one of three single dose levels of PHVS416 and placebo. The study compares symptom relief during HAE attacks and the safety of each dose of PHVS416 with placebo. In Part I of the study, participants in a non-attack state received the assigned single dose of PHVS416 at the study center to assess its pharmacokinetics and safety. In Part II, participants self-administer blinded study drug at home to treat three physician-confirmed HAE attacks with PHVS416 or placebo.

The primary endpoint of the study is the change of a three-symptom composite (skin pain, skin swelling, abdominal pain) visual analogue scale (VAS-3) score from pre-treatment to four hours post-treatment, as captured electronically using numerically assisted input. Topline data from 147 attacks collected by 62 patients show that dose levels of PHVS416 significantly reduces attack symptoms.

The statistical tests for the primary and all key secondary endpoints followed a pre-specified multiple comparison procedure to assess statistical significance for PHVS416 20 mg and 30 mg, supported by a nominal statistical analysis for PHVS416 10 mg.

PHVS416 was generally well tolerated with no treatment-related serious adverse events and no adverse events leading to treatment discontinuation. In the non-attack phase, two treatment-related adverse events were experienced by two patients; in the attack treatment phase, three treatment-related adverse events were reported for one attack treated with PHVS416 30mg (2.8%) and one treatment-related adverse event was reported for one attack treated with placebo (1.9%).

Marcus Maurer, M.D., Professor of Dermatology and Allergy at the Charité – Universitätsmedizin Berlin, and principal investigator on the RAPIDe-1 study, comments: "The expectation of people living with HAE is that next-generation HAE therapies should achieve the same or better efficacy than current standard of care while offering an improved duration of effect and better convenience. Given the study design with physician-confirmed attacks, these data showing consistent results across all endpoints are an encouraging step in that direction for PHVS416."

Peng Lu, M.D., Ph.D., Chief Medical Officer of Pharvaris, states: "The data demonstrate rapid onset of action, symptom relief, and resolution of attacks, which support the further development of PHVS416 as a potential on-demand therapy for HAE. Further, study participants used substantially less rescue medication when taking PHVS416 to treat attacks versus when treating with placebo. The strength and durability of effect shown in the top-line data from RAPIDe-1, as well as the observed safety profile, has further enhanced our confidence in the clinical development strategy."

Berndt Modig, CEO of Pharvaris, adds: "Seven years ago, we embarked on our journey to bring novel, oral therapies to people living with HAE based on our deep insight into the biology of HAE and an experiment, the bradykinin challenge, that guided our trial design and dose selection. The results of the RAPIDe-1 study represent another step towards a potential new, oral on-demand HAE treatment. We sincerely thank the clinical trial participants and their families, the site investigators and staff, the HAE community, and the Pharvaris team for their contributions to the RAPIDe-1 study."

In August 2022, the U.S. Food & Drug Administration (FDA) placed clinical studies of PHA121 in the U.S., including RAPIDe-1, on hold. Pharvaris had previously announced the achievement of target enrollment across 33 sites in Canada, Europe, Israel, the UK, and the U.S. Subsequent to the clinical holds, the company continues to evaluate PHVS416 for the treatment of acute attacks for continuing participants enrolled outside the U.S.

(Source: Pharvaris)

15 December 2022

Astria Therapeutics, Inc. announces positive preliminary results from the Phase 1a clinical trial of STAR-0215 in healthy subjects establishing early proof of concept of STAR-0215 as a potential long-acting preventative treatment for HAE. STAR-0215 was well-tolerated at all doses studied. The results showed rapid and sustained drug levels consistent with clinical benefit and sustained target engagement with plasma kallikrein inhibition for at least three months, supporting the potential for STAR-0215 to be dosed once every three months or less frequently. Astria plans to initiate the ALPHA-STAR Phase 1b/2 trial in HAE patients in Q1 2023.

"These results mark a significant milestone for STAR-0215 and Astria. We are excited that STAR-0215 has shown early proof of concept for its target profile: of being a long-acting preventative therapy for HAE, with a best-in-class PK profile, and dosing once every 3 months or less frequently," says Jill C. Milne, Ph.D., CEO at Astria. "We aim to change the way those affected by HAE live with their disease and see these preliminary results as a critical step bringing us closer to improving patients' lives. We are looking forward to bringing STAR-0215 to patients in the ALPHA-STAR trial early next year."

"Patients want treatment options that can normalize their lives. I am pleased to see STAR-0215 moving forward in clinical development to patients," says William Lumry, M.D., Founder and Medical Director of the AARA Research Center. "We understand the need from the HAE community for an effective treatment with less burdensome dosing administration and are excited to see that potential in STAR-0215."

STAR-0215 is a monoclonal antibody inhibitor of plasma kallikrein designed to provide long-acting, effective HAE attack prevention. The Phase 1a randomized, double-blind, placebo-controlled single ascending dose trial of STAR-0215 evaluated the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of STAR-0215 at a single U.S. center. Twenty-five healthy adult subjects each received a single subcutaneous administration of one of three dose levels of 100mg, 300mg, or 600mg of STAR-0215 or placebo, and subjects are being followed for safety, PK, and PD for a total of 224 days. Preliminary data includes safety through 84 days for all three cohorts, PK and PD for the 100 mg and 300 mg cohorts through 84 days and PK and PD through 56 days for the 600 mg cohort.

Blinded safety results showed that STAR-0215 was well-tolerated at all dose levels. The most common treatment-related adverse event was mild (Grade 1), self-resolving injection site reaction, which most commonly was site redness. There were no clinically relevant changes in liver enzymes or coagulation parameters, serious adverse events or discontinuations. In the 300 and 600 mg dose groups, PK and PD results were consistent with clinical benefit up to three months, with an estimated half-life of STAR-0215 up to 110 days. Rapid and sustained drug levels consistent with clinical benefit support the potential for dosing STAR-0215 once every three months or less frequently. PD results showed rapid and robust target engagement with plasma kallikrein inhibition through at least three months with a single dose of STAR-0215. The levels of inhibition, 40 to 60% decrease in FXIIa-activated cleaved high molecular weight kininogen, are consistent with the levels shown to prevent attacks in people living with HAE.

The results support advancing STAR-0215 to a Phase 1b/2 trial, ALPHA-STAR, expected to initiate in Q1 2023. This global, multi-center, open-label, single and multiple dose proof-of-concept clinical trial in people with HAE, will evaluate safety, tolerability, HAE attack rate, PK, PD, and quality of life in patients. Initial results are expected from the single and multiple dose cohorts in mid-2024. The results from the Phase 1a trial also suggest that there could be an opportunity to dose STAR-0215 less frequently. Astria plans to evaluate the potential for 6-month dosing with additional healthy subject cohorts in the Phase 1a trial starting in Q1 2023 with initial results expected in Q4 2023.

(Source: Astria)

6 January 2023

Intellia Therapeutics, Inc. announces its strategic priorities for the upcoming two years as the Company enters its next phase of pipeline execution and platform innovation.

Among the 2023-2024 Strategic Priorities are to initiate global pivotal trials for Intellia's investigational in vivo CRISPR-based therapy NTLA-2002 for HAE.

"2022 proved to be another outstanding year for Intellia, with several significant clinical milestones achieved across our pipeline, further reinforcing the ability of our modular CRISPR genome editing platform to target a broad range of diseases," says Intellia President and CEO John Leonard, M.D. "These accomplishments reflect steady execution against our core strategy: to harness the immense power of genome editing, both for in vivo and ex vivo applications. As we look ahead, our highest priority will be to prepare for the initiation of global pivotal trials for our investigational in vivo CRISPR-based therapy NTLA-2002 for HAE. As this program continue to progress, we believe we are moving closer to setting a new standard of care for people living with HAE and other serious diseases. In addition, we are advancing the next wave of platform capabilities, such as in vivo gene insertion and our proprietary allogeneic solution. Importantly, while the possibilities to apply our industry-leading genome editing technology are expansive, we are taking a disciplined approach with our portfolio by deploying resources on high-impact opportunities and collaborating with a network of other scientific leaders to expand the applications of our innovative technologies."

Based on the strategic priorities, which will be the Company's focus over the next two years, Intellia anticipates to initiate Phase 2 portion of the ongoing NTLA-2002 Phase 1/2 study in 1H 2023, to submit an IND in 1H 2023 to support the inclusion of U.S. sites in the Phase 2 study of NTLA-2002, and to present additional clinical data from the ongoing first-in-human study of NTLA-2002 in 2023.

