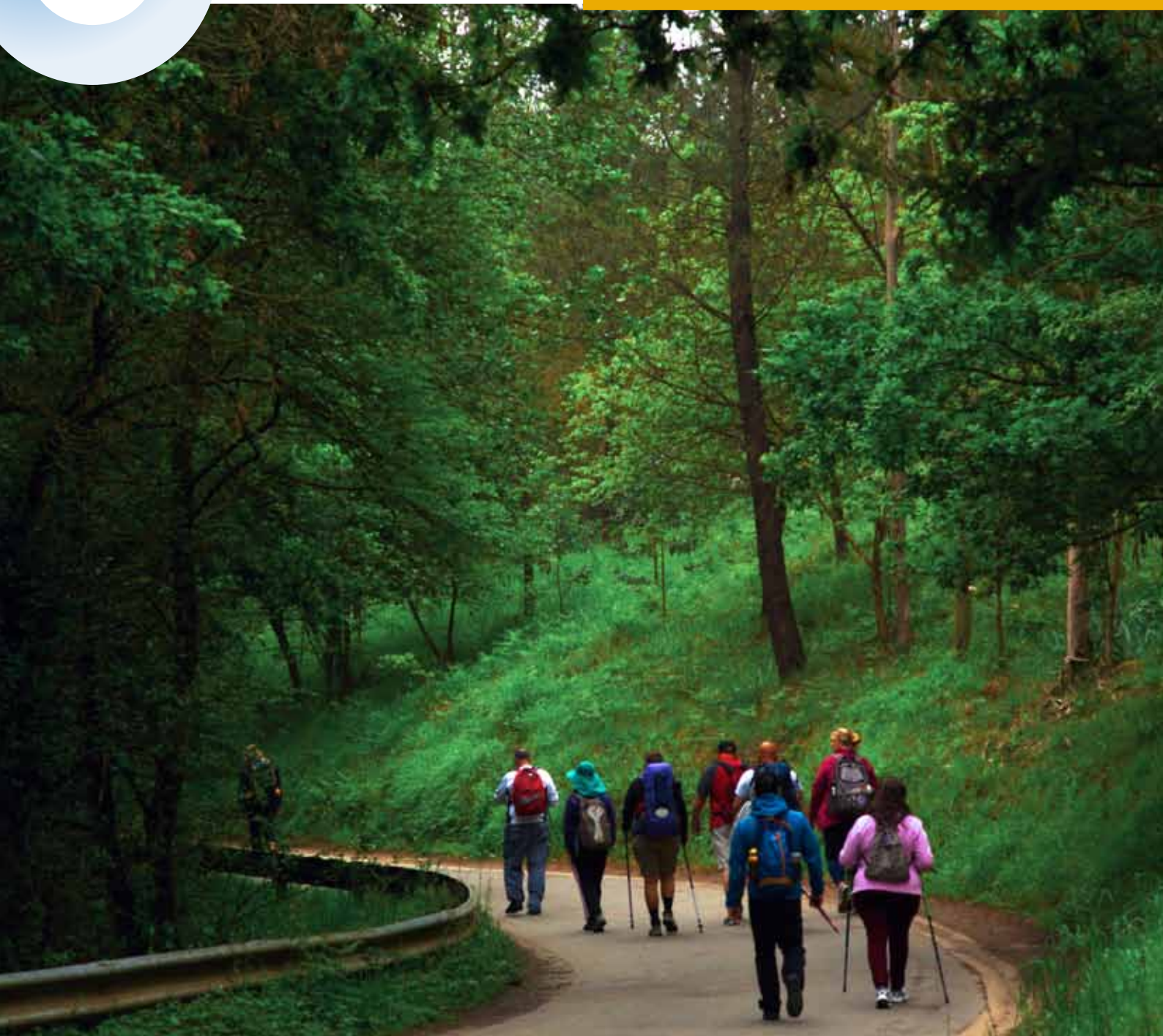


# Global perspectives:

HAEi MAGAZINE · ISSUE 1/2019



## **HAEi/AEDAF Camino Walk 2019**

Following the successful planning and execution of the HAEi/AEDAF Camino Walk events in northwestern Spain in 2016 and 2017 as well as the HAEi Jakobsweg Walk in Vienna, Austria in 2018 HAEi has once more teamed up with the Spanish organization AEDAF for the third Camino Walk in Spain.





**HAE  
GLOBAL  
CONFERENCE  
FRANKFURT  
14-17 MAY  
2020**

## **Welcome to the 5th HAE Global Conference**

“2012 Copenhagen, 2014 Washington D.C., 2016 Madrid, 2018 Vienna. And now we are ready to present the venue for the 5th HAE Global Conference as it will be taking place in Frankfurt am Main, Germany from 14 to 17 May 2020”, says HAEi President & CEO Anthony J. Castaldo.

“Frankfurt was an obvious choice as its airport serves as a hub for many destinations worldwide. We have also chosen the Sheraton Frankfurt Airport Hotel as our venue. This hotel is located directly at Terminal 1 at Frankfurt International Airport. More information about the 2020 HAE Global Conference will follow during 2019,” says, HAEi Executive Vice President & Chief Operating Officer Henrik Balle Boysen.





## Dear HAEi Friends,

The first quarter of 2019 has been a particularly busy and productive time for HAE International (HAEi). HAEi now has member organizations in 74 countries. The pages that follow in this edition of Global Perspectives offer clear evidence that the global HAE patient movement continues to build momentum!

Please join me in congratulating Fiona Wardman on her appointment as Chief Regional Patient Advocate. Fiona oversees a group of skilled and experienced Regional Patient Advocates (RPA), who (1) deliver HAEi's programs, activities, and specialized expertise to our member organizations, and (2) are available to help member organization's leadership grow their organizations and sharpen their advocacy programs. The RPAs are also responsible for helping to both form and support new patient organizations and, as you will read in the pages that follow, HAEi sponsored and organized the first patient meeting in India.

On 18 May 2018 HAEi member organizations unanimously passed a resolution directing HAEi to broaden governance by establishing Regional Advisory Groups and reduce the current amount of income tax and VAT. As described in the lead article, we are moving forward with a plan that maximizes member organization representation and participation in HAEi governance. We have also taken steps to ensure that our financial resources are spent on programs and activities rather than paying taxes.

Finally, it is with great sadness that we acknowledge the death of Dr Dumitru Moldovan from Romania. Dr Moldovan worked diligently to bring modern HAE medicines to his country and was an important contributor to the international clinical and scientific HAE community. He will always be remembered as a friendly and compassionate person who cared deeply about HAE patients.

Anthony J. Castaldo  
President & CEO, HAEi

*Global* perspectives

**Global Perspectives**  
Issue 1/2019  
April 2019

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Read more about the HAEi/AEDAF  
Camino Walk 2019 on page 17

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



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## HAEi fulfills the General Assembly mandate

At the HAEi General Assembly on 18 May 2018 HAEi member organizations unanimously voted to pass a resolution authorizing the Executive Committee of HAEi to make changes to the HAEi charter in order to:

- Broaden HAEi governance by establishing Regional Advisory Groups
- Reduce the current amount of income tax and value added tax (VAT) HAEi currently pays

HAEi would like to update you on the changes that have been made in order to fulfill these ambitious goals.

### **BROADEN HAEi GOVERNANCE BY ESTABLISHING REGIONAL ADVISORY GROUPS**

Regional Advisory Groups will be established to ensure that member organizations have a mechanism to provide their insights and advice to HAEi. The Regional Advisory Groups will correspond with the areas that are covered by the current Regional Patient Advocates.

Each member organization in a region with a Regional Patient Advocate will be invited to appoint a representative to participate in Regional Advisory Group meetings. During these meetings, the representatives will be asked to provide feedback about HAEi programs, discuss their own programs, and make recommendations on what HAEi should focus on in the future.

### **REDUCE THE AMOUNT OF TAXES HAEi CURRENTLY PAYS**

The second part of the resolution provided the HAEi Executive Committee with the mandate to increase monies available to support patient programs by minimizing the tax and VAT burden.

To fulfill this mandate, HAEi conducted a worldwide search for a country that offers a full tax-exempt for a non-profit organization but has no country-specific requirements for physical presence of employees or members of the leadership and/or governing team. The United States of America was identified as the only stable country globally where a registered charitable organization can be both tax and VAT exempt, with no requirements with regard to any specific US involvement in that charity by either US citizens or US businesses.

The United States of America requires that a Board of Directors govern every charitable organization. Therefore the HAEi Executive Committee is now called the Board of Directors and consists of:

- Anthony J. Castaldo, President & Chief Executive Officer
- Michal Rutkowski, Vice President
- Fiona Wardman, Treasurer
- Sarah L. Smith Foltz
- Jørn Schultz-Boysen
- Rachel Annals
- Beverley Yamamoto
- Natasha Jovanovska Popovska

HAEi was officially registered as a charitable organization in the United States of America at the beginning of 2019.

“HAEi is proud to deliver on the General Assembly resolutions, which will increase member organization representation and participation in HAEi governance, and ensure that our financial resources are spent on programs and activities rather than paying taxes”, says President & CEO Anthony J. Castaldo.

Some changes have also been made to the HAEi operational staff. Here you will now find:

- Henrik Balle Boysen, Executive Vice President & Chief Operating Officer
- Nevena Tsutsumanova, Operations Manager
- Steen Bjerre, Communications Manager
- Deborah Corcoran, Chief Specialist Projects and Research
- Ole Frølich Christensen, Enterprise Technology Manager
- Rikke Sørensen, Communication Design and Graphics Manager



## Board of Directors



Anthony J. Castaldo  
President & CEO



Michal Rutkowski  
Vice President



Fiona Wardman  
Treasurer



Sarah L. Smith Foltz



Jørn Schultz-Boysen



Rachel Annals



Beverley Yamamoto



Natasha Jovanovska Popovska

## Operational staff



Henrik Balle Boysen  
Executive Vice President  
& Chief Operating Officer



Nevena Tsutsumanova  
Operations Manager



Steen Bjerre  
Communications Manager



Deborah Corcoran  
Chief Specialist  
Projects and Research



Ole Frølich Christensen  
Enterprise Technology Manager



Rikke Sørensen  
Communication Design  
and Graphics Manager

# HAEi now has a Chief Regional Patient Advocate

As the readers of Global Perspectives may know, the HAEi Regional Patient Advocate (RPA) program was started a few years ago with Chief Specialist Projects and Research Deborah Corcoran at the helm.

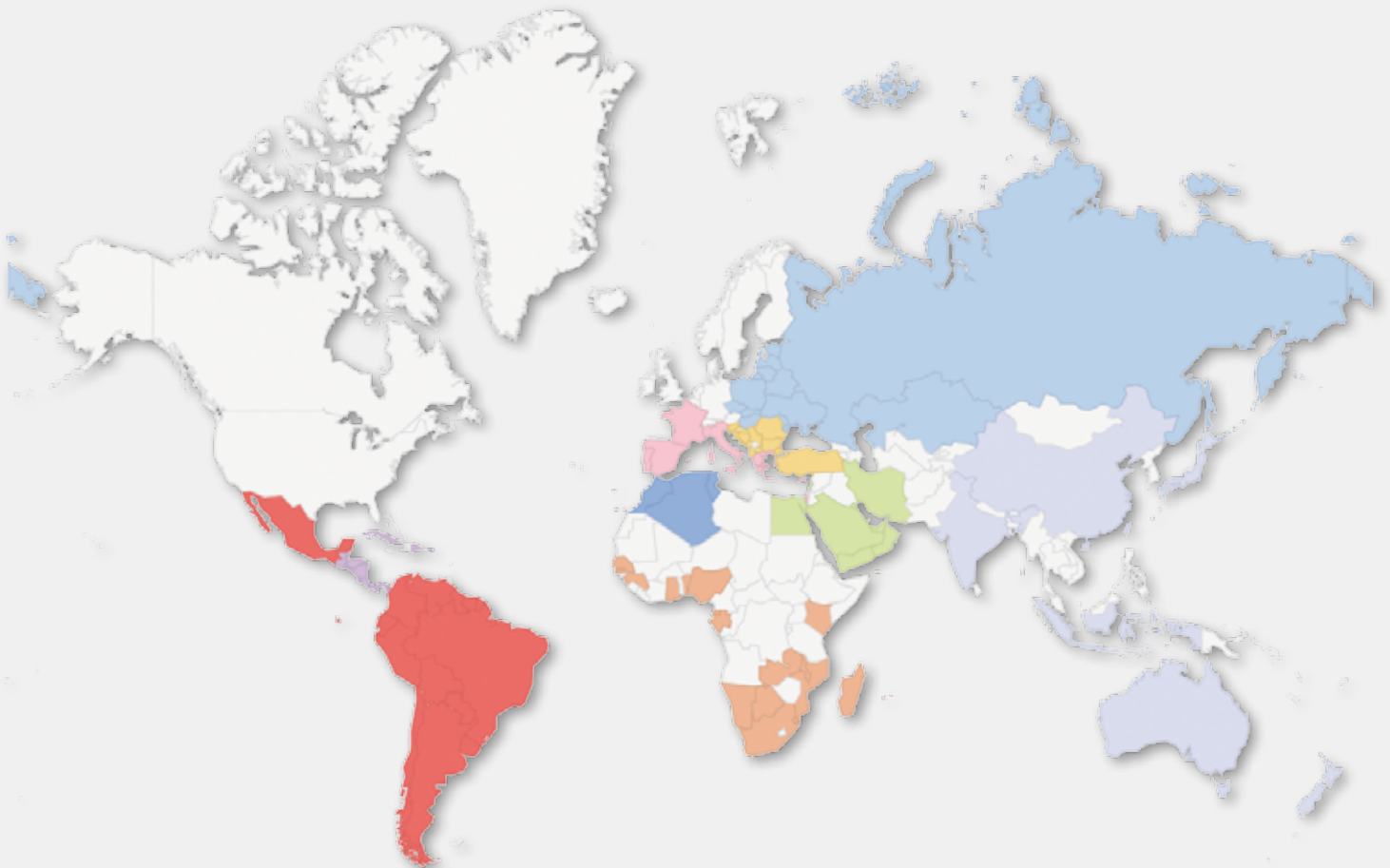
“Our growing RPA program has become the backbone of HAEi and the experienced and talented people who serve in this role are delivering HAEi’s expertise and programs to our member organizations and achieving results. Given the increased activity in the RPA program, I am