(Source: Intellia)

Intellia THERAPEUTICS

9 January 2023

Pharvaris provides business updates and company highlights:

- Meeting minutes from Type A meeting with U.S. Food and Drug Administration (FDA) received. Pharvaris will conduct a 26-week rodent toxicology study to resolve the clinical holds in the U.S. The protocol for this nonclinical study has been submitted to the FDA for review.
- FDA approval of dosing of final U.S. participants in RAPIDe-1 received. The FDA has agreed to partially lift the hold on on-demand to allow the two remaining U.S. participants in RAPIDe-1 to complete treatment of the last attack per the protocol. Positive top-line data from RAPIDe-1 was announced in December 2022. RAPIDe-2, a long-term extension study of PHVS416 for the on-demand treatment of HAE, is currently on hold in the U.S. and is underway outside the U.S.
- Top-line data from CHAPTER-1, a global Phase 2 study of PHVS416 for the prophylactic treatment of HAE attacks, anticipated 2H2023. CHAPTER-1 is currently on hold in the U.S. All active sites outside of the U.S. continue to recruit participants in the CHAPTER-1 clinical study. After being notified of the clinical holds in the U.S. by the FDA, Pharvaris informed country-specific regulatory authorities in Canada, Europe, Israel, and the UK regarding the clinical holds in the U.S. To date, the regulatory status of the CHAPTER-1 study outside the U.S. remains unchanged. Based on the Company's current assumptions regarding ex-U.S. regulatory status and enrollment, Pharvaris anticipates announcing top-line data from the CHAPTER-1 trial in 2H2023.

(Source: Pharvaris)

PHARVARIS

9 January 2023

At the presentation of the preliminary, unaudited ORLADEYO® (berotralstat) net revenue for the fourth quarter and full year 2022, Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc.**, says:

"In our second year on the market, we more than doubled our first-year ORLADEYO sales. This continues to be an exceptional launch of an oral rare disease drug, and we expect this success to continue creating

real value for patients and for shareholders this year and for many years to come."

The number of patients on therapy at the end of 2022 was in-line with the company's expectations as patients continued to switch to ORLADEYO in the fourth quarter. BioCryst sees continued growth in 2023 in the U.S. and around the world.

(Source: BioCryst)

12 January 2023

The U.K. Medicines and Healthcare products Regulatory Agency (MHRA) has awarded the Innovation Passport for **Intellia Therapeutics, Inc**.'s NTLA-2002, an in vivo genome editing candidate being developed for the treatment of HAE. The Innovation Passport is the point of entry into the U.K.'s Innovative Licensing and Access Pathway (ILAP), which is designed to accelerate time to market and facilitate patient access to innovative medicines.

"With the high treatment burden of currently available chronic therapies for HAE, we are pleased to receive the ILAP designation, which will enable us to further accelerate the clinical development of NTLA-2002," says Intellia President and CEO John Leonard, M.D. "We expect to begin the Phase 2 portion of the NTLA-2002 clinical study in the first half of this year, and we look forward to working with the U.K. and other regulatory agencies to bring this investigational single-dose genome editing treatment to patients as quickly as possible."

The Phase 1/2 study evaluating NTLA-2002 in adults with Type I or Type II HAE is currently ongoing, with the Phase 2 portion expected to initiate in the first half of 2023.

Delivered in partnership by the All Wales Therapeutics and Toxicology Centre (AWTTC), the Medicines and Healthcare products Regulatory Agency (MHRA), the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC), the Innovation Passport prioritizes innovative medicines in early clinical development stages for the treatment of diseases with a significant patient or public health need. Benefits of the ILAP include access to a Target Development Profile, which defines key regulatory and development features and creates a roadmap for advancement through regulatory approval.

Intellia's multi-national Phase 1/2 study is evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2002 in adults with Type I or Type II HAE. This includes the measurement of plasma 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)

21 January 2023

ADARx Pharmaceuticals, Inc. announces the dosing of the first cohort in a Phase 1 clinical study of ADX-324 for the treatment of HAE.

"We are very excited to be advancing our first candidate that utilizes our proprietary PLR™ delivery platform and SPE™ technology into the clinic," says Zhen Li, President and CEO. "ADX-324 represents an innovative and differentiated approach for the treatment of HAE."

"Dosing of our first participants in this trial is a major milestone for ADARx; in addition to its potential best-in-class efficacy, our pre-clinical studies in non-human primates have confirmed the likelihood for a bi-annual, and possibly annual, low volume subcutaneous dose regimen for ADX-324," says Feriandas Greblikas, Vice President of Clinical Development.

ADX-324 is a short-interfering RNA (siRNA) designed to reduce the production of PKK, a protein critical to the etiology of HAE. The study is being conducted in Australia as a randomized, placebo-controlled, double-blind, single ascending dose trial in healthy volunteers with an expansion cohort in patients with HAE. The primary objective of the study is to evaluate the safety and tolerability of ADX-324 when administered by subcutaneous injection.

(Source: ADARx)

23 January 2023

BioCryst Pharmaceuticals, Inc. enters into a collaboration with Swixx BioPharma AG to commercialize ORLADEYO® (berotralstat) in Central and Eastern Europe.

"We continue to build partnerships with companies that have deep expertise in commercializing rare disease therapies as we advance our mission of bringing ORLADEYO to patients living with hereditary angioedema around the world. The team at Swixx is highly skilled at launching rare disease therapies in Central and Eastern Europe, and we are thrilled to work alongside them to bring our oral, once-daily prophylactic treatment for HAE to patients in this region," says Charlie Gayer, Chief Commercial Officer of BioCryst.

"Based on our unrivaled understanding of the rare disease landscape in Central and Eastern Europe, we believe we are best suited to help BioCryst bring ORLADEYO to patients living with HAE in the countries within this region. It goes without saying that there are significant unmet needs among HAE patients in Central and Eastern Europe, and our experienced commercial team is well equipped to bring this important long-term prophylactic therapy to the people who need it most," says Jean-Michel Lespinasse, CEO of Swixx.

Under the terms of the agreement, Swixx will be responsible for commercializing ORLADEYO in 15 markets within Central and Eastern Europe.

Swixx is a Swiss-based biopharmaceutical company that has extensive experience with providing end-to-end services to its partner companies to bring therapies for rare diseases to patients living in CEE, with a strategic business unit focused on rare and ultra-rare diseases.

(Source: BioCryst)

26 January 2023

BioCryst Pharmaceuticals, Inc. announces the enrollment of the first patient in the pivotal APeX-P trial evaluating oral, once-daily ORLADEYO® (berotralstat) in pediatric HAE patients who are 2 to <12 years of age.

"Today's announcement marks a very important step in our continuing efforts to reduce the burden of therapy for people living with HAE around the world with oral, once-daily ORLADEYO. Pediatric patients are a particularly important group where the challenges posed by disease and treatment can be significant to these children and their families, especially given the uncertainty they face as they are newly diagnosed during childhood. It is imperative that we strive to help normalize patients' lives, as early experiences can have a lasting impact on how HAE is perceived – and managed – for their entire lifetimes. We are excited by the opportunity to introduce this new pediatric formulation of ORLADEYO that could significantly reduce the treatment burden for children and families impacted by HAE," says Dr. Ryan Arnold, Chief Medical Officer of BioCryst.

ORLADEYO is the first and only oral therapy designed specifically to prevent HAE attacks in adult and pediatric patients 12 years and older. First approved by the U.S. Food and Drug Administration (FDA) in December 2020, ORLADEYO is available in many global markets.

APeX-P is an open-label trial designed to evaluate the pharmacokinetics (PK) and safety of ORLADEYO in pediatric HAE patients (2 to <12 years of age). The trial will consist of an initial 12-week standard-of-care (SOC) treatment period, followed by a subsequent open-label ORLADEYO treatment period lasting 48 weeks, with continuation up to 144 weeks. Patients will be enrolled into four dose cohorts, with body weight being used to determine assignment to each cohort. Higher weight cohorts (Cohorts 1 and 2) will enroll first and in parallel, and safety assessments and PK modelling from all available PK data will then be used to confirm the weight bands for sequentially enrolling Cohorts 3 and 4. The effectiveness of ORLADEYO in APeX-P will be summarized using descriptive statistical methods. The primary endpoint of APeX-P is the characterization of the PK profile of ORLADEYO in patients aged 2 to <12 years.

Following the completion of APeX-P, BioCryst plans to submit a supplemental New Drug Application (sNDA) for the potential expanded use of ORLADEYO for prophylaxis to prevent attacks in pediatric HAE patients.

(Source: BioCryst)

5 February 2023

The U.S. Food and Drug Administration (FDA) has approved the supplemental Biologics License Application (sBLA) for the expanded use of **Takeda**'s TAKHZYRO® (lanadelumab-flyo) for prophylaxis to prevent attacks of HAE in pediatric patients 2 to <12 years of age. Prior to the approval, the only approved routine prophylaxis treatment options for children 6 to <12 years of age required dosing every three to four days, and children with HAE 2 to <6 years of age had no approved prophylaxis treatment, making TAKHZYRO the first prophylaxis treatment for this age group. The recommended dose is 150 mg/1 mL solution in a single-dose prefilled syringe every four weeks in patients 2 to <6 years of age and every two weeks in patients 6 to <12 years of age.

"The approval for TAKHZYRO in pediatric patients as young as 2 years of age brings a welcome and important addition to treatment options available for children living with HAE," says Anthony Castaldo, President and CEO of the U.S. Hereditary Angioedema Association (HAEA).

The sBLA approval was supported by extrapolation of efficacy data from the HELP Study, a Phase 3 trial that included patients 12 to <18 years of age, and additional pharmacokinetic analyses showing similar drug exposures between adults and pediatric patients, as well as safety and pharmacodynamic data from the SPRING Study, an open-label Phase 3 trial in 21 HAE patients 2 to <12 years of age. The primary objectives of the SPRING Study were the safety and pharmacokinetics of TAKHZYRO. The most common treatment-related treatment emergent adverse events in the study were injection site pain (29%), injection site erythema (14%), injection site swelling (5%), administration site pain (5%) and injection site reaction (5%). The prevention of HAE attacks was measured as a secondary objective. TAKHZYRO reduced the rate of HAE attacks in pediatric patients by a mean of 94.8% compared to baseline, from 1.84 attacks per month to 0.08 attacks during the 52-week treatment period (N=21). The majority of patients (76.2%, n=16) were attack-free with an average of 99.5% attack-free days. These efficacy results are from an open-label, non-controlled trial, and the study was not designed for statistical hypothesis testing. Further confirmatory studies are required to draw any conclusions from these data.

"Today's approval of the expanded indication of TAKHZYRO represents a significant step forward for the HAE community as it helps some of its youngest patients who are living with the disease to have a long-term prophylaxis treatment available to them," says Julie Kim, President, U.S. Business Unit and U.S. country head at Takeda. "Takeda is a committed leader in the rare disease space, and today's approval underscores our confidence in TAKHZYRO, as well as our dedication to addressing the needs of HAE patients through continued research, clinical programs and real-world data collection."

TAKHZYRO was originally approved in the U.S. in 2018 for prophylaxis to prevent attacks of HAE in adult and pediatric patients 12 years and older.1 It is currently available in more than 60 countries around the world and is supported by a robust clinical development program, which includes one of the largest prevention studies in HAE with the longest active treatment duration.

(Source: Takeda)

7 February 2023

KalVista Pharmaceuticals, Inc. presents three posters at the Western Society of Allergy, Asthma & Immunology 60th Annual Scientific Session in Kona, the United States.

The first highlights that KONFIDENT-S (NCT05505916) is a prospective trial to evaluate the effectiveness and safety of sebetralstat, an investigational oral plasma kallikrein inhibitor, for short-term prophylaxis. The second reports phase 1 data evaluated the pharmacokinetic and pharmacodynamic parameters of sebetralstat in Japanese adults. These positive Phase 1 data support the expansion of the KONFIDENT (NCT05259917) phase 3 trial to Japan. Finally, KalVista presents a post hoc analysis of phase 2 trial data demonstrating that sebetralstat provided similar symptom relief, reduction in attack severity, and use of rescue regardless of abdominal or peripheral attack location.

Targeted Literature Review to Assess the Studies Supporting Short-term Prophylactic Treatment Options for the Preprocedural Prevention of Attacks in Patients with HAE – Dr. Marc A. Riedl, Division of Rheumatology, Allergy and Immunology, University of California San Diego, United States:

The literature review confirms that there are few prospective and no controlled studies in the short-term prophylaxis setting that support the present first-line treatment options for preprocedural prevention of acute HAE attacks. Consistent with prior studies, therefore, we have designed a 2-year, open-label, phase 3 extension trial (KONFIDENT-S, NCT05505916), which will evaluate the safety of sebetralstat, an investigational oral plasma kallikrein inhibitor for the on-demand treatment of HAE attacks, while also prospectively evaluating the effectiveness and safety of sebetralstat in the preprocedural short-term prophylaxis setting. KONFIDENT-S is the first prospective trial that will evaluate an oral on-demand therapy for short-term prophylaxis.

Pharmacokinetic, Pharmacodynamic, and Safety Profile of Sebetralstat in Healthy Japanese and White Adults: Results from a Phase 1, Randomized, Double-Blind, Placebo-Controlled Trial – Matthew Iverson, KalVista Pharmaceuticals Inc., Cambridge, MA, United States:

Sebetralstat has comparable pharmacokinetic, pharmacodynamic, and safety profiles in healthy Japanese and White adults. These findings support the inclusion of Japanese patients with HAE in the KONFIDENT phase 3 trial (NCT05259917) to assess sebetralstat as on-demand treatment for HAE attacks.

Efficacy of the Oral Plasma Kallikrein Inhibitor Sebetralstat (KVD900) by Attack Location in a Phase 2 Clinical Trial in Patients with HAE – Dr. Paul K. Audhya, KalVista Pharmaceuticals Inc., Cambridge, MA, United States:

Sebetralstat treatment resulted in rapid symptom relief for both abdominal and peripheral attacks, with approximately 80% achieving symptom relief within 12 hours regardless of attack location as evaluated by a score of "A Little Better" or higher for 2 consecutive timepoints on the PGI-C scale. Abdominal attacks tended to resolve more quickly than peripheral attacks as evaluated on PGI-S and VAS scales. Faster symptom relief for abdominal versus peripheral attacks observed in this study is consistent with previously reported findings for other acute therapies. The use of rescue medication for abdominal and peripheral attacks treated by sebetralstat was also similar, although somewhat more abdominal attacks were rescued earlier, while more peripheral attacks were rescued later. The results of this post hoc analysis demonstrate that sebetralstat provides symptom relief and attack resolution for people living with HAE, regardless of abdominal or peripheral attack location.

(Source: KalVista)

KalVista Pharmaceuticals

10 February 2023

The Lancet, the international weekly medical journal, publishes results from the phase 2 trial evaluating the efficacy and safety of **KalVista Pharmaceuticals, Inc**.'s oral sebetralstat for the on-demand treatment of HAE.

The phase 2 study was a two-part, randomized, double-blind, placebo-controlled clinical trial. The trial included a total of 68 patients with HAE and showed that oral sebetralstat was well tolerated and led to rapid suppression of plasma kallikrein activity, resulting in significantly increased time to use of conventional treatment, reduced attack severity, and faster time to symptom relief and resolution compared to placebo.

"All currently available on-demand treatments in HAE require injections and are associated with substantial treatment burden and delays due to the time required for medication preparation and administration, and associated pain and discomfort," says Dr. Emel Aygören-Pürsün, Head of the HAE Center at the University Hospital Frankfurt, Germany, co-lead author of the manuscript, and Principal Investigator for the phase 2 clinical trial. "In this study, patients were able to orally administer treatment early after attack onset, minimizing time to improvement. This suggests that sebetralstat has the potential to enable patients to improve clinical outcomes."

"Sebetralstat was rapidly absorbed after oral administration, halting attack progression and expediting symptom relief and attack resolution," adds Dr. Andrea Zanichelli, Unità di Medicina, IRCCS Policlinico San Donato, Università degli Studi di Milano, Italy, and co-lead author. "Importantly, sebetralstat was well-tolerated in this trial with very few adverse events. The preliminary safety profile contrasts favorably with the labelled adverse reactions for currently approved on-demand therapies."

"The publication of these phase 2 results in The Lancet underscores their significance and represents further validation of the promise of sebetralstat as potentially the first oral on-demand treatment for people living with HAE," says Andrew Crockett, CEO of KalVista. "We anticipate clinical results from our ongoing phase 3 KONFIDENT trial for sebetralstat for on-demand treatment in HAE in the second half of this year as we work to bring this innovative therapy to the HAE community."