honored to have been appointed as the Chief Regional Patient Advocate for HAEi along with my regional work in Asia Pacific and India”, says Fiona Wardman:

“Over the last few months, I have been working more closely with each Regional Patient Advocate and have gained insight into the great work that is being done by them all. It’s my pleasure to introduce the summaries of just some of the fantastic work that is continuing around the globe in this latest edition of Global Perspectives.”

- **Michal Rutkowski** – Central and Eastern Europe
- **Natasa Angjeleska** – South East Europe
- **Maria Ferron** – Mediterranean
- **Rashad Matraji** – Gulf Region and Middle East
- **Javier Santana** – Central America

- **Patricia Karani** – Sub-Sahara Africa
- **Fernanda Martins** – South America and Mexico
- **Fiona Wardman** – Asia Pacific
- **Maria Ferron and Rashad Matraji**







**Patricia Karani**  
Sub-Sahara Africa



### **SOUTH AFRICA**

The first patient meeting was held 14 March 2019 in Cape Town. In attendance were doctors and patients who learned more on HAE and how best to gain access to emergency medication.



### **SENEGAL**

HAEi has been able to reach collaboration with the Africa Society of Primary Immunodeficiency and look for ways of raising HAE awareness amongst its medical members.



**Fiona Wardman**  
Asia Pacific



### **TAIWAN**

Plans are being made for HAEi to meet with a Taiwanese doctor and his HAE patients in May 2019. This will be the first time a meeting of this type has taken place. Hopefully this will be the beginning of improvements for patients in the country.



### **HONG KONG**

Fiona has established contact with a doctor in Hong Kong who has HAE patients. The doctor is corresponding with his colleagues for them to contact their patients in the view to holding an informal meeting in the next few months.



### **INDIA**

The first patient meeting was held 9 March 2019 – please see extensive coverage elsewhere in this magazine.



**Fernanda de Oliveira Martins**  
Mexico and South America

### GENERAL

Fernanda is presently working on the agenda for a regional meeting that is to take place 27-28 April 2019 in Bogotá, Colombia.



### PARAGUAY

Fernanda is in contact with a doctor interested in supporting the creation of a Paraguayan HAE Association.



### ECUADOR

The HAE organization is working on a letter to the Ministry of Health to include HAE as a serious illness.



**Natasa Angjeleska**  
South Eastern Europe



### SERBIA

In February 2019 Natasa participated in the annual patient meeting of HAE Serbia delivering a presentation entitled "The incredible power of advocacy". The program also included addresses from two physicians about the therapeutic options for HAE and patients heard about the bureaucratic procedures regarding receiving medication.



### ALBANIA

Natasa has agreed to visit patients and physicians in Albania as support to the national patient group and in order to explore options for Albanian patients to receive access to modern HAE medications.





**Michal Rutkowski**  
Central & Eastern Europe



### LITHUANIA

Michal is in contact with a doctor from Vilnius who has shown interest in joining the HAE Global Registry project. The doctor sees around 10 HAE patients.



### RUSSIA

Michal has been invited to attend the “Scientific and Practical International HAE Conference” that HAE Russia will be organizing in Moscow, Russia 19-20 June 2019.



### ARMENIA

At this point Armenia does not have an HAE organization and HAE patients do not have access to any modern therapies. Michal has established contact with an HAE physician in Yerevan with a few HAE patients under her supervision. This doctor is very interested in collaborating with HAEi.



### SLOVAKIA

Michal has been helping the management of HAE Slovakia out with the preliminary considerations regarding a national HAE summit for Slovakian patients later this year.



### BELARUS

HAE Belarus is working on a new national website under the HAEi umbrella. Also, the organization is preparing a national HAE summit dedicated to patients and physicians - this is likely to take place in late June.

## Roles of the Regional Patient Advocates

- Supporting the member organizations already in place
- Assisting in setting up new groups in countries with no existing organization



**Javier Santana**  
Central America and the Caribbean



### PANAMÁ

Javier is planning a trip to Panama to meet with the patient group and offer a workshop on how to create awareness events, media interviewing tips, and addressing government issues.



### COSTA RICA

In February 2019 HAE Costa Rica held the first conference on HAE in the Medical Faculty of the University of Costa Rica. Attendees and speakers included medical professors, Costa Rican allergist specialists, HAE patients, government representatives, as well as medical students.

During the event, several patients described their experiences with HAE attacks, hospital misdiagnosis, failure in treatments, and the lack of effective therapies. Doctors discussed the disease state, symptoms and triggers, as well as the need for effective treatments. As a direct result of the participation of the Deputy Minister of Health of Costa Rica, the State Hospital was ordered to initiate/perform HAE relevant testing to identify patients with HAE.

Furthermore, Javier has been talking with several medical specialists to identify more HAE patients. He has also met with the new head of HAE Costa Rica and with several patients to discuss local strategies. Most recently, a patient contacted Javier through the new Facebook group, and he helped with contact with HAE Costa Rica.

The new head of HAE Costa Rica is Angie Leitón. She can be reached at [aleiton1694@gmail.com](mailto:aleiton1694@gmail.com) and +506 8553 5295.



### EL SALVADOR

Javier has been helping HAE El Salvador with collecting the information needed for a national website under the HAEi umbrella. Additionally, he has supported in the process of applying to attend the Global Youth Advocacy Program taking place in Atlanta, USA this summer. Javier has also provided HAE El Salvador with informative and promotional material in Spanish to share with patients and doctors.



### CUBA

Javier has been in contact with a Cuban who is both doctor and HAE patient. He already knows of some other HAE patients in the country – and he is willing to lead a national organization in Cuba, identify more patients, educate about the disease, and identify processes needed to facilitate access to treatments in Cuba. With this point-of-contact in place Cuba has been added to the HAEi world map.



### DOMINICAN REPUBLIC

Together with a doctor from Puerto Rico Javier is planning on visiting doctors in the Dominican Republic to identify HAE patients and help in the diagnosis and treatment process.







**Rashad Matraji**  
Gulf Region and Middle East

 **LEBANON**

Together with a Lebanese doctor Rashad has been working on a meeting leading up to the WAO International Scientific Conference in Beirut in April 2019.

 **KUWAIT, QATAR**

In both countries Rashad has helped in identifying patients who have agreed to become the national HAE point-of-contact. Therefore, both Kuwait and Qatar have been added to the HAEi world map.

 **SYRIA**

A Syrian patient with HAE in his family has been identified via Facebook – Rashad is working on developing more contacts. Due to the war there is no access to medication but together with a local doctor Rashad is trying to assist with information.

 **YEMEN**

Rashad has located a number of patients. However, there seems to be no HAE knowledgeable doctors and no medication.



**Maria Ferron**  
Mediterranean

 **MOROCCO**

19 January 2019 AMMAO (HAE Morocco) held the first meeting as an official association with 115 attendees. Maria attended on behalf of HAEi introducing the association, projects, and activities to the Moroccan community. Presently Maria is supporting AMMAO on hosting their website under the HAEi umbrella.

 **PORTUGAL**

Maria is trying to locate more patients willing to support the association ADAH (HAE Portugal). Home treatment is not yet available for most of the patients so Maria is working on trying to improve this situation as well.





## 44 HAE pilgrims to walk the Camino

Following the successful planning and execution of the HAEi/AEDAF Camino Walk events in northwestern Spain in 2016 and 2017 as well as the HAEi Jakobsweg Walk in Vienna, Austria in 2018 HAEi has once more teamed up with the Spanish organization AEDAF for the third Camino Walk in Spain.

“We had hoped to be able to attract around 30 participants, but at this point 44 HAE pilgrims have signed up for the 2019 edition of the HAEi/AEDAF Camino Walk. Once more people will be coming from four continents as we cover Spain, the USA, Italy, Denmark, Hungary, South Africa, Chile, and Norway”, says Steen Bjerre from the organizing team.

The pilgrims will be meeting in Madrid Airport on the morning of Wednesday 15 May 2019 from where a bus will take them some 600 km to El Ferrol.

“The first stage is appropriately coinciding with **hae day :-)** this year as we will start Thursday morning and walk some 15 km from El Ferrol to Puentedeume. The following day we will walk from Puentedeume to Betanzos – that is around 18 km. Finally, Saturday morning the third and final stage will be taking us the approximately 14 km from Sigüeiro to Santiago de Compostela”, says Steen Bjerre.

The participants will round off the HAEi/AEDAF Camino Walk 2019 by taking part in the pilgrim’s mass at the cathedral in Santiago de Compostela before the bus brings them back to Madrid.

### You can follow the Camino Walk on a number of social media:

- Open HAEi Facebook page: [www.facebook.com/haeinternational](http://www.facebook.com/haeinternational)
- Closed HAEi Facebook group: [www.facebook.com/groups/HAEinternational](http://www.facebook.com/groups/HAEinternational)
- Closed HAEi Camino Amigos group: [www.facebook.com/groups/1704846256399874](http://www.facebook.com/groups/1704846256399874)
- Twitter: [twitter.com/HAEDAY](https://twitter.com/HAEDAY)
- Instagram: [haecamino](https://www.instagram.com/haecamino)
- Website: [www.haei.org](http://www.haei.org)

**The official hashtag is #haecamino19**



## HAEi brings hope to India

*By Fiona Wardman, HAEi Chief Regional Patient Advocate*

Early March 2019 patients, their families, physicians, industry and other rare disease experts along with HAEi came together for the first HAE meeting in India. For most of the patients, this was also the first time they had met anyone outside of their family who knew exactly what they had been going through all their lives.

A group of 40 of us gathered at the Aloft Hotel in Aerocity, Delhi where the morning session opened with a welcome and introduction by Dr Shaibal Guha, who is head of HAE India, and myself. Our first two presentations were by Dr Aleena Banerji who presented remotely from the USA on “What every patient needs to know about HAE” and “The History of HAE Treatments and what is on the horizon”. The next speaker was patient Pravlika who shared her story with candidness and hope.

Following a morning tea break, Dr Anuradha Udumudi – the founder of Genetech – discussed Genetics of HAE and presented on her experience with HAE, which was very insightful.

Professor Binay Biswas then spoke about the in-hospital management of HAE patients in India with limited options and unlimited challenges.

After lunch, Dr Ankur Jindal spoke on the Indian perspective of HAE and presented case studies. We then heard from Mr Prasanna Shirol and Ms Shami Ravishankar from the Organisation for Rare Diseases India on their initiatives helping patients create awareness in India. Furthermore, our own Henrik Balle Boysen and Anthony J. Castaldo presented on HAEi experiences around the globe and shared information on resources and the support that HAEi can offer.

The afternoon session was an opportunity for everyone to have their questions answered by the panel of experts; this was then followed by discussions on the next step for HAE India.