Topline Phase 2 Sebetralstat Results

- Time to use of conventional treatment within 12 h of study drug administration was significantly longer with sebetralstat versus placebo; (p=0·0010)
- Sebetralstat significantly reduced time to onset of symptom relief (p=<0.0001) on the Patient Global Impression of Change scale (PGI-C), with a median time of 1.6 hours versus 9 hours for attacks treated with placebo
- Time to conventional attack treatment use or worsening in severity by 1 level or more on the PGI-S, whichever came first, within 12 h of study administration was significantly longer after treatment with sebetralstat than after treatment with placebo (p<0.001)
- The median time to attack resolution, defined as a PGI-S rating of "none" within 24 h after study drug administration, was significantly shorter with sebetralstat than with placebo (p=0·0021)
- Sebetralstat was well-tolerated and no serious adverse events were reported. The proportion of drug-related treatment-emergent adverse events was similar in attacks treated with sebetralstat and placebo

(Source: KalVista)

KalVista Pharmaceuticals

13 February 2023

Astria Therapeutics, Inc. initiates the ALPHA-STAR Phase 1b/2 clinical trial of STAR-0215 in people living with HAE. Initial proof-of-concept results in HAE patients from single and multiple-dose cohorts are expected in mid-2024.

"Our vision for STAR-0215 is to develop a long-acting, safe, and effective preventative therapy that normalizes the lives of people living with HAE," says Chris Morabito, M.D., Chief Medical Officer at Astria Therapeutics. "After seeing promising Phase 1a clinical results at the end of last year, we are proud to be taking the next step forward by evaluating STAR-0215 in HAE patients in our proof-of-concept clinical trial. We believe that STAR-0215 has the potential to change the way that people live with their HAE."

"We are thrilled that STAR-0215 is moving forward in development with a thoughtfully planned clinical trial that takes our patient community into consideration by allowing all qualifying participants to receive STAR-0215," says Dr. Marcus Maurer, M.D., Professor of Dermatology and Allergy at Charité Universitätsmedizin in Berlin, Germany. "The HAE community is looking for treatments that have the potential to be less burdensome on their lives. ALPHA-STAR is designed to efficiently assess the potential of STAR-0215, and I am looking forward to the expected proof-of-concept results mid-next year."

The ALPHA-STAR trial is a global open-label Phase 1b/2 proof-of-concept trial enrolling patients with HAE types I and II evaluating safety and tolerability, changes in HAE attack rate, pharmacokinetics, pharmacodynamics, and quality-of-life assessments. Following an initial run-in period, qualifying participants will be enrolled in either a single or multiple-dose cohort. Data from up to 18 participants will evaluate efficacy and safety, and comparisons will be made against data collected during the run-in period. Initial results from the single and multiple-dose cohorts from the ALPHA-STAR trial are expected in mid-2024, and pending positive results, Astria expects to progress directly to a pivotal trial.

STAR-0215 is a monoclonal antibody inhibitor of plasma kallikrein in development for the treatment of HAE. Preliminary results from a Phase 1a trial in healthy subjects support STAR-0215's target profile: a long-acting preventative therapy, best-in-class PK profile, and dosing once every three months or less frequently. Based on results seen to date, Astria is planning to

evaluate the potential for six-month administration of STAR-0215 in additional cohorts in the Phase 1a trial, with preliminary results expected in the fourth quarter of 2023.

(Source: Astria)

14 February 2023

KalVista Pharmaceuticals, Inc. provides multiple clinical trial and regulatory updates for its lead compound sebetralstat, as a potential oral on-demand therapy for HAE attacks.

- KalVista has enrolled more than 50% of the 114 targeted number of patients in the pivotal phase 3 KONFIDENT clinical trial. The trial will conclude once 84 of the patients enrolled complete the three-attack treatment sequence. As per previous guidance, topline data for the trial remains expected in the second half of 2023.
- KONFIDENT is currently enrolling patients at more than 50 active sites in 17 countries, and the KONFIDENT-S open label extension study also continues to enroll in accordance with plan.
- The Company recently received additional FDA regulatory guidance for the oral disintegrating tablet (ODT) formulation of sebetralstat that confirmed the requirements to support a supplemental NDA (sNDA) filing. The guidance from FDA included that no efficacy trials with the ODT formulation will be required prior to filing the supplemental NDA (sNDA) filing. KalVista anticipates that the ODT formulation will follow the expected initial launch formulation in the US and EU, although it may become the initial launch formulation in other geographies.
- KalVista also recently received guidance from the Japanese regulatory authority (PMDA) on the clinical development pathway to a regulatory submission in that country. KalVista will now be enrolling Japanese patients in both KONFIDENT and KONFIDENT-S to support the filing, and clinical sites for Japanese enrollment have been selected and start up activities are underway.

"We are very pleased with the recent progress of the sebetralstat development program," says Andrew Crockett, CEO of KalVista. "We have already exceeded our recruitment target goals for KONFIDENT in the US, and recruitment outside the US continues to accelerate as new sites come online. We continue to believe that sebetralstat can fill an important unmet need for efficacious and safe oral, on-demand therapy, and we expect to be the first to provide this important therapeutic advance to people living with HAE."

(Source: KalVista)

21 February 2023

BioCryst Pharmaceuticals, Inc. reports financial results for the fourth quarter and full year ended 31 December 2022, and provides a corporate update.

"It has been exciting to build on our strong initial launch by doubling ORLADEYO revenues in our second year, and to see the expanding global reach of an oral, once-daily therapy that is changing the lives of patients with HAE and their families," says Jon Stonehouse, President and CEO of BioCryst.

Program Updates and Key Milestones (excerpts)

- New patient demand for ORLADEYO was strong in the fourth quarter, consistent with the steady growth trajectory observed since launch.
- The ORLADEYO prescriber base continues to grow significantly, with approximately half of the new prescriptions in the fourth quarter coming from the top 500 prescribers.
- The total number of patients on ORLADEYO at year-end 2022 was consistent with the company's expectations.
- The company expects patient growth in Q1 2023 to remain strong.
- The Canadian Agency for Drugs and Technologies in Health Canadian Drug Expert Committee has recently issued a final draft positive recommendation for ORLADEYO to be reimbursed for the routine prevention of HAE attacks in adults and pediatric patients 12 years of age and older.

"Underlying demand from patients and physicians for ORLADEYO continues to be strong and consistent in the U.S., and our initial European launches are gaining traction with ORLADEYO now commercially available in 15 countries. All of this enables more and more patients to benefit from ORLADEYO", says Charlie Gayer, Chief Commercial Officer of BioCryst.

(Source: BioCryst)

22 February 2023

Ionis Pharmaceuticals, Inc. announces additional positive interim data from a Phase 2 open-label extension (OLE) study of donidalorsen, an investigational antisense medicine for the treatment of patients with HAE. Positive interim data presented in November 2022 showed that treatment with donidalorsen resulted in an overall sustained mean reduction in HAE attack rates of 95% from baseline. In the latest update, patients treated for one year with donidalorsen showed a clinically meaningful 24-point mean improvement in their Angioedema Quality of Life (AE-QoL) total score relative to baseline with improvements observed in all domains. An improvement of 6 points or more is considered clinically meaningful.

"The improvement in quality of life demonstrated in patients treated with donidalorsen for one year were clinically meaningful and further support our belief in this medicine's potential to be a best-in-class prophylactic treatment for patients with HAE," says Richard S. Geary, PhD, Executive Vice President and Chief Development Officer at Ionis. "We continue to be pleased with the progress of the Phase 3 OASIS study of donidalorsen, which remains on track to complete enrollment this year."

(Source: Ionis)

24 February 2023

BioCryst Pharmaceuticals, Inc. announces new data from the APeX-S and APeX-2 clinical trials which evaluated oral, once-daily ORLADEYO® (berotralstat) for the prophylactic treatment of HAE demonstrating sustained reductions in attack rates and improvement in quality of life (QoL) among patients living with HAE, highlighting its profile as a well-tolerated, effective and convenient prophylactic HAE therapeutic option.

The company also announces additional analyses from new real-world data that further demonstrate a meaningful reduction in attack rates experienced by patients on ORLADEYO, in addition to findings from a survey that underscore a significant disease and treatment burden among pediatric HAE patients, as reported by their caregivers.

"The final results from the long-term APeX-S study show that ORLADEYO was consistently well-tolerated, with no new safety signals observed, and attack reduction was sustained through 96 weeks. These results are complemented by the analyses from APeX-2, in which clinically meaningful patient-reported improvements in QoL across subgroups was shown at 96 weeks," says Emel Aygören-Pürsün, M.D., Internal Medicine and Hemostaseology, Division of Oncology, Hematology and Hemostaseology, Department for Children and Adolescents, University Hospital Frankfurt, Germany.

"We are excited to report the final results of our ORLADEYO clinical studies, as these new datasets are being reinforced by what we have observed in the real-world use of ORLADEYO. This real-world evidence supports the continued need for an oral, once-daily option for patients and physicians who are seeking control of their HAE attacks," says Dr. Ryan Arnold, Chief Medical Officer of BioCryst.

The data are being presented at the 2023 American Academy of Allergy, Asthma & Immunology (AAAAI) annual meeting.

The posters being presented at AAAAI include analyses from the APeX-2 and APeX-S clinical studies, as well as real-world data from patients taking ORLADEYO in the United States. APeX-2 was a Phase 3, double-blind, placebo-controlled, parallel-group, three-part study evaluating ORLADEYO versus placebo for the prevention of HAE attacks in patients with HAE Type I or Type II. APeX-S was a Phase 2, open label, international study evaluating the safety and effectiveness of ORLADEYO 110 mg once daily (QD) and 150 mg QD in patients with HAE Type I or Type II for up to 96 weeks in the US and 240 weeks in all other countries.

Overall, treatment-emergent adverse events (TEAEs) reported in APeX-2 and APeX-S were mild and transient, indicating that ORLADEYO was generally well tolerated.

Real-World Outcomes in Patients with HAE Treated with Berotralstat:

- This analysis assessed patient-reported HAE attack rates of HAE Type I or Type II patients on ORLADEYO 110 mg or 150 mg QD for at least 120 days based on review of data from a sole-source pharmacy from December 2020 to May 2022 (n=213). Baseline attack rates were captured by pharmacist progress notes for the previous 90 days prior to initiation of ORLADEYO and converted to a 30-day average for each patient.
- Overall, attack rates subsequently decreased upon initiation with ORLADEYO and remained consistently

low through 360 days on therapy. The median reported attack rate was ⩽0.5 attacks/month across all reporting periods through 360 days, and the median reported attack rate was 0.0 in half of the 30-day reporting periods.
- These real-world findings suggest that ORLADEYO is a durable and effective long-term prophylactic treatment for patients with HAE.

Disease and Treatment Burden of HAE in Pediatric Patients: Assessment by Caregivers:
- This analysis focused on a blinded, cross-sectional study based on results from an online survey of U.S. adults (n=35) who self-reported being the caregiver of pediatric HAE Type I or Type II patients (age 2-12 years old). They were asked to share perceptions of their experiences with disease management, current HAE treatments and the potential impact of an oral HAE treatment in pediatric patients.
- Key findings from the survey included:
  - Only 17 percent of pediatric patients (n=6) were on prophylactic HAE treatment.
  - 40 percent of caregivers (n=14) reported ⩾1 attack experienced by the pediatric patient in the past six months.
  - 75 percent of school-age pediatric patients (⩾ 5 years old; n=12) who had ⩾1 attack missed at least one day of school in the last six months because of HAE and 33 percent missed 6-15 days.
  - Caregivers of pediatric patients who had ⩾1 attack not on prophylactic therapy (n=12) most commonly reported infusion requirements (33 percent) and administration inconvenience (25 percent) as reasons why pediatric patients were not on prophylactic therapy.
  - These findings demonstrate significant disease and treatment burden experienced by pediatric patients and underscore the need for a more convenient option to help increase adoption of prophylactic treatment for HAE in this patient population.

Long-term HAE Prophylaxis with Berotralstat Is Well Tolerated and Effective: Analysis for the APeX-S Study:
- This analysis characterizes the final safety and effectiveness results of APeX-S through 96 weeks. Patients (n=387) were initially allocated to once-daily ORLADEYO 110 mg or 150 mg until superior efficacy at 150 mg was demonstrated in APeX-2 and patients on the 110 mg dose at that time transitioned to 150 mg (n=100).
- No new safety signals were observed. Overall, TEAEs were generally mild and transient, indicating that ORLADEYO was generally well tolerated.
- Clinically meaningful and sustained reductions in HAE attack rates were observed in patients receiving ORLADEYO 150 mg (n=287). In patients who received ORLADEYO 150 mg, a median attack rate of 0.0 attacks/month was observed in 20 of 24 months. Following one month of ORLADEYO treatment, the mean (SEM) adjusted HAE attack rate was 1.1 (0.1). Subsequently, SEM adjusted HAE attack rates declined to 0.9 (0.1) at Month 6, 0.7 (0.1) at Month 12, and 0.8 (0.1) at Month 24.
- Patients experienced sustained reductions in attacks throughout treatment through 24 months, consistent with previously reported data, further supporting the long-term safety and effectiveness of ORLADEYO.

Berotralstat Improved Quality of Life through 96 Weeks Across Multiple Subgroups of Patients with HAE:
- This analysis focused on the changes in QoL assessed in APeX-2 using the validated patient-reported Angioedema Quality of Life Questionnaire (AE-QoL), specifically AE-QoL scores in patients randomized to ORLADEYO 150 mg in part 1 of the study through Week 96 in part 3 of the study (n=40).
- Results were stratified by four baseline characteristics: age (<35 years old, 35-50 years old, >50 years old); sex (male, female); baseline attack rate (<2 attacks/month, ⩾2 attacks/month); prior prophylaxis (prior treatment with androgens or C1 esterase inhibitor). Additionally, AE-QoL results were stratified by the presence or absence of gastrointestinal adverse events (GI AEs) in part 1.
- Mean patient-reported improvements from baseline to Week 96 in total AE-QoL score exceeded the minimal clinically important difference (MCID) value starting at Week 4 and were sustained through Week 96.
- Improvements were also observed in all domains of the AE-QoL (functioning, fatigue/mood, fear/shame, nutrition) regardless of stratification, with the largest improvement occurring in the functioning domain in almost all stratification groups.
- These data illustrate that long-term prophylaxis with ORLADEYO led to sustained and clinically meaningful improvements in patient-reported QoL across multiple subgroups after 96 weeks of treatment, and that patients reported improvements in total AE-QoL score and all AE-QoL domains, regardless of the presence or absence of GI AEs.

(Source: BioCryst)

25 February 2023

Astria Therapeutics, Inc. presents new STAR-0215 data in two presentations at the American Academy of Allergy, Asthma, and Immunology Annual Meeting 2023, that demonstrate early proof-of-concept for STAR-0215's profile as a long-acting preventative therapy for HAE.

In the poster "Initial Results from a Phase 1a Single Ascending Dose Clinical Trial of STAR-0215, an Investigational Long-Acting Monoclonal Antibody Plasma Kallikrein Inhibitor for HAE, in Healthy Subjects Followed for at Least 3 Months", Chris Morabito, M.D., Chief Medical Officer at Astria Therapeutics, shares clinical data including unblinded safety data that showed that STAR-0215 was well-tolerated, with no serious adverse events or discontinuations due to an adverse event. Additionally, there were no clinically significant changes in laboratory assessments, and there were no treatment-emergent anti-drug antibodies (ADAs) detected. STAR-0215 demonstrated dose-dependent pharmacokinetics (PK), with an estimated half-life of up to 117 days. At Day 84, mean concentrations remained above the threshold for potential efficacy after a single 300 mg subcutaneous dose. Suppression of cleaved high molecular weight kininogen (cHMWK) to levels consistent with robust plasma kallikrein inhibition was achieved through Day 84 in both Western Blot and Chromogenic assays. These results demonstrate early proof of concept for STAR-0215 as a potential long-acting therapy for HAE, and additional cohorts have been added to the Phase 1a trial to assess the potential for once every six-months administration, with preliminary results expected in the fourth quarter of 2023.

The second poster "Structure of STAR-0215 Bound to Active Plasma Kallikrein Reveals a Novel Mechanism of Enzyme Inhibition" presented by Nikolaos Biris, Ph.D., Director of Assay Development at Astria Therapeutics, shows that STAR-0215 binds allosterically to a site that is unique to plasma kallikrein. This allosteric binding of STAR-0215 blocks the formation of the active site of plasma kallikrein to potentially inhibit its activity and gives rise to the high selectivity for plasma kallikrein compared with prekallikrein and related serine proteases. These findings, together with the additional Phase 1a clinical data that established long half-life in healthy subjects, support that STAR-0215 is a potential best-in-class therapy for the prevention of HAE attacks.