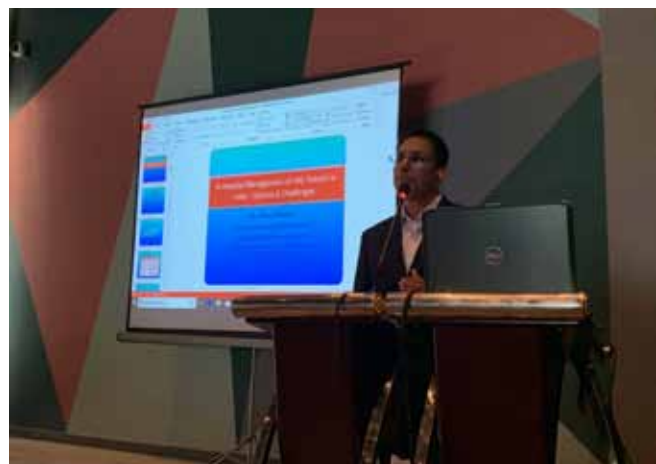


All presentations and speakers were warmly received, and from the feedback, the meeting was a very positive and worthwhile experience for everyone. Here is just some of the feedback we have received following the meeting:

- “It was great to meet you all personally. I am very happy that we were able to share our experiences with fellow patients and were able to get detailed replies from all experts. Each and every speaker was excellent and my thnx to all of them. My special thnx to Fiona and HAEi team for the wonderful coordination.”
- “Thanks a lot to everyone. We have to keep our move on and today was indeed a great day for all of us. Please be in touch”
- “Thank you very much Fiona and other team members for all the wonderful arrangements for meeting today. Wish HAE India all the very best to support patients and families.”
- “Informative, interactive, inspirational HAE meet. Thank you very much”
- “Thanks Fiona and other delegates and my fellow friends coming from long way and gathering a HAE meet in India for first time”
- “Many thanks to Fiona and HAEi team for organizing this and for everything else you do to make better treatment options available to HAE community”
- “Our special thanks to Dr Shaibal also for his support and follow up.”
- “Thank you Fiona and Dr Shaibal for giving us an opportunity to come together share and discuss stuff. It was really wonderful meeting you guys. Stay strong and positive. And if you are having any attack or if you need any emotional support we can always count on each other to understand”
- “What I saw at the meeting yesterday was truly inspiring! Commendable job by Fiona, HAEi and HAE India. If any of you need information or advise on inheritance of HAE and genetic testing or counseling for your family or other family members, please write to me. I will be glad to help. I hope the registry will grow in numbers and most needed drugs will be available to all in India. Good luck to all of you! Dr Anuradha Udumudi from GeneTech.”

Discussions and plans are already in motion to set up a Physician forum and work on ways to educate and create further and necessary awareness in India. We have a long way to go, but the first steps have been taken.

It was great to see new friendships formed, to feel the positivity, and see the willingness to continue to strengthen the unified patient voice by everyone who attended the meeting.



APRIL  
2019

**HAEi**  
Youngsters

## INSPIRING STORIES FROM HAEI YOUNGSTERS' COMMUNITY:



### RARE DISEASES, RARE PEOPLE

Youth and young adult-focused digital media and broadcasting company recently interviewed Eirini, an active member of the HAEi Youngsters' Community, to discuss and learn about HAE. In the interview Eirini talks about what it's like to be a rare disease patient living in Greece. She shares the story of her journey to diagnosis and how her life changed following it:

"At first, I thought it was completely weird that it could be treated. Growing up like this and being the only thing I knew, I thought that this was just the way my body works."

Read Eirini's story and find out where to watch the interview:

<https://haei.org/youngsters/vice-specials-rare-diseases-rare-people/>



### THE HAEI YOUNGSTERS COMMUNITY - TAKING ACTION!

In early March 2019 our very own HAEi Youngsters' Community and Advisory Group member, Nanna Maria Boysen (17), was invited to take part at AEDAF's patient meeting in Madrid, Spain. We are very excited that Nanna got a chance to meet with some of the Spanish youngsters and tell them more about our goals and vision for the young generation of HAE patients.

"The HAEi Youngsters Community is not only a place where youngsters can share their experiences and stay connected but also a place to help each other advocate for HAE, express our thoughts, hopes and goals for the future - all while having lots of fun!", says Nanna.

See Nanna's upcoming blog post on <https://haei.org/youngsters/>





## FINDING WORLDWIDE FRIENDSHIP WITH HAEI

Naty Galárraga, an HAE patient from Ecuador, has always enjoyed exploring new places and experiencing new things. She used to wonder how HAE would affect her travelling aspirations but she never expected that HAE would enable her to meet a whole community of people who would support and enrich her travels:

“From that first four-day HAEi Summer Camp, I never would have imagined forming these friendships, much less finding so many people like myself. Although we don’t see each other every day, and even though we’re separated by hundreds and thousands of kilometers, we Youngsters find ways to help each other, keep in touch, and share our favorite experiences with each other.”

Read more of Naty’s story:

<https://haei.org/youngsters/finding-worldwide-friendship-with-haei/>

## HAEI YOUNGSTERS' COMMUNITY

You can follow all the Youngsters' Community's activities via their blog at [haei.org/youngsters](https://haei.org/youngsters).

If you're a young person living with HAE and are interested in joining the HAEi Youngsters' Community or want to share your own inspiring story get in contact using Facebook, Instagram or email.



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[instagram.com/haeiyoungsters](https://www.instagram.com/haeiyoungsters)



HAEi Youngsters Community  
[facebook.com/groups/470967886612519](https://www.facebook.com/groups/470967886612519)



[youngsters@haei.org](mailto:youngsters@haei.org)





## Dr Moldovan in memoriam

*By Dr. Marco Cicardi, Co-Chair, HAEi Medical Advisory Panel*

On 11 February 2019, the HAE world lost a cherished colleague when Dr Dumitru Moldovan (known to all as Itu) passed away at home in Targu Mures, Romania surrounded by family and close friends.

The global HAE scientific community responded to Itu's passing with countless messages expressing sadness over losing a great friend and leader in the HAE field. Itu will be remembered for his thoughtful commitment to advancing the science of HAE, creating an HAE Center of Excellence despite scarce financial resources, and willingness to fight for Romanian patients. His commitment to the HAE cause knew no limits, and despite failing health, Itu organized an important international conference that took place last year in Bucharest, Romania.

Above all we will miss his warm smile, and "down to earth" approach to people and solving problems.

*By Anthony J. Castaldo, HAEi President & CEO*

On behalf of HAE International's member organizations, we would like to express our sincere condolences to Dr Moldovan's family and friends.

His interest in HAE was enduring and global in its impact. An inspiration to us all, he steadfastly and bravely continued his presence on the global HAE stage by most recently (and successfully) fulfilling a vitally important leadership role in the HAE Global Registry.

We have fond memories of a friendly and compassionate person, physician, and scientist who made a distinct and significant contribution to improving the quality of life for HAE patients. He will be missed, but not forgotten.

# HAEi is ready to host your website

Still more national HAE organizations across the globe are letting HAEi host their websites – for pretty obvious reasons if you ask HAEi Enterprise Technology Manager Ole Frölich:

“We have established an advanced system under the HAEi website allowing us to host national websites as well as provide them with templates for an individualized website – naturally all in their native language. And not to forget: This service is for free for all HAEi member organizations.”

At this point, there are four new website templates to choose from – and in the backend, there are powerful editing tools for the website administrator. Furthermore, the HAEi solution supports your organization’s own domain name just as it supports https// secure protocol.

At this point 16 countries have an HAEi hosted website. These countries are Australia, Ecuador, Greece, Hungary, Iceland, Kenya, New Zealand, North Macedonia, Peru, Poland, Romania, Serbia, South Africa, Spain, Turkey, and Uruguay.

“We are in contact with a further 11 countries and hope to able to launch the majority of these websites during 2019”, says Ole Frölich:

“These national organizations are Albania, Belarus, Brazil, Bulgaria, Czech Republic, Croatia, India, Ireland, Montenegro, Slovenia, and EL Salvador.”





## Still more countries on HAEi Connect

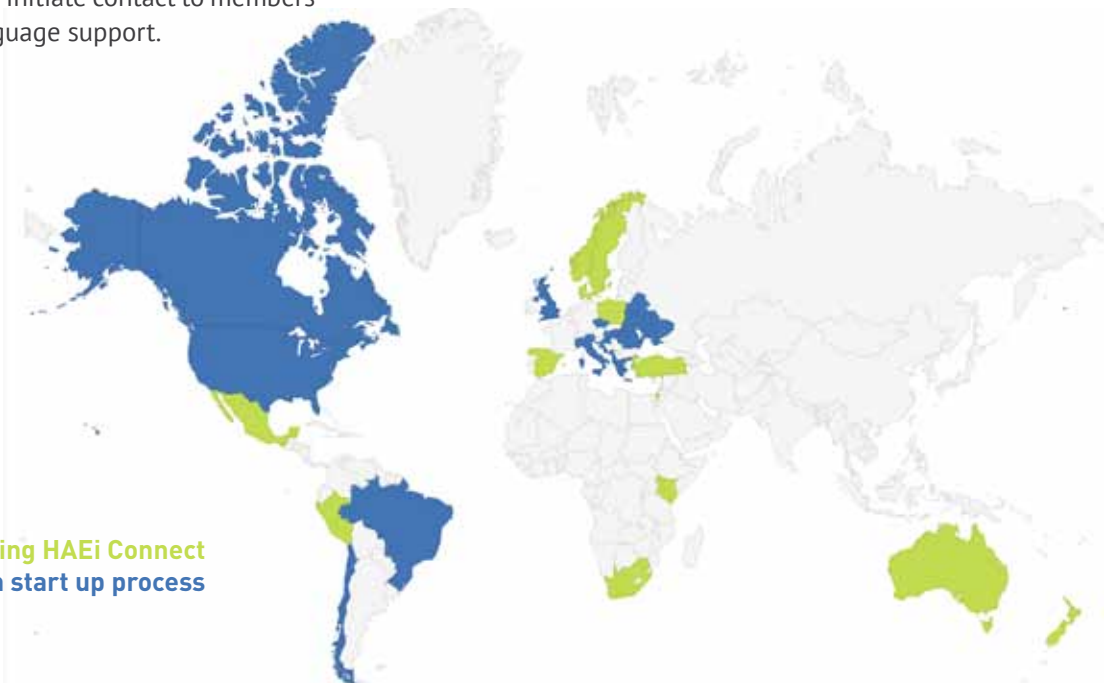
In 2018 HAEi presented HAEi Connect – a cloud-based member database for national organizations to manage their members. Due to popular demand, this free-of-charge offer has been updated in February 2019 with a number of highly useful features. HAEi Enterprise Technology Manager Ole Frölich explains:

“First and foremost HAEi Connect includes an easy to use editor for creating emails to members as well as a template for saving and re-using emails. Another addition to the system is the possibility of contacting members via text message.”

Other updated features are four new sections in the HAEi Connect dashboard to initiate contact to members as well as right-to-left language support.

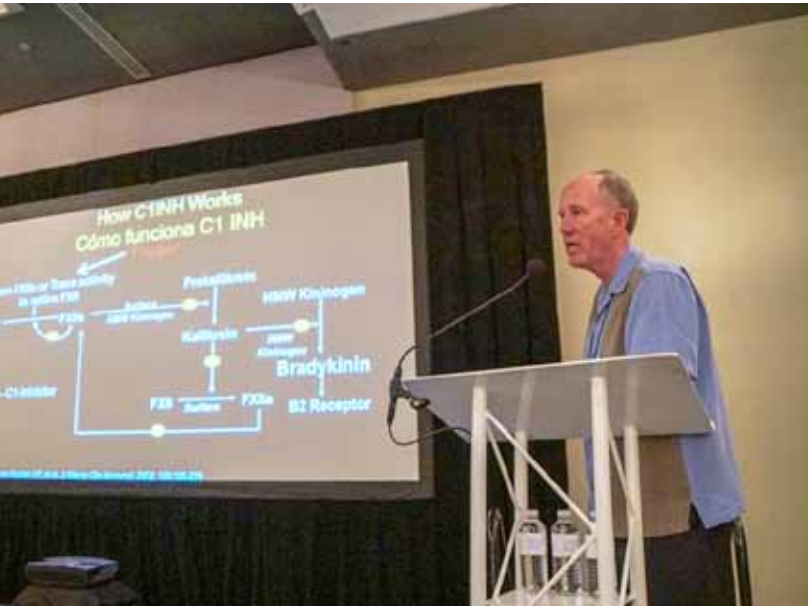
At this point, 17 countries are using HAEi Connect: Australia, Bulgaria, Denmark, India, Israel, Kenya, Mexico, New Zealand, North Macedonia, Norway, Peru, Poland, Slovenia, South Africa, Spain, Sweden, and Turkey.

“Furthermore, we are presently talking to the national organizations in Albania, Belarus, Brazil, Czech Republic, Croatia, Greece, Hungary, Italy, Japan, Montenegro, Romania, Slovakia, Ukraine, United Kingdom, and the United States of America”, says Ole Frölich.



17 countries using HAEi Connect  
15 countries in start up process





SEVEN IN TEN!  
WILLIAM R. LUMRY, M.D.

## SEVEN IN TEN!

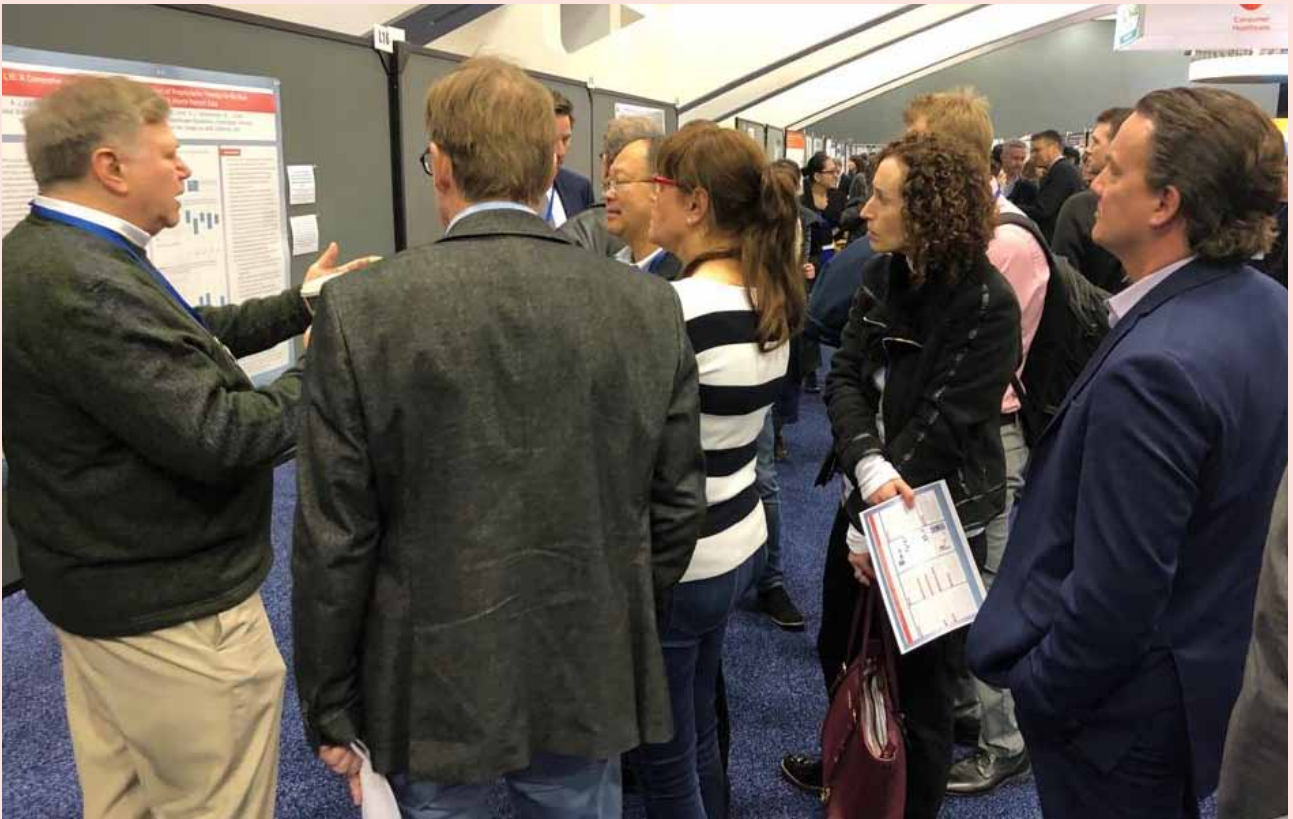
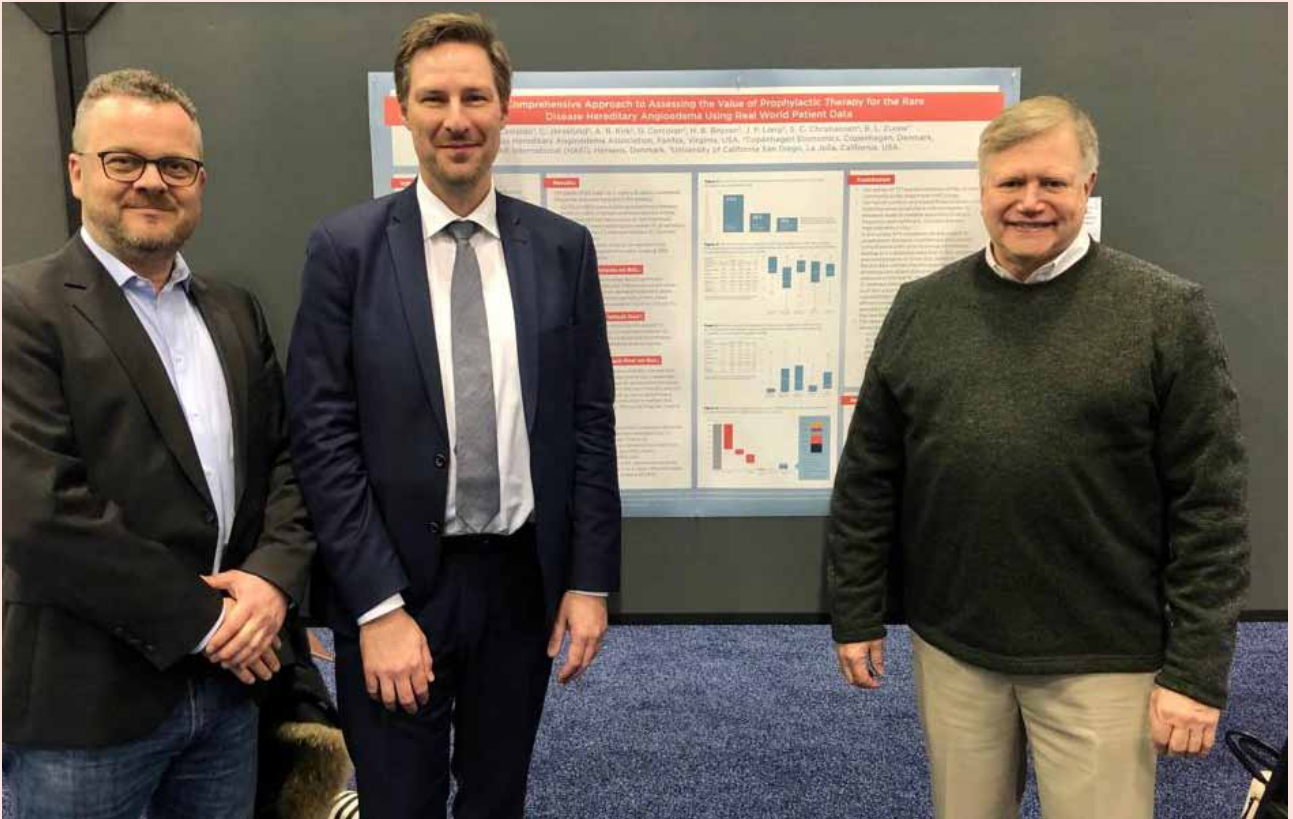
By William R. Lumry, M.D., Allergy Immunology Specialist, Clinical Professor of Internal Medicine, University of Texas Southwestern Medical School.

Seven safe and effective treatments for treatment and prevention of HAE attacks have been approved and are available for treatment in various countries around the world. This occurred in only ten years! I think all of us who have or care for individuals with HAE are thankful for these life-changing and life-saving treatments.

Who do we thank? First and foremost thank you to those of you in the HAE community who volunteered your time and energy and bodies to participate in the clinical research trials that proved these treatments were effective and safe allowing them to be approved. Without your efforts this amazing accomplishment, (7 IN 10), would not have happened. You are the heroes in our community! We also should thank HAEi for advocating for us, encouraging pharmaceutical companies to take the risk to develop these products, the pharmaceutical companies who did the drug development and the physicians and researchers who coordinated and managed the trials.

As a physician who conducts clinical research for HAE patients, I encourage you to become a hero. There is more work to be done to develop new and innovative treatments for HAE. You can help. Please know these trials do require you to make some sacrifices for the greater good. You will need to make time to keep your appointments, take your study medication, keep track of your progress and occasionally have some blood drawn. It is important for you to carefully and truthfully report your experience with the study medication. Some of the trials last months or years but it is vitally important that you stay in the trial until the end of it so a complete picture of your experience can be captured.

THANK YOU to all of you who made 7 IN 10 possible! And THANK YOU to those who will continue to support these important research efforts.





# The Value of Prophylactic Therapy

**A study sponsored by the US HAEA and HAEi assess the value of the new subcutaneous prophylaxis therapies to on-demand only treatment.**

The results of the study were presented as a poster at the annual meeting of the American Academy of Allergy, Asthma & Immunology (AAAAI) in San Francisco, USA 22-25 February 2019. The presenters of the poster with the title “A Comprehensive Approach to Assessing the Value of Prophylactic Therapy for the Rare Disease Hereditary Angioedema Using Real World Patient Data” were HAEi President & Chief Executive Officer Anthony J. Castaldo and Executive Vice President & Chief Operating Officer Henrik Balle Boysen.

“The study involved a survey of 737 patient members of the US HAEA community is the largest ever HAE survey. The results confirm and extend those of recent clinical trials that show prophylaxis with the newest subcutaneous therapies leads to sizeable reductions in attack frequency and significant, clinically relevant improvement in the quality of life”, says Anthony J. Castaldo:

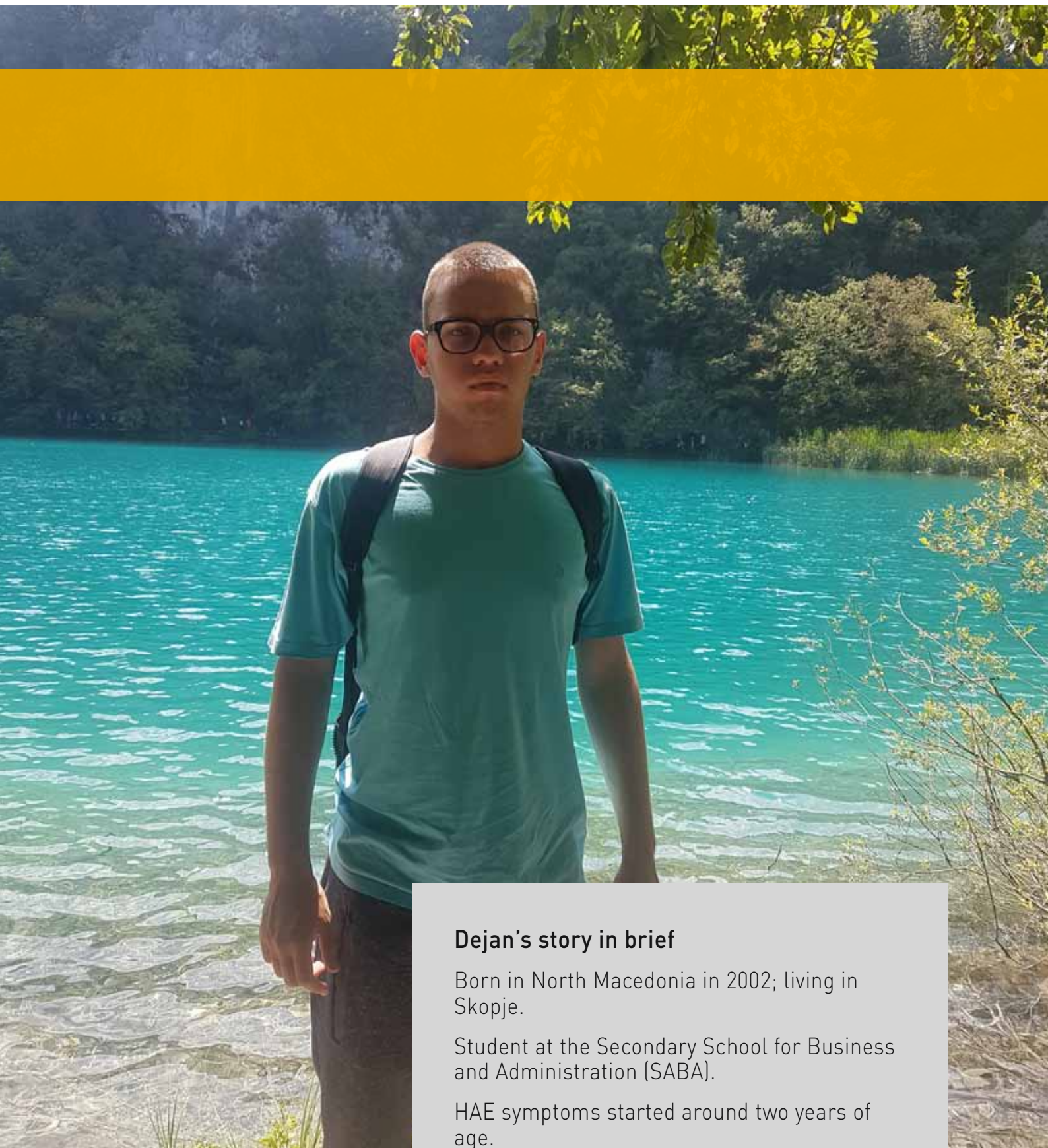
“Our data shows that 57 percent of patients on the newest subcutaneous prophylactic therapies experienced zero attacks in the three months prior to survey completion, leading to a substantial reduction in quality of life impairment and normalization of some quality of life domains”.