STAR-0215 is a monoclonal antibody inhibitor of plasma kallikrein in development for the treatment of HAE. Initial results from a Phase 1a trial in healthy subjects support STAR-0215's target profile: a long-acting preventative therapy, best-in-class PK profile, and dosing once every three months or less frequently. The Phase 1b/2 ALPHA-STAR trial evaluating STAR-0215 in people living with HAE is ongoing, with initial results from single and multiple dose cohorts expected in mid-2024.

(Source: Astria)

27 February 2023

CSL presents results from the pivotal placebo-controlled Phase 3 VANGUARD clinical trial of garadacimab (CSL312), CSL's investigational first-in-class monoclonal antibody being developed as a long-term prophylactic treatment for patients with HAE. Results from the trial, the first to investigate targeting activated Factor XII (FXIIa) to prevent HAE attacks, showed that once-monthly subcutaneous injections of garadacimab significantly reduced the attack rate compared to placebo.

"Targeting FXIIa and the HAE cascade from the start, as opposed to intervening downstream, is an innovative treatment approach that could help stop the process in its tracks," says Dr. Timothy Craig, Tenured Professor of Medicine, Pediatrics and Biomedical Sciences at Penn State University, United States, and Principal Investigator of the study. "The Phase 3 data we are presenting support the potential use of garadacimab as a prophylactic therapy for HAE."

Key Data from the Phase 3 VANGUARD Trial

During the double-blind, randomized, placebo-controlled, multicenter, parallel-group study, patients taking once monthly garadacimab (n=39) experienced a statistically lower monthly attack rate versus placebo (n=24) ($p< 0.001$), resulting in a mean attack rate reduction of 86.5% versus placebo, and a median attack rate reduction of 100% versus placebo. The mean attack rate reduction compared with placebo after adjusting for baseline attack rate was 89.2%.

Overall, during the six-month trial, a majority (61.5%) of patients taking garadacimab were attack-free, whereas no patients on the placebo arm were attack-free; 74.4%

of patients taking garadacimab achieved ⩾90% attack reduction versus the run-in period.

The study also showed that garadacimab demonstrated a favorable safety and tolerability profile. There were no adverse events that led to treatment discontinuation. Five injection site reactions, all mild, were reported in two (5.1%) patients treated with garadacimab and three patients (12%) on placebo.

"The data being shared at AAAAI showcase the efficacy and safety profile of garadacimab administered as a convenient monthly subcutaneous injection. The clinical trial results support garadacimab as a novel, first-in-class potential treatment that could offer a significant benefit to patients with HAE," says Catherine Milch, Vice President R&D Immunology, CSL. "Garadacimab represents the next chapter in delivering on our promise to bring disruptive innovation and treatment options to patients living with rare diseases."

Based on the full study data, which are consistent with the positive top-line results announced in August 2022, CSL plans regulatory submissions to global health authorities later this calendar year for approval of garadacimab.

About the Pivotal Phase 3 VANGUARD Trial
The multicenter, randomized, double-blind, parallel-group VANGUARD trial evaluated the efficacy and safety of garadacimab, an investigational first-in-class monoclonal antibody, as a prophylactic treatment for patients with HAE. Patients aged 12 years and older with HAE type I or II underwent screening and a run-in study period to verify a baseline attack rate. Patients were randomized 3:2 to receive a loading dose of 400mg followed by 200 mg of garadacimab monthly (n=39) or volume-matched placebo monthly (n=25) subcutaneously. After the six-month treatment period, patients were given the opportunity to continue into the open-label extension study, which is currently ongoing.

The ongoing open-label extension of the Phase 3 VANGUARD study evaluates the long-term safety and efficacy of garadacimab (200 mg monthly) in patients with HAE.

(Source: CSL Behring)

CSL Behring

27 February 2023

KalVista Pharmaceuticals, Inc. presents five posters at the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting in San Antonio, Texas, United States.

"The real-world data presented at AAAAI highlight the significant treatment burden and anxiety associated with existing injectable on-demand therapies, and the potential for sebetralstat, an investigational oral plasma kallikrein inhibitor, to improve the treatment experience for people living with HAE," says Andrew Crockett, CEO of KalVista. "Additionally highlighting this potential are the data from our phase 2 trial assessing sebetralstat for on-demand of HAE attacks demonstrating that early treatment decreased cumulative attack and symptom severity compared to placebo, as well as new data supporting continued advancement of our orally disintegrating tablet formulation."

All five presentations can be found online at www.kalvista.com/healthcare-providers/publications.

(Source: KalVista)

KalVista Pharmaceuticals

3 March 2023

The U.S. Food and Drug Administration (FDA) has cleared **Intellia Therapeutics, Inc**.'s Investigational New Drug (IND) application for NTLA-2002 for the treatment of HAE, enabling the company to include the United States in the global Phase 2 portion of its ongoing Phase 1/2 study. NTLA-2002 is an in vivo genome editing candidate designed to inactivate the target gene, kallikrein B1 (KLKB1), to permanently reduce plasma kallikrein protein activity and thus prevent HAE attacks after a single-dose treatment.

"The FDA's acceptance of our IND application to initiate clinical evaluation of NTLA-2002 brings us one step closer to introducing a potentially paradigm-shifting treatment for people living with HAE," says Intellia President and CEO John Leonard, M.D. "The NTLA-2002 IND clearance marks an important milestone for Intellia as we continue our track record of execution as the leader in the genome editing field. We are thrilled to advance the development of NTLA-2002 in the U.S. and are working to rapidly enroll patients in the Phase

2 portion of the study. We look forward to presenting additional data from the first-in-human, Phase 1 portion of the study later this year."

Intellia's multi-national Phase 1/2 study is evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2002 in adults with Type I or Type II HAE. This includes the measurement of plasma kallikrein protein levels and clinical 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 two dose levels of NTLA-2002 that will be further evaluated in the randomized, placebo-controlled Phase 2 portion of the study. In 2022, Intellia reported positive interim results from the Phase 1 study demonstrating deep, dose-dependent reductions in plasma kallikrein and robust reductions in patient HAE attacks. The Phase 2 portion of the study has recently initiated patient screening outside of the U.S.

(Source: Intellia)

9 March 2023

At the operational update and release of the financial results for the third fiscal quarter ended 31 January 2023, the **KalVista Pharmaceuticals, Inc**. CEO Andrew Crockett says:

"We have made significant advances at KalVista over this quarter, including completing a financing that funds us into 2025, well beyond our phase 3 data results, which remain on track for the second half of this year. We continue to publish sebetralstat data across a wide variety of outlets, including influential medical journals such as The Lancet, and make presentations at prestigious medical and patient meetings. We remain committed to addressing the unmet needs of the HAE community by providing sebetralstat as a significant advancement in treatment for this disease."

(Source: KalVista)

16 March 2023

At the presentation of the **Pharming Group N.V.** preliminary (unaudited) financial report for the full year ended 31 December 2022, CEO Sijmen de Vries comments:

"2022 was a pivotal year for Pharming. It was a year in which we prioritized our efforts in rare diseases and affirmed our commitment to our purpose of serving the unserved rare disease patient. It is this priority and commitment that forms the foundation as we build Pharming into a leading, global rare disease company across multiple geographies, with multiple products, a well-defined pipeline and with the necessary commercial infrastructure in place to enhance our future ambition.

In 2022, we prioritized our efforts on rare diseases and executed on a number of our strategic objectives to help build a sustainable global rare disease business focused on RUCONEST® sales. We significantly expanded our organization and headcount in 2022. These investments are in line with our strategy to become a global, multi-product, rare disease company.

In line with our renewed focus on rare diseases, we are advancing the development of our pipeline through a combination of internal development projects - including OTL-105 as a gene therapy for HAE.

Pharming has an ongoing strategic collaboration with Orchard Therapeutics to research, develop, manufacture and commercialize OTL-105, a newly disclosed investigational ex vivo autologous hematopoietic stem cell (HSC) gene therapy for the treatment of HAE. The program has made good progress developing the lentiviral vector to enhance C1-inhibitor expression and is now testing in preclinical HAE disease models. We anticipate providing further updates as we move towards preparing an Investigational New Drug (IND) filing.

While Pharming faces competition within the HAE market, the continued need for effective and reliable treatments for acute attacks, including breakthrough attacks in patients on prophylactic therapy, as well as RUCONEST®'s distinct advantages as the only recombinant treatment that targets the root cause of HAE by replacing missing or dysfunctional C1-INH, allows for sustainability in RUCONEST®'s revenues."

(Source: Pharming)

18 March 2023

At the 2023 HAEi Regional Conference APAC in Bangkok, Thailand, **Pharvaris** presents positive data from its Phase 2 RAPIDe-1 study of PHVS416 for the on-demand treatment of HAE attacks.