Recent data indicate that the population of patients achieving zero attack status increases with sustained exposure to the newest subcutaneous therapies. Data from the C1-esterase inhibitor subcutaneous (human) phase 3 open-label trial and a postdoc analysis performed as part of the lanadelumab clinical trial indicate that treatment efficacy increases over time. This suggests the strong possibility that a substantial majority of patients on the new therapies will be attack free.

Further, in the conclusion it says that the value of new subcutaneous prophylactic HAE treatments should be assessed in the context that:

- a substantial majority of patients using the newest subcutaneous prophylaxis therapies are likely to become attack free
- there is potential for remarkable improvement in health outcomes, quality of life and potential socioeconomic gain, and
- the on-demand only treatment model is associated with high direct and indirect costs.

A comprehensive health economics analysis of patients using on-demand only treatment revealed costs of 417,100 USD per patient per year. Direct costs – including on-demand only treatment, emergency room visits, hospital stays, and HAE-linked co-morbidities totalled 364,500 USD while the indirect socioeconomic costs, calculated using the cost of missed work due to sick days, reduced wages, and underemployment, totalled 52,600 USD.



### **Dejan's story in brief**

Born in North Macedonia in 2002; living in Skopje.

Student at the Secondary School for Business and Administration (SABA).

HAE symptoms started around two years of age.

Other HAE patients in his family: None.

## Patient story: Dejan Angeleski, North Macedonia

# An HAE patient organization can raise awareness, advocate, and lobby for patient rights

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I do not quite recall when my first HAE attack was since the condition has been part of me for as long as I can remember. My mom always says it started very early, even at the age of two when I had swellings on different parts of my body: feet, palms, hands, arms, cheeks, and so on.

### What is your own first memory of an HAE attack?

When I was six years old my parents and I went to the small and very beautiful mountain town Krusevo in order for me to learn skiing. We arrived in the afternoon and immediately went to the skiing slope to arrange for me to have my first lessons. It was such fun and joy. There was a lot of snow, and it was a shiny sunny day. I did not stop being active for a single minute, and my mom was getting a bit worried as I did not even want to take a break to have a snack or a hot drink. I was determined to learn how to ski! During that night and early in the morning of the next day I was not feeling that well. The area around my left eye was swollen, and my parents decided to go to the Emergency Unit at a nearby hospital. Unfortunately, they had no idea what was wrong with me and just said that it was probably an

allergic reaction from the sun. My parents did not want to risk giving me allergy medications so we rushed back to Skopje so I could get to the Clinical Hospital. During the ride home, both of my eyes swelled so much that I could not see anything by the time we arrived. At that point, I realized that my mom was already familiar with my condition as I heard her discuss with a senior doctor trying to figure out why my symptoms had started so early.

### A turning point of your life I guess?

Yes, it became quite an ordeal of constant and long hospitalizations. Most of the time my face was swollen so much that I experienced difficulties in seeing and even breathing. I had abdominal attacks very frequently, and those were the worst as I was unable to get out of bed because I had lost too much liquid and I was in pain. I used to be in a hospital bed for hours on and receiving many plasma packages to make me better.

In the first two years of primary school, I was barely there, and I had to go to a specialist school to work with special educators and psychologists to catch up with the curriculum.





## Talk a bit about your HAE medication.

At a point, my mom decided to learn how to give me injections so we could be more independent when traveling. She was terrified at first, and I could see in her eyes that she hated needles as well as hospitals and was very frustrated. However, I knew she would do anything to make my life – our lives – easier, so she completed a course with the nice nurses at the Children’s Hospital in Skopje. Mom is not aware of this, but she is now much better than the professionals when she injects me – I can tell the difference. This dramatically changed our lives.

However, even when my mom and I were very disheartened, we made a firm decision not to weep and wail and feel sorry for ourselves. I needed to do something to let go of the frustrations I had, so I enrolled in a basketball club. I was attending training three times a week, and in between the training I played tennis with my mom and grandma and I cycled along the river Vardar and the Ohrid Lake. I was especially happy during the summer holidays because I enjoy swimming and I’m lucky enough that my grandparents live in a beautiful town by the lake. We would go to the beach early in the morning and late afternoon and enjoy the clear water. I also like diving and all water activities. We have visited many waterparks during our holidays, and I always try multi slides, simvoli slides, family rafting slides, and even looping rockets! When we are tired, we have cold drinks and relax.

## No limitations?

Well, it has not always been ideal to say the least. After all, I have been in situations for instance in a foreign country where a hospital was the only place we could seek medical assistance when I had an attack. Even when I was able to bring my own HAE medication, the hospitals would charge a lot for giving it to me, and that meant we had to reduce a couple of days from our holiday whenever I had to go to a hospital outside my home country.

Our HAE patient organization has managed to win over the medical regulators, and we are now allowed to have home treatment, which makes life much easier. Whenever I have an attack, when I feel the first symptoms, my mom prepares the injection, and I have my medication at home. It is such a relief not to have to rush to the hospital and wait for an hour or two for all the administrative work to be completed before the nurses can give me the medicine. At home, the whole procedure takes 30 minutes, and after that, I can go to school, go out with my friends, or just rest at home, play on my computer and relax. Now I feel freedom!

## Your mother has been involved in the national HAE organization since it was established. How would you describe the value of such an organization?

Having an HAE patient organization as we have in my country is very helpful as it can raise awareness, advocate, and lobby for patient rights. I was particularly glad when HAE Macedonia organized a screening of the HAE documentary “Special Blood” in Skopje. My mom invited my teachers to come, and I was pleased that the film could help me explain the facts of HAE to them – based on more than my personal experiences, I mean. Indeed, afterwards my teachers and school administrators understood me much better and became more supportive – and I was able to finish my primary education with fewer worries and difficulties.

You have been sharing your HAE story before?

Yes, the first time I decided to tell my personal story I gave an interview with a young journalist working for a student and youth radio as well as a web page. They also filmed the interview for social media, and it ended up being among the top 10 most viewed videos in the country in 2016. I was happy because I tried to express myself about the challenges and things that interest me most. I was even filmed during one of the training sessions in my jiu-jitsu club.





You were among the participants in the HAEi Youngsters Summer Camp in Frankfurt, Germany in 2017. What did you think about that gathering?

I met many HAE patients and their siblings and friends from all over the world. It was an amazing experience to feel free and discuss things that bother you and not care if someone would be surprised when you talked about needles and injections, pain and fear. We were all the same at the camp, although with so many different backgrounds and interests. I realized that many teenage HAE patients from around the world are experiencing similar things as I am. I was glad to hear that they travel, do sports, and go to college without any constraint because of their condition.



Speaking of education: What are your plans for the future?

I have two more years before I finish my secondary education, so it is a bit early for me to plan for my university studies. Initially, I was into computer programming, but now I am not quite sure what I will choose as my professional carrier. I am currently studying law, and it might be useful for me since I am attracted by the topics that I study covering human rights. The right to health care and support is a universal human right. Therefore, I can maybe choose to become a human rights advocate and contribute to improving the rights of HAE patients in and outside my country. Until I decide what my profession will be, I intend to enjoy life, be active and happy.

How do you see your future with relation to HAE?

I now feel more confident that I can become more independent. I am informed about the latest treatment options. Preventative therapies seem to have good results, and I strongly believe that by the time I start living on my own I can rely on those, so my quality of life can improve without frequent attacks. Even this year I feel I have more control of my condition as I have fewer swellings. It is because I feel less stressed now that I have my medication at home and because we have improved access to therapy in my country.

I would describe myself as a very active and attractive young man – ha-ha! Indeed, I think that I live my life to the fullest and I want to enjoy every minute of it in the company of my friends and family.

### HAE in the Macedonia

- *Member Organization*  
HAE Macedonia  
– established 2009  
[www.haei.org/haemacedonia](http://www.haei.org/haemacedonia)
- *Diagnosed patients*  
24
- *Points of HAE interest*  
Hospitals: Skopje (2)
- *Available medication*  
Berinert and Ruconest





# News from around the Globe



## HUNGARY

From Henriette Farkas and Lilian Varga, Co-chairs of the 11th C1-INH Deficiency Workshop:



### 11<sup>th</sup> C1 Inhibitor Deficiency and Angioedema Workshop

Budapest, Hungary, 23-26 May 2019

The 11th C-1 Inhibitor Deficiency and Angioedema Workshop will be held 23-26 May 2019 in Budapest, Hungary. This series of conferences organized every other year is devoted to the presentation and discussion of the latest scientific findings related to bradykinin-mediated angioedemas in the first place. It has long been known that in addition to C1-inhibitor deficiency, the background of these angioedematous disorders might also include further – genetic and other – factors. Therefore, the title of the conference has been supplemented with the word 'Angioedema', in order to harmonize it with its agenda. The final scientific program will be assembled under the leadership of the C1-Inhibitor Working Group, based on the submitted abstracts. In addition to oral and poster presentations selected from the latter, guest lecturers will be invited to discuss the latest achievements in the research of C1-inhibitor deficiency and/or hereditary angioedema.



## PERU

President Suzet Lam Torres of HAE Peru writes:

After eight years, on 22 February 2019, the Regulation of the Law of Rare Diseases was promulgated, declaring treatment for people with rare diseases of national interest. The norm establishes the elaboration of a national plan of prevention, diagnosis, integral attention of health, treatment, rehabilitation, and monitoring of the rare diseases in charge of the Ministry of Health and will have a validity of five years.



## SINGAPORE

Tan Tock Seng Hospital has been added as an HAE knowledgeable hospital in Singapore.

See <http://haei.org/location/hospital-singapore>.



## KUWAIT

Kuwait is now also an official member of the HAEi family, bringing it to 70 countries globally.

HAEi welcomes Mubarak Al Ajami as the HAEi point of contact to be reached at [mubalajami@gmail.com](mailto:mubalajami@gmail.com).



## SOUTH KOREA

Yet another physician has been added to the HAEi map – this time in Seoul, South Korea:

<http://haei.org/location/physician-seoul-3-korea>.



## MOROCCO

A pretty sure sign of the establishment of a HAE organization is the introduction of a logo. Here is the one from Morocco:







## MONTENEGRO

**From Marija Kaludjerovic Nikolic, President of HAE Montenegro:**

In the past year, HAE Montenegro had its first participation at the HAEi SEE Workshop in Skopje, Macedonia where we presented our mission and goals – and became a full member HAEi.

In December 2018 the Centre for Civic Education organized the FAST FORWARD Human Rights Film Festival ([www.ubrzej.me/en](http://www.ubrzej.me/en)) for the ninth time – and this one was quite special to us as we had the national premiere screening of the film “Special Blood” directed by Natalie Metzger. This was at the same time our first activity in Montenegro with the aim of giving the general public a closer look at HAE as well as the beginning of raising awareness about HAE in our country. After the screening of the film, there was a panel discussion in which Immunologist Maja Gavranovic and I participated. The debate and the premiere of the movie were quite successful. Furthermore, on Montenegro's national television I had the opportunity to announce the showing of the film and for the first time to publicly speak about HAE and point out the problems that HAE patients face within our country and in the world.