Marc A. Riedl, M.D., M.S., Professor of Medicine, Clinical Director of the US Hereditary Angioedema Association (HAEA) Angioedema Center at the University of California San Diego (UCSD), and Clinical Service Chief for Allergy/Immunology at UCSD, comments:

"Currently approved on-demand therapies for HAE attacks are administered intravenously or subcutaneously and can be associated with treatment burden. The time required for preparation and administration, as well as potential occurrence of pain, discomfort, or other injection site reactions can lead to treatment delays or untreated HAE symptoms. An unmet need exists for on-demand oral therapies that are effective and well-tolerated, and that may reduce the treatment burden, enabling prompt administration as recommended by clinical guidelines. The consistent results across all endpoints in the RAPIDe-1 trial provide evidence supporting the efficacy and well-tolerated profile of PHVS416 in treating HAE attacks and provide a foundation for its further development as a potential on-demand therapy."

RAPIDe-1 is a Phase 2, double-blind, placebo-controlled, randomized, cross-over, dose-ranging trial of PHVS416, the oral softgel capsule formulation of PHA121, for the treatment of HAE type 1 and type 2 (HAE-1/2) attacks. The trial enrolled participants in Canada, Europe, Israel, the United Kingdom, and the United States. Eligible participants were between the ages of 18 and 75 years, diagnosed with HAE type I or II and experienced three or more attacks in the last four months or two or more attacks in the last two months prior to screening.

74 participants were enrolled and 62 of them experienced 147 qualifying HAE attacks that were treated with double-blinded study drug (either placebo or PHVS416 10, 20, or 30 mg doses). Analysis of the primary endpoint demonstrated that PHVS416 significantly ($p<0.0001$; nominal p value for 10 mg dose) reduced attack symptoms measured as change in the mean 3-symptom composite (skin pain, skin swelling, abdominal pain) visual analogue scale (VAS-3) score during HAE attacks, at four hours compared with placebo (LS mean difference of change in VAS-3: -16.75, -15.02, and -16.28 for PHVS416 10, 20 and 30 mg, respectively, vs. placebo). All key secondary efficacy endpoints were also met. Participants on PHVS416 also used substantially less rescue medication compared to placebo (10 mg=18.9%, 20 mg=10.7%, 30 mg=6.5%, placebo=60.8%). PHVS416 was generally well tolerated with three treatment-related adverse events (TRAEs) reported for one PHVS416 30-mg-treated attack (2.8%) and one TRAE reported for one placebo-treated attack (1.9%).

(Source: Pharvaris)

PHARVARiS

23 March 2023

At the presentation of the company's financial results for the fourth quarter and full year ended 31 December 2022, **Astria Therapeutics, Inc**.'s CEO Jill C. Milne, Ph.D., says:

"We made excellent progress with our STAR-0215 program in 2022, culminating in the promising initial Phase 1a results. These results support our vision for STAR-0215 to be the first-choice preventative therapy for HAE. The recent initiation of our ALPHA-STAR Phase 1b/2 trial marked an important step towards our goal of reducing the disease and treatment burden as we work to normalize the lives of people with HAE. We look forward to the initial proof-of-concept results from ALPHA-STAR expected in mid-2024."

STAR-0215 Clinical Development

- Positive preliminary results from the Phase 1a clinical trial of STAR-0215 in healthy subjects were announced in December 2022 and initial unblinded results from the first three cohorts were presented at the American Academy of Allergy Asthma, and Immunology Annual Meeting (AAAAI) in February 2023. STAR-0215 was well-tolerated at all doses studied. The results showed rapid and sustained drug levels, with an estimated half-life of up to 117 days and sustained target engagement with plasma kallikrein inhibition for at least three months. These results establish early proof of concept for STAR-0215 as a long-acting preventative therapy for HAE.
- The Company initiated the ALPHA-STAR Phase 1b/2 trial of STAR-0215 in people with HAE in February 2023. Initial proof-of-concept results are expected in mid-2024. The ALPHA-STAR trial is a global, open-label, proof-of-concept trial enrolling

patients with HAE types I and II that is evaluating safety and tolerability, changes in HAE attack rate, pharmacokinetics, pharmacodynamics, and quality-of-life assessments. Following an initial run-in period, qualifying participants will be enrolled in either single or multiple dose cohorts. Data from up to 18 participants will evaluate efficacy and safety, and comparisons will be made against data collected in the run-in period. Pending proof-of-concept results from the ALPHA-STAR trial, Astria expects to progress directly to a pivotal trial.

- Astria is also evaluating the potential for administration of STAR-0215 every six months in additional cohorts in the Phase 1a trial, with preliminary results expected in the fourth quarter of 2023. These data, in conjunction with the ALPHA-STAR results, are expected to inform plans for the pivotal trial.

(Source: Astria)

27 March 2023

The U.S. Food and Drug Administration (FDA) grants Regenerative Medicine Advanced Therapy (RMAT) designation to **Intellia Therapeutics, Inc**.'s NTLA-2002 for the treatment of HAE. NTLA-2002 is an in vivo CRISPR-based investigational therapy designed to inactivate the target gene, kallikrein B1 (KLKB1), to potentially prevent life-threatening swelling attacks in people with HAE.

"The RMAT designation is important recognition for our early clinical data. It indicates that a single dose of NTLA-2002 has the potential to address serious unmet medical need for people living with HAE," says Intellia President and CEO John Leonard, M.D. "We look forward to continuing our productive dialogue with the FDA to accelerate the development of NTLA-2002, an investigational in vivo CRISPR-based therapy, with the goal of bringing forth a potentially transformative treatment to patients more quickly."

The RMAT designation was established under the 21st Century Cures Act to expedite the development and review of promising therapeutic candidates, including genetic therapies, which are intended to treat, modify, reverse or cure a serious or life-threatening disease. RMAT designation includes benefits, such as early interactions with the FDA, including discussions on surrogate or intermediate endpoints that could potentially support accelerated approval and satisfy post-approval requirements, and potential priority review of a product's biologics license application (BLA).

The RMAT is the third special regulatory designation received by Intellia for NTLA-2002. NTLA-2002 was also granted Orphan Drug Designation by the FDA and the Innovation Passport by the U.K. Medicines and Healthcare products Regulatory Agency.

(Source: Intellia)

5 April 2023

At the presentation of the **Pharvaris** financial results for the fourth quarter and year ended 31 December 31 2022, CEO Berndt Modig says:

"Our first in-patient data readout of deucrictibant in people living with HAE was a significant milestone for the company. The positive outcome of the RAPIDe-1 clinical study, announced in December 2022, demonstrates the potential of PHVS416 to offer meaningful improvement over the standard of care for people living with HAE in their on-demand treatment of attacks. With the non-clinical study underway, we believe we have a path forward to address the remaining clinical holds in the U.S. We anticipate important milestones this year, including the announcement of top-line Phase 2 CHAPTER-1 data, the activation of our first ex-U.S. clinical sites for a Phase 3 on-demand study, and the submission of our non-clinical toxicology data to the FDA. The unique clinical insights of the Pharvaris team and our strong financial position have enabled us to effectively execute toward our goals; we will continue to operate with a disciplined approach as we aspire to bring best-in-class oral therapies to the HAE community."

(Source: Pharvaris)

27 April 2023

BioCryst Pharmaceuticals, Inc. announces new data from the APeX-S clinical trial, which evaluated oral, once-daily ORLADEYO® (berotralstat) for the prophylactic treatment of HAE, showing sustained reduction in disease burden for patients across multiple subgroups through 96 weeks of treatment.

"We continue to generate evidence that further strengthens confidence in ORLADEYO as a safe, effective and more convenient therapeutic option for people living with HAE. These data demonstrate how our oral, once-daily prophylactic treatment can consistently help patients spend more of their days without disruption from HAE attacks, regardless of their age, gender and experience with prior prophylactic treatment, including among pediatric patients aged 12-17. These additional analyses of long-term data reflect our continued commitment to define the potential benefits and bring ORLADEYO to as many HAE patients around the world as possible," says Dr. Ryan Arnold, Chief Medical Officer of BioCryst.

Attack-free status across subgroups of patients with hereditary angioedema after 96 weeks of berotralstat treatment:

- This analysis assessed the attack-free status of patients receiving ORLADEYO 150 mg through 96 weeks in APeX-S (n=287), stratified by baseline age, gender, and prior HAE prophylaxis treatment. The three subgroups included patients who were 12-17 (n=23), 18-64 (n=253) and ≥ 65 years of age (n=11), female (n=180) and male (n=107) and had prior experience with androgens (n=142) or C1-inhibitors (n=105).
- Overall, a reduction in mean adjusted HAE attack rates was observed compared to Weeks 0-24 in patients treated with ORLADEYO 150 mg QD. Mean adjusted HAE attack rates decreased from 1.08 from Weeks 0-24 (n=287) to 0.69 and 0.59 from Weeks 25-48 (n=214) and Weeks 49-96 (n=158), respectively.
- Attack-free status was consistently high through 96 weeks of treatment with ORLADEYO 150 mg regardless of patients' age, gender and prior prophylactic treatment.
- Patients aged 12-17, 18-64 and ≥ 65 remained attack free an average of 97, 94 and 98 percent of days, with a mean (SEM) of 196.8 (30.4), 99.3 (9.5) and 275.9 (104.4) days and a maximum duration of 461, 1,101 and 1,182 days between attacks, respectively.
- Female patients remained attack free an average of 94 percent of days, with a mean (SEM) of 106 (11.8) days and a maximum duration of 1,182 days between attacks. Male patients remained attack free an average of 94 percent of days, with a mean (SEM) of 127.2 (17.4) days and a maximum duration of 1,101 days between attacks.
- Patients who had prior treatment with androgens remained attack free an average of 93 percent of days, with a mean (SEM) of 87.1 (12.7) days and a maximum duration of 1,026 days between attacks. Patients who had prior treatment with C1-inhibitors remained attack free an average of 91 percent of days, with a mean (SEM) of 75.8 (9.8) days and a maximum duration of 584 days between attacks.
- Long-term prophylaxis with ORLADEYO 150 mg led to a durable treatment effect and sustained reduction in disease burden through 96 weeks of treatment regardless of baseline characteristics including patients' age, gender and prior prophylactic treatment.

(Source: BioCryst)

3 May 2023

"The strong new patient growth in the first quarter, building on our large patient base with ORLADEYO, positions us very well to achieve our expectations for 2023. This growing revenue stream, alongside our robust balance sheet, has dramatically reduced our reliance on the capital markets as we drive value with continued commercial execution and disciplined investment in our pipeline," says Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc.**, at the presentation of the financial results for the first quarter ended 31 March 2023.

The launch has recently surpassed the milestone of 1,000 patients in the U.S. on ORLADEYO therapy. New patient growth remained strong, with a 20 percent increase in U.S. patient start forms in the first quarter of 2023 compared to the first quarter of 2022. There were more new U.S. patient start forms in the first quarter of 2023 than in three of the four quarters in 2022.

As expected, the percentage of U.S. ORLADEYO patients receiving free drugs in the first quarter increased, primarily because many patients went through the annual re-authorization process with payors.

"As we enter our third year on the market, 1,000 of 7,500 U.S. HAE patients are already benefitting from ORLADEYO. Demand is very strong in the U.S. and in international markets, and our market data from patients and physicians tells us that ORLADEYO is still in the early stages of its growth trajectory," says Charlie Gayer, Chief Commercial Officer of BioCryst.

(Source: BioCryst)

8 May 2023

KalVista Pharmaceuticals, Inc. delivers two oral presentations and one poster presentation at the 13th C1-inhibitor Deficiency & Angioedema Workshop (C1 Workshop) in Budapest, Hungary.

Rationale for the Short-term Prophylaxis Regimen with Sebetralstat in KONFIDENT-S: Michael D. Smith, KalVista Pharmaceuticals Inc., Cambridge, MA, USA:
KalVista presents data providing the rationale for the sebetralstat regimen for short-term prophylaxis (STP) for medical and dental procedures in people living with HAE in the phase 3 KONFIDENT-S trial, which is an ongoing, up to 2-year, open-label extension of the phase 3 KONFIDENT trial.

HAE Patients Decision to Carry On-demand Treatment When Away from Home: Stephen Betschel, Division of Allergy and Immunology, Department of Medicine, St. Michael's Hospital, University of Toronto, Toronto, ON Canada:
This oral presentation is based on real-world survey data collected from people with HAE and shows that only one-third of patients always carry on-demand attack treatment with them when away from home. Of note, those that did not carry treatment would routinely travel for several hours without it for a variety of reasons, including a preference to treat with injectables at home.

Route of Administration Preferences of People with Hereditary Angioedema for On-demand Treatment: A US-based Qualitative Study: Laurence Bouillet, Internal Medicine, Grenoble Alpes University, National Reference Center for Angioedema, Grenoble, France:
The poster presentation, based on qualitative interviews with adolescents and adults with HAE, demonstrates that both groups had a strong preference for oral medication for on-demand treatment of attacks over self-administered injectable treatments when efficacy and safety profiles were similar.

"The data we have gathered from a comprehensive survey focused on the experience of patients experiencing HAE attacks has been eye-opening and reveals the real-world impact injectable treatments have on the lives of people living with HAE," says Andrew Crockett, CEO of KalVista. "Strong patient preference data for oral treatments over injectables reflects these challenges. We believe that sebetralstat may have the potential to improve patients' current treatment experience. Given the challenges with access to and logistics surrounding the use of injectables for short-term prophylaxis prior to routine medical and dental procedures, the oral regimen being assessed in KONFIDENT-S may represent yet another opportunity to enhance the lives of people living with HAE."

(Source: KalVista)

11 May 2023

Astria Therapeutics, Inc. reports financial results for the first quarter ended 31 March 2023 and provides a corporate update.

"We are excited to be administering STAR-0215 to patients in the Phase 1b/2 ALPHA-STAR clinical trial. We on track to share initial proof-of-concept results which are anticipated in mid-2024," says Jill C. Milne, Ph.D., CEO at Astria. "We are also encouraged by human mechanistic modeling data that supports the potential for STAR-0215 to be administered once every three or six months for robust suppression of HAE attacks with low treatment burden. The modeling results, in conjunction with our clinical momentum, bring us closer to our goal of making STAR-0215 the first-choice preventative treatment for HAE to help normalize the lives of the HAE community."

22 May 2023

The Public Health Institute (ISP) of Chile has granted marketing authorization for oral, once-daily ORLADEYO® (berotralstat) for the prophylaxis of HAE attacks in patients 12 years of age or older.

"The announcement marks the first approval of ORLADEYO in Latin America, which is an important step forward in addressing the significant unmet needs of HAE patients who live in the region. With this approval, we continue our mission to bring ORLADEYO to patients around the world who could benefit from an oral, once-daily prophylactic treatment option to improve control of their HAE attacks," says Charlie Gayer, Chief Commercial Officer of **BioCryst Pharmaceuticals, Inc**.

BioCryst has an exclusive collaboration with Pint Pharma GmbH to register and promote ORLADEYO in the pan-Latin America region. Under the terms of the agreement, Pint is responsible for obtaining and maintaining all marketing authorizations and for commercializing ORLADEYO in the region.

1 June 2023

Ionis Pharmaceuticals, Inc. announces positive clinical progress with donidalorsen, its late-stage investigational prophylactic therapy for HAE. Topline two-year open-label extension (OLE) results continue to demonstrate consistent efficacy and safety, with an overall sustained mean reduction in HAE attack rates of 96% from baseline through two years across dosing groups. The company also announces that it has completed enrollment in the Phase 3 OASIS-HAE study, which is evaluating the safety and efficacy of donidalorsen in preventing angioedema attacks. Topline data from the study are expected in the first half of 2024.

"By completing enrollment in the Phase 3 study, we are one step closer to bringing a potentially transformative and differentiated prophylactic treatment to HAE patients," says Richard S. Geary, Ph.D., Executive Vice President and Chief Development Officer at Ionis. "We are also encouraged by the long-term safety and durable efficacy results seen in patients treated for two years in our ongoing open-label extension study. We look forward to the Phase 3 data readout in the first half of 2024 and are advancing our go-to-market preparations to commercialize donidalorsen."

The two-year Phase 2 OLE results will be presented at an upcoming medical congress.

In the Phase 2 study, through week 17, donidalorsen 80 mg monthly demonstrated a 90% reduction in angioedema attacks compared with placebo after the first dose, and a 97% reduction in angioedema attacks starting with the second dose. The Phase 2 results also showed a significant improvement in quality of life as assessed by the Angioedema Quality of Life Questionnaire (AE-QoL), in the patients treated with donidalorsen. Donidalorsen continues to demonstrate a favorable safety and tolerability profile with added two-year OLE data.

(Source: Ionis)

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