## AUSTRALIA AND NEW ZEALAND

**From HAE Australasia CEO Fiona Wardman:**

HAE Australasia is excited by the interest and number of registrations for our upcoming Patient and Carers Conference on the Gold Coast 13-14 April 2019. With 95 participants including 21 youngsters, HAE Australasia has had to close off any further registrations.

The agenda has been finalized and the speakers confirmed. We are looking forward to Dr Marc Riedl, and a host of wonderful international and local speakers and facilitators share their knowledge with everyone attending over the two days.



HAE Australasia took part in Rare Disease Day activities at the Shire/Takeda office in Sydney. I was given the opportunity to share her story and speak about the benefits of a dedicated patient support group for HAE to their staff.

Great news was received from Shire/Takeda with the announcement that Firazyr (Icatibant) is now indicated for paediatric patients in New Zealand. This will undoubtedly make a difference to children who currently have not been able to access any other on-demand therapy for their attacks.

In HAE Australasia's commitment to continue to work with our partners such as the Australasian Society of Clinical Immunology and Allergy, our Chair Anne Wilkinson took part in the National Immunodeficiency Strategy meeting held in Melbourne to discuss ways to improve the patient journey and better support patients with Primary Immune Deficiencies and HAE.







## RUSSIA

### From Elena Bezbozhnaya, Chairman of HAE Russia:

In the first quarter of 2019, the Interregional Public Organization “Society of Patients with Hereditary Angioedema” organized many important events for residents from different regions of Russia.

On 8 February 2019, we held a webinar, which gathered patients with HAE from Moscow, St. Petersburg, Siberia, and the Central and Southern Federal Districts of Russia, and also many who recently became members of the organization. The webinar focused on the protection of patient rights. Deputy Chairman Denis Bezbozhny reported on the main activities of the Society and cooperation with HAEi. Our lawyer Ilya Ushankov and I answered the questions of the webinar participants. Most of these issues dealt with medicine supply issues as the most serious problem for the members. Patients with HAE are not always provided with essential drugs, or receive only a small part of the required amount, although they are legally entitled this. During the meeting, the patients discussed their personal medicine supply situations and how to act in certain conditions.

On 2 March 2019, the Regional School for Patients with HAE gathered the residents of St. Petersburg and the Leningrad region within the Right for Life project in St. Petersburg. The problem of medicine supply in the region is very dramatic as HAE patients receive about 50 percent of drugs from real need and many months of delays in the provision of essential medicines for people. Speakers at this meeting lawyer Ilya Ushankov, Professor Andrei Prodeus, psychologist Yulia Faykova and myself. The patients discussed life safety issues, i.e. improving medicine supply process as well as receiving qualified medical care in unusual situations, for example, pregnancy follow-up for patients with HAE and dental procedures. I promised the participants that we would draw up a petition to the St. Petersburg Healthcare Committee based on the issues discussed at the seminar. At the end of the meeting, Yuliya Faykova offered art therapy training for the participants and focused on psychological techniques to cope with anxious states.



## News from around the Globe



### DENMARK, NORWAY & SWEDEN

The previous day the Armory Chamber of the Museum-Preserve "Moscow Kremlin" provided the grand opening of the social exhibition "The World through the Eyes of a Rare Child". The event was dedicated to the International Rare Disease Day. Supported by the Ministry of Culture of the Russian Federation, the event was organized by our Society. The exposition presented the photographic portraits by author and photographer Eugene Drobyshev of children diagnosed with HAE. The exhibition organizers decided to include non-professional photos by children diagnosed with HAE and their parents. These photos helped the visitors to see the everyday life of "rare" children. In addition, the exhibition presented the photos with views of European cities authored by Dasha Bezbozhnaya, a fourteen-year-old patient with HAE. Representatives of the Moscow Kremlin Museum, as well as parents and children, attended the opening ceremony – and all children were presented with memorable gifts. At the end of the ceremony, the participants enjoyed the permanent exhibition of the museum.

At the exhibition, I took the opportunity to thank the leadership and the staff of the Russian Ministry of Culture and Moscow Kremlin Museums. At the same time, I noted that the primary purpose of the exhibition was to draw public attention to rare diseases and to show that people with rare diseases appreciate every moment of life despite the pain, showing the most precious quality and making the life worth living.

In addition to these events, the Society regularly provides legal and psychological support to members of the organization, closely interacting with the medical community and medical authorities on all issues of HAE patient care.

Leading HAE experts from Scandinavia will be speaking at the third HAE Scandinavia conference taking place in Oslo 8-10 November 2019. Among the speakers are:

- Christian Jervelund from Copenhagen Economics – speaking on health and socioeconomic topics underlining the importance of access to the right treatment,
- Dr Linn Landrø from Oslo University Hospital, Norway – speaking on how to prepare children for prophylactic treatment,
- Dr Robert Brudevold from Ålesund Hospital, Norway – focusing on how the daily life of HAE patients has changed as still more have gained access to prophylactic treatment,
- Dr Anette Bygum from Odense University Hospital, Denmark – among other topics on the role of the HAE patient in the society and the new possibilities arising,
- The German HAE expert Markus Magerl from the university hospital Charité in Berlin – speaking on the exciting development within new HAE treatments,
- HAE patient Nanna Maria Boysen from Danmark - talking about the work of HAE youngsters globally in order to create a network crossing borders.

Furthermore, the Danish motivational speaker Mark Anthony will inspire the participants and Scandinavian nurses will provide advice and give a mini course in self-administration.

# News from around the Globe



## SWITZERLAND

**From President Helene Saam, HAE Switzerland:**

18 May 2019 the 20th meeting of patients in HAE Switzerland will take place in Novotel in Bern. The first part of the program includes:

- "HAEi – a global umbrella organization" – HAEi Executive Vice President & Chief Operating Officer Henrik Balle Boysen,
- "HAE from the doctor's point of view" - Prof. Dr. med. Walter A. Wuillemin from HAE- Zentrum Luzern, Switzerland,
- "Information from the HAE Switzerland management" – Helene Saam, Nicole Hodler, Fabienne Resenterra, and Greber Ernst.



After lunch the participants will be taken on a guided tour to the production facilities of CSL Behring AG to hear about the production of bio therapeutics from human plasma. CSL Behring AG in Bern is a specialized producer of bio therapeutics with more than 100 years of experience in the treatment of a number of diseases.

There are now numerous HAE Care Centers in the country. To the previous ones in Basel, Luzern, and Zürich you can add yet another one in Basel as well as one in Bern, St. Gallen, Sion, and Genève.



## QATAR

HAEi can now add country no. 71 to the global HAE family – please welcome Qatar represented by Ameera Elawad who can be reached at [ameeraelawad7@gmail.com](mailto:ameeraelawad7@gmail.com).



## KOSOVO

Two HAE knowledgeable physicians have been added in Pristina: One at Children's Clinic (Pediatrijska Klinika) and the other at KBC-Pediatria – Nephrology department. Contact information can be found at <http://haei.org/location/physician-pristina-1-kosovo> and <http://haei.org/location/physician-pristina-2-kosovo>.



## BRAZIL

ABRANGHE (HAE Brazil) has been reaching out to Mara Gabrilli, a senator who is defending rare diseases, in order to raise awareness of the needs of HAE patients and to strengthen relationship.

There is a shortage of Berinert in Brazil. CSL Behring has informed ABRANGHE that medication might only be available at end of March 2019.



## UNITED ARAB EMIRATES

Mrs Elizabeth Stott – located in Abu Dhabi – has been added as HAE contact. See new contact information at <http://haei.org/location/hae-in-united-arab-emirates>.





## NORTH MACEDONIA

From Natasa Angjeleska, HAE Macedonia:

HAE Macedonia initiated and organized the marking of the national Rare Disease Day on behalf of the National Alliance for Rare Diseases in Macedonia. It involved two interesting events within the project Systematic solutions for rare disease patients, funded by the European Union. First of all, a press conference on 28 February 2019 that was attended by the highest healthcare officials, including the Minister of Health, the Deputy Minister, the State Secretary for Health, and a member of the Parliamentary Health Commission.

Secondly, HAE Macedonia organized a Children Creative Workshop taking place 2 March 2019 with the purpose of introducing youngsters to diversity and rarity. We invited an animator from Skopje Zoo to attend the event and talk to the children about his favorite animal, the one that inspired the legend of the unicorn – the okapi, which is a rare animal. He surprised everyone when he brought a big lizard and a python for children. Other entertainers involved a juggler and students from the Medical Faculty, who had an act called Teddy Bear Hospital, where a big teddy explained to the children the importance of having healthy habits. The Minister of Labor and Social Work, who also attended the event and addressed the children, afterwards stated that the present government aims at building systematic support and that they would let neither the future of children nor the life of rare disease patients or their families be defined by their disease.

Furthermore, I have had a meeting at the Ministry of Health to clarify the needs of HAE patients. Afterwards, the Bid Opening for 2019 was published for medications with sufficient increase in the number of vials of Berinert and Ruconest to be procured.



## USA

From Managing Director Michelle Cuevas, US HAEA:

**US HAEA presents original research at the national conference of American Academy of Allergy, Asthma & Immunology:** On 25 February 2019 the US HAEA CEO Anthony J. Castaldo, along with HAEi Executive Vice President & Chief Operating Officer Henrik Balle Boysen, presented findings of new, HAEA/HAEi driven research: A Comprehensive Approach to Assessing the Value of Prophylactic Therapy for the Rare Disease Hereditary Angioedema Using Real-World Patient Data. This happened at the American Academy of Allergy, Asthma & Immunology (AAAAI) in San Francisco, USA. Supporting this research, members of US HAEA completed an anonymous online survey designed to obtain a comprehensive profile of the HAE patient experience regarding education, employment, attack frequency, treatments, comorbidities, caregiver economic costs, and actual billed costs for attack-related hospitalizations, physician office visits, or emergency room admissions. The survey results confirm and expand upon those from recent clinical trials. It shows that prophylaxis with the newest subcutaneous therapies leads to sizable reductions in HAE attack frequency and that it provides significant, clinically relevant improvements in Quality of Life.



**Twenty years of serving the HAE community:** The next HAEA National Patient Summit will take place in Atlanta, Georgia 25-28 July 2019. The Summit will commemorate the 20th anniversary of dedicated patients joining together to establish what today is a strong and vibrant advocacy community. The Summit theme for 2019 is "Imagine the Possibilities", and it will frame a program that will provide participants with a sense of the past, a realistic assessment of the present, and a positive look to the future. With the advent of new therapies and the prospect for continued innovation,

the 2019 Summit will offer a unique opportunity to educate participants and motivate them to Imagine the Possibilities by evaluating their personal situation and exploring alternatives to improve their current quality of life. This 20th-anniversary gathering will offer an innovative format and unique programs that further unites the HAE community and guarantees a memorable and empowering experience. For this year, two exciting programs will be added: (1) a Professional-Scientific Track will offer informative sessions on the latest research, the new US HAEA Medical Advisory Board Treatment Recommendations, and HAE therapies, and (2) a three-day Global Youth Advocacy program designed to teach our youngest members from the US and national member organizations around the globe important advocacy techniques, boost leadership skills, friendships, and mutual support. Participants will earn an HAEi Advocacy Certification after the completion of the program.

The Summit agenda will focus on the HAEA's foundational pillars: Health, Advocacy, Engagement, and Advances in Research, and cover the most pressing issues facing the US community.

**Meet & Greet Program across America:** As part of the anniversary celebrations, we are hosting a new Meet & Greet Program to engage directly with our members. The Meet & Greet offer family members and/or caregivers, a unique opportunity to learn about the numerous HAEA programs and services designed specially to help them raise HAE awareness, educate, advocate, and inspire within their local communities. During the Meet & Greet, US HAEA Patient Advocates answer participant questions and provide informative materials that can be shared with physicians, schools, and workplaces, helping to facilitate a discussion on HAE with others. These special gatherings also allow our members to meet each other and share their experiences. Meet & Greet programs are scheduled to take place in places such as Los Angeles, Dallas, San Francisco, Union, Philadelphia, New York City, Cincinnati, Northern Virginia, Tampa, and Ann Arbor.

**Defending Patient Access to Therapy:** We continue to defend patients' rights to access to life-saving therapies. In recent years, additional challenges have threatened this access as health insurers look to deny coverage to patients who were receiving non-profit patient assistance from charitable organizations,

keeping essential treatments and services out of reach for many of those most in need. Furthermore, insurers are imposing additional requirements making it difficult for patients to afford or even have access to their HAE therapies. To protect patient rights and their access to therapies, this year we will lead a coalition of patient advocacy organizations that will identify policy priorities, determine opportunities for proactive engagement, and develop messaging campaigns to reach key decision-makers. The coalition of 20+ patient advocacy organizations will launch a coordinated public affairs campaign to pursue legislative and regulatory solutions to protect patient access and assistance.



## SPAIN

**From President Sarah Smith Foltz, AEDAF (HAE Spain):**

**Patient Workshops:** AEDAF held its 15th regional patient workshop on 13 February 2019 in Expo Hotel Valencia, Valencia. The workshop was attended by more than 30 people, including patients, family members, nurses, and physicians. Dr Ramón Almero Ves of the Allergy Department of Valencia's La Fe University Hospital, Vice President Dr Concepción Lopez Serrano and I presented the activities of AEDAF and HAEi, gave an update of HAE, and informed about the current treatment options and the situation of HAE in the Valencian region.




 nd the Globe

AEDAF plans to hold at least two more regional workshops in 2019.



**Annual Meeting and General Assembly:** AEDAF held its 21st Annual Meeting and General Assembly in Hospital Universitario La Paz in Madrid 9 March with the participation of around 80 people.

Following the General Assembly with items such as an overview of the organization's activities in 2018 and plans for **hae day :-)** 2019, the Annual Meeting opened with an update of HAE in Spain delivered by Dr Teresa Caballero Molina. Then Dr Carmen Marcos Bravo spoke on HAE with normal C1 INH before HAEi Communications Manager Steen Bjerre gave a short status on the HAEi/AEDAF Camino Walk 2019 and greeted the participants on behalf of the HAEi President and Executive Director who were unable to come as they were engaged in the first HAE meeting in India. The final items before the lunch break was a presentation on HAEi activities by HAEi Regional Patient Advocate Maria Ferron Smith and a Q&A session with Dr Caballero Molina and Dr Marcos Bravo.

After lunch, the meeting continued with three individual tracks. One was a self-administration workshop, another was a discussion on the different types of bradykinin-mediated angioedema, and the third was a youngsters' session run by Danish HAE patient Nanna Boysen with the support of Maria Ferron Smith.

As usual, all participants then assembled for a final round of debate on HAE and AEDAF related topics.

**HAEi/AEDAF Camino Walk:** AEDAF is supporting HAEi in the organization of the 3rd Camino Walk in Galicia (northwest Spain), to commemorate **hae day :-)** 2019 and raise awareness of HAE. We now have nearly a full bus of pilgrims who will be travelling to Galicia from Madrid on 15 May 2019, walking three stages of the English Way (Camino Inglés) on 16, 17 and 18 May and returning to Madrid on 19 May 2019. ¡Buen Camino!

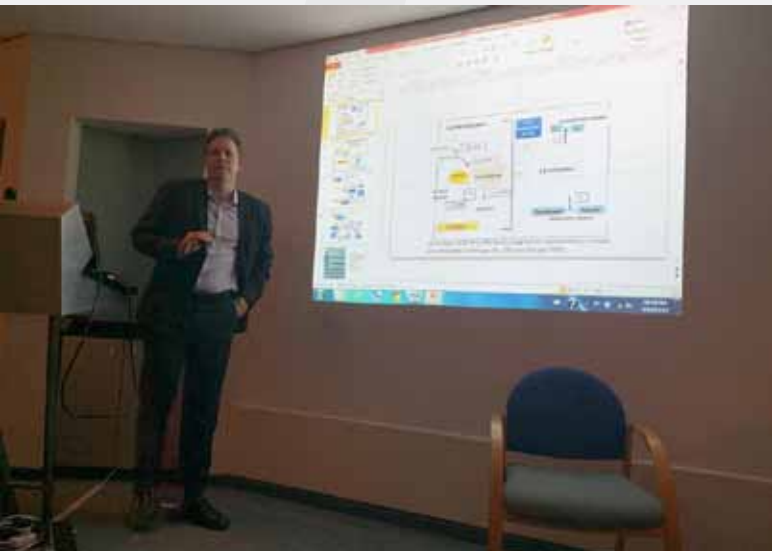




## SOUTH AFRICA

**From Patient Representative Adrienne de Jongh, HAE South Africa:**

We held our second patient meeting on 15 March 2019 in Cape Town which was attended by 19 patients, Professors Pater and Levin plus other interested members of the medical and dental professions. In total approximately 30 people attended. HAEi Chief Regional Patient Advocate Fiona Wardman visited for the first time, and HAEi Regional Patient Advocate for Sub-Sahara Africa Patricia Karani provided an update on recent events in Africa.



In the intervening year, we established an extensive social media network on Facebook, Instagram and Whatsapp. We developed a web presence on the HAEi site and linked with the South African Allergy Foundation (AFSA) site. We participated in the making of a local HAE film clip which is now featured on both sites. We have also set up HAEi Connect which is working extremely well. We registered with rare diseases too so that we can in future develop our presence there as well.

We have worked on establishing the patient treatment guide on the website as the go-to place to access the correct treatment protocol. This is really important as it is available 24/7, in all areas and accessible to everyone. It furthermore features emergency numbers so there should be no excuse for incorrect treatment.

We have increased our patient numbers to 82.

We have also just received the first order of Ruconest on the HAEi Global Access Program and look forward to extending this program to more patients.

The BCX drug trial has been extended for another year, and we have the largest sample in the trial.

As for our organization, we have a small committee consisting of MJ Dafel, Tamsin van Vlaanderen, Hana Foulds and myself. Hana will be attending the youth camp in Atlanta, USA in July this year.



## GUATEMALA

HAEi Regional Patient Advocate Javier Santana has helped country no. 72 to join the global HAE family. HAEi welcomes Guatemala represented by Mrs Samantha Alvarado who can be reached at [samata.saga@gmail.com](mailto:samata.saga@gmail.com).



## CUBA

Country no. 73 can now be added to the HAEi world map, as there is now also an HAE point-of-contact in Cuba. The man to reach out to is Carlos Velázquez Jomarrón – both doctor and HAE patient – who can be contacted via email [carlosvj82@ltu.sld.cu](mailto:carlosvj82@ltu.sld.cu) and phone 54765528.

Cuba also has an HAE knowledgeable hospital: Instituto de Hematología e Inmunología at Plaza de la Revolución in La Habana.



## News from around the Globe



### KENYA

**From President Patricia Karani, HAE Kenya:**

**First organization meeting:** HAE Kenya held its first member organization meeting with patients 22 February 2019 in celebration of Rare Disease Day. Angioedema patients who have joined HAE Kenya got to discuss and share about their conditions and they sought a way forward to endeavor to get proper diagnosis and better management of their conditions. Kenya has also launched an awareness campaign to collaborate with clinics willing to raise awareness and serve as referral clinics for HAE and other related angioedema cases.

**Allergy Society of Kenya:** After successful meetings between HAE Kenya, HAEi and members of the Allergy Society of Kenya (ASOK), HAE Kenya was able to attain collaboration with ASOK to carry out awareness campaigns in our country. This was made possible by the willingness of the Chairman of ASOK, Dr Adil Waris who is a pulmonologist and pediatrician at Aga Khan University Hospital in Nairobi to incorporate angioedema, urticaria and HAE as part of their organization's Continuous Medical Education program.

The meeting was attended by the HAEi Chief Executive Regional Patient Advocate and myself in my capacity as the HAE Kenya founder and HAEi Regional Patient Advocate for Sub Sahara Africa. Fiona shared about HAEi work around the globe and the willingness for HAEi to collaborate with doctor associations that are willing to cooperate with HAE patient support groups.

ASOK is willing to use their social media platform to raise awareness amongst doctors as well as include HAE in their continuous medical education program which they conduct every other month in the country.

**The Allergy Clinic:** The Allergy Clinic in Nairobi has been identified to be a focal point for referral for patients with suspected HAE. This was discussed in a meeting held between Dr Priya Bowry of The Allergy Clinic, Fiona Wardman and myself. Fiona highlighted on some of our HAEi tools including the Global Access Program and the HAE Global Registry to better assist patients living with HAE.



### JAPAN

**From President Beverley Yamamoto, HAE Japan (HAEJ):**

Icatibant has now been approved for acute attack in Japan and now for the first time patients have access to a therapy that can self-inject. It is making a big difference to patient lives already.

We are still working hard to get self-administration of C1-inhibitor approved and making progress. As we feel authorization may be on the horizon, we have started to consider what training should look like. HAEJ successfully applied for funding for a small research grant from EFPIA to carry out a qualitative study of key stakeholders on the theme of creating a training program for intravenous self-administration for the Japanese setting. We are now part way through the study, and the results are extremely promising.

On 23 February 2019, we hosted the Rare Disease Day event in Kobe again. We had a lot of visitors to our event, both HAE patients and stakeholders and other disease patients and stakeholders. It was a very uplifting event and an important way of sharing capacity and other resources.

HAEJ has been working with the RUDY Japan team in the School of Medicine at Osaka University Hospital. Dr Kassim and his team at the University of Oxford originally created RUDY. The idea of RUDY is to create an IT platform that will enable patient-driven medical research around rare diseases. Osaka University has created RUDY Japan under the leadership of Professor Kazuto Kato. On 31 October 2018 items specifically relating to HAE were added to the platform and launched. There was a big press release event, and national television and newspapers covered the event. HAEJ are working with the RUDY Japan team at Osaka to push forward patient-centric initiatives in rare disease research. On 9 March 2019 four HAEJ members joined a workshop with medical researchers and policymakers to brainstorm about how patients can help set the agenda for rare disease research.

## POLAND

**From Michal Rutkowski, President of the Swelling Beautifully Association (HAE Poland):**

The beginning of 2019 has been extremely busy for our association, permanently striving to improve patients' quality of life by organizing numerous events and projects dedicated to HAE patients and their relatives.

The biggest challenge for 2019 is an on-going project called HAE Regional Workshops organized from 1 January to 31 December in 13 venues around Poland, which aims at increasing awareness of HAE and in particular to:

- help HAE patients and their families to accept the disease,
- improve patients' knowledge of the available modern HAE therapies,
- educate, teach and improve patients' skills in self-administration with iv and sub-q injections,
- explain and understand that the self-preferences regarding HAE medicines should depend solely on the patients' experience and decision,
- create patients' ideal behavioral pattern during an HAE attack.

We have already organized four Regional Workshops in Łódź (19 January), Olsztyn (23 February), Rzeszów (2 March), and Lublin (23 March) with a total number of around 100 participants attending and another four meetings are expected before the end of June. This project has been so far a magnificent example of a perfect collaboration between HAE Poland and our partners Takeda, CSL Behring, and Pharming Group NV.

Another challenging but very much needed and anticipated project focuses on the pediatric patients and their families. One of the surveys organized by the Swelling Beautifully Association indicated a significant burden of the disease among parents and children diagnosed with HAE at age 5 and older. To provide them with enough awareness, education and most of all support, we have been working on the implementation of the US HAEA Brady Club, an online safe space customized for children diagnosed with HAE and their siblings. This website, together with a mobile app and an activity book, will help the youngest HAE patients to better understand, manage, and cope with their disease while offering fun ways for them to feel inspired, empowered, and connected to other kids. Thanks to US HAEA the Polish HAE patients will soon join Brady Club International.

On 29 January 2019, I was invited to the Pharming Group NV headquarter in Leiden, Netherlands, to introduce the situation of HAE patients in Poland and other countries in the Central and Eastern European region. One of the points in the meeting agenda was the presentation of "Beautiful Blood", the documentary about living with HAE from the perspective and reality of Polish patients. The meeting gathered around 50 employees of Pharming coming from different departments, who had the opportunity to find out what their daily work means to the patients and how it influences and increases the patients' quality of life.

February ended with a Rare Disease Day, and Swelling Beautifully was invited by Takeda to celebrate this feast together in Warsaw. I had the pleasure of presenting in front of some 70 of Takeda's employees and introduce HAE from the patients' perspective. The successful presentation was followed by detailed questions from the audience regarding the disease, access to





## News from around the Globe

medications, and life with this rare and potentially life-threatening disorder. Also, we attended the conference and meeting organized by the Polish Rare Disease Association and celebrated this day together with patients and patients' organizations from different therapeutic areas.

15 March 2019 we presented at the HAE Conference organized by Polish Society of Allergology in Warsaw. The theme of the presentation was "Can the patient with diagnosed HAE feel safe in the Polish healthcare system reality?"

All the news and latest information regarding 'Swelling Beautifully' activities can be found at [www.piekniepuchne.org](http://www.piekniepuchne.org) and [www.haerw.org](http://www.haerw.org).



### CANADA

From Paige Gunderson, HAE Canada Youth member:



HAE Canada was pleased to be part of the celebration in Ottawa to recognize International Rare Disease Day 2019. On 28 February 2019, HAE Canada's Volunteer Coordinator Daphne Dumbrille joined a large group of supporters for a flag raising ceremony on Parliament Hill, followed by a catered reception; thankfully, indoors. Attendees of the event enjoyed speeches from different individuals, including, David Cox, the Executive Director of the Rare Disease Foundation, Maureen Smith, the Secretary of the Board for the Canadian Organization for Rare Disorders (CORD) as well as from Members of Parliament from Canada's four major political parties. Each speaker gave their perspective on the importance of recognizing rare diseases in Canada. The event, organized by the Rare Disease Foundation, hoped to not only recognize International Rare Disease Day but also to encourage the federal government to implement Canada's Rare Disease Strategy, including adopting a federal Orphan Drug Regulatory Framework. Events such as these are a great reminder that many dedicated organizations and individuals work hard each day for Canadians with rare diseases and we are proud to be part of this community.

HAE Canada President Jacquie Badiou and HAE Canada Treasurer Richard Badiou along with two volunteers, attended the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting in San Francisco, California, from 22 to 25 February 2019. Jodi Valois, a





## PUERTO RICO

representative from Yang Medicine in Ottawa, joined them to present four posters developed from data collected from our National Report Card, specifically Demographics, Attack Profile, Treatment Utilization and Treatment Satisfaction. Not only did HAE Canada share our important research, but also helped raise awareness of our rare disease at this important annual event.

We have exciting news from the newly established Youngsters side of HAE Canada. Makayla Gunderson and I were chosen through the Youngster volunteers and accepted to travel to Atlanta, USA to attend the HAEi Youngsters Camp 2019 in the hot summer month of July. I am happy I will reunite with my sister Makayla, who will be coming from the opposite side of the country, to learn and reconnect with the HAE youth community once again. We hope to bring back new ideas and initiatives which will help us develop our Youngsters program and strengthen our volunteering skills gained through volunteering with HAEC over the past two years.

With the HAEi Youngsters website and magazine launched from the HAE Global Conference 2018, I am quite electrified to see what we youngsters have in store for the bright future. With the HAE Canada Youngsters program kicking off here we are also excited to see what adventures will come with that. Look out world, we HAE Youngsters are diving head first into our futures, with each other at our backs.

Stay tuned for news on our upcoming **hae day :-)** here in Canada!

In the second half of March, HAEA Puerto Rico held its Patient Summit 2019 in San Juan. The main speakers were Professor Sandra Christiansen from the US HAEA Angioedema Center at UCSD, Director Bruce Zuraw from the US HAEA Angioedema Center at UCSD, MD Rafael Zaragoza who is President of the Puerto Rican Association of Allergy Physicians, MD Cristina Ramos from Puerto Rico, the US Allergy & Asthma Specialist William Lumry, and Anthony J. Castaldo, President of the US HAEA.

During the event, the doctors talked about advances in HAE treatments, new studies presented by the physicians, and about a new Puerto Rican study on HAE patients, Post Traumatic Stress Disorder, and the impact of Hurricane Maria in Puerto Rico.



## LIBYA

With the addition of Libya HAEi now have a point of contact in 74 countries around the globe.

The person in question in Libya is Ahmed Ali Abudahair who is located in Tripoli. He can be contacted via e-mail [abodher\\_a@yahoo.com](mailto:abodher_a@yahoo.com) and phone 00218913869369.

HAE patients in Puerto Rico currently have access to Cinryze, Firazyr, Kalbitor, and Ruconest. Tahkzyro is expected to enter the market in late spring 2019 – and discussions with CSL Behring regarding the possibility of Haegarda entering Puerto Rico is going on at the moment.



## Medical Papers

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

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**Consequences of Misdiagnosed and Mismatched HAE Angioedema Laryngeal Attacks: An Overview of Cases from the Romanian Registry** – by D. Moldovan, Romanian Network for Hereditary Angioedema, et al.:

Due to the unpredictable and potentially fatal nature of laryngeal HAE attacks, rapid and appropriate emergency care is critical. Emergency physicians should be able to recognize the symptoms of HAE attacks, distinguish HAE from other forms of angioedema, and be aware of effective HAE medication. Misdiagnosis and mismanagement of laryngeal attacks are a continuing challenge. We welcome the recommendations made in recent guidance documents for the emergency departments and highlight the importance of their implementation. Furthermore, national education programs are essential to raise awareness amongst patients, relatives, and emergency department physicians and to improve access to appropriate treatments. (*Hindawi Case Reports in Emergency Medicine, 2018*)

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**Lessons learned from founding a rare disease patient organization for HAE in Japan: moving from a paternalistic to a power-sharing model of the physician-patient relationship** – by B.A. Yamamoto, HAE Japan, and N. Kitano, Wakayama Medical University, Japan:

A dedicated rare disease patient organization has the potential to function as a catalyst for moving from a paternalistic to a power-sharing model of the patient-physician relationship. It can be viewed as a resource for generating new knowledge and social capital, which may translate directly or indirectly into improved patient quality of life and lower disease burden. (*European Journal for Person Centered Healthcare, 2018*)



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### **The use of tranexamic acid for on-demand and prophylactic treatment of HAE – A systematic review**

– by T. Horiuchi, Kyushu University Beppu Hospital, Japan, et al.:

Particularly in Japan, tranexamic acid is an important treatment option for many patients with HAE, particularly for long-term prophylaxis. Although C1-INH has been demonstrated to be safe and effective, self-administration and long-term prophylaxis are not licensed, and accessibility to treatment is challenging for many patients. Awareness of HAE among physicians is low and the limited availability of effective therapies increases the burden of HAE.

While danazol is available for off-label use, it has been associated with numerous side effects, including virilization, headaches, depression, and acne. The risk of adverse events in response to androgens increases the longer the duration of treatment. There is a need for increased awareness of available treatment options and an increase in the availability of more effective options to allow HAE patients to access the best available therapies. Tranexamic acid is not recommended for on-demand treatment or prophylaxis. This is particularly relevant in Japan, considering that alongside danazol, tranexamic acid is the only other option available for long-term prophylaxis. Neither treatment can be considered both safe and effective in the majority of patients with HAE. As such, these findings highlight a significant unmet need in Japan with regard to the paucity of clinically effective treatment options, and suggest the need for increased awareness among patients and physicians to ensure more options become available in the near future. The use of tranexamic acid is advocated in selected patients that have already been shown to benefit; however, it is likely that once more options become more widely available, the requirement for tranexamic acid in both on-demand and prophylactic treatment of HAE may be significantly reduced. Tranexamic acid may be more effective than no treatment, particularly for short-term prophylaxis. However, the efficacy of tranexamic acid varies widely between patients, and in many cases, the effect is negligible. For on-demand treatment, there is clear evidence that newer therapies such as icatibant and pdC1-INH are more effective. Although there have been no direct comparisons between ecallantide and tranexamic acid, ecallantide might also be considered superior given its clear advantages when compared with no treatment. For prophylaxis, while some efficacy

is observed in selected patients, tranexamic acid is inferior to many other options, including C1-INH replacement therapy. As such, there may be limited utility for tranexamic acid in short-term prophylaxis prior to dental procedures and minor surgery; however, where available, newer, more effective therapies should be used in place of tranexamic acid for long-term prophylaxis. (*J Cutan Immunol Allergy*, 2018)

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### **Indirect comparison of intravenous vs. subcutaneous C1-inhibitor placebo-controlled trials for routine prevention of HAE attacks**

– by J.A. Bernstein, University of Cincinnati, the United States of America, et al.:

For prophylaxis of HAE attacks, replacement therapy with human C1-INH treatment is approved and available as intravenous [C1-INH(IV)] (Cinryze) and subcutaneous [C1-INH(SC)] HAEGARDA preparations. In the absence of a head-to-head comparative study of the treatment modalities, an indirect comparison of data from two independent but similar clinical trials was undertaken. This analysis suggests greater attack reduction with twice-weekly C1-INH (subcutaneous) 60 IU/kg as compared to twice-weekly C1-INH (intravenous) 1000 U for the routine prevention of HAE attacks. (*Allergy Asthma Clin Immunol.*, March 2019)

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### **Serum fetuin-A, tumor necrosis factor alpha and C-reactive protein concentrations in patients with HAE with C1-inhibitor deficiency**

– by B. Márkus, Semmelweis University, Hungary, et al.:

Patients with C1-INH-HAE have decreased serum fetuin-A concentrations during the symptom-free period. Given the anti-inflammatory properties of fetuin-A, the increase of its levels may contribute to the counter-regulation of edema formation during C1-INH-HAE attacks. Human fetuin-A is a multifunctional glycoprotein that belongs to the proteinase inhibitor cystatin superfamily and has structural similarities to the high molecular weight kininogen. Fetuin-A is also known a negative acute phase reactant with anti-inflammatory characteristics. (*Orphanet J Rare Dis.*, March 2019)

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**HAE in Austria: prevalence and regional peculiarities** – by C. Schöffl, Medical University of Graz, Austria, et al.:

Patients with HAE still face an excessive diagnostic delay in some parts of Austria, or their disorder may even remain unrecognized by specialists. The median age at the onset of symptoms was 6.5 years, and the median age at the time of correct diagnosis 21.0 years. The median delay in diagnosis was 15.0 years for newly diagnosed patients without a family history of HAE. Patients with a family history of HAE received an immediate diagnosis. HAE patients without a family history of HAE and born before 1960 had to wait a median of 16.0 years until they were diagnosed correctly. Patients born after 1980 still experienced a median diagnostic delay of 6.5 years. This underlines the need for better awareness of the disease. (*J Dtsch Dermatol Ges.*, March 2019)

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**HAE: a Chinese perspective** – by S. Liu et al., Peking Union Medical College, China:

Research on HAE in China began in the 1980s, and later studies identified some clinical characteristics of HAE patients that differ from the western population. Type 1 HAE (98.73%) accounts for the majority of HAE patients while no type 3 HAE patient has been diagnosed to date. Compared with other populations, the onset age (21.25 years) of Chinese HAE patients is older and the percentage of abdominal attacks (34.18%) is lower. A total of 56 mutations have been reported. Currently, there is no approved drug for acute attacks, and the choices for long-term prophylaxis are limited to danazol and tranexamic acid. Danazol has demonstrated good efficacy and is tolerated in most Chinese patients, although it has some side effects, especially at the beginning of the treatment with higher doses. Oedematous attacks are effectively prevented with a dosage of  $\leq 200$  mg/day in 80% patients. (*Eur J Dermatol.*, March 2019)

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**Clinical profile and quality of life of Puerto Ricans with HAE** – by Y.M. Arce-Ayala, University of Puerto Rico, et al.:

A cross-sectional study was performed in 32 Puerto Rican patients with HAE. Puerto Rican Hispanics showed a similar epidemiologic and clinical profile to previous studies, however; higher frequency of attacks was prominent. The study demonstrates a substantial and noteworthy decrease in quality of life in HAE patients and an increase risk for depression, particularly among women. (*Allergy Asthma Proc.*, March 2019)

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**Long-Term Outcomes with Subcutaneous C1-Inhibitor Replacement Therapy for Prevention of HAE Attacks** – by T. Craig, Penn State University, the United States of America, et al.:

In patients with frequent HAE attacks, long-term replacement therapy with C1-INH (subcutaneous) is safe and exhibits a substantial and sustained prophylactic effect, with the vast majority of patients becoming free from debilitating disease symptoms. (*Allergy Clin Immunol Pract.*, February 2019)

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**Treatment effect of switching from intravenous to subcutaneous C1-inhibitor for prevention of HAE attacks: COMPACT subgroup findings** – by T. Craig, Penn State University, the United States of America, et al.:

Patients previously using C1-INH (intravenous) at various doses as routine prophylaxis can experience a substantial and clinically meaningful reduction in HAE attack rate when switching to C1-INH (subcutaneous). (*J Allergy Clin Immunol Pract.*, January 2019)



# Clinical Trials

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

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

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

**A Long Term Safety Study of BCX7353 in HAE**

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

**A Study to Investigate CSL312 in Subjects With HAE**

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

**Biomarker for HAE Disease Type 1**

– recruiting in Egypt, Georgia, Germany, and India.

**C1 Inhibitor Registry in the Treatment of HAE Attacks**

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

**Cloud-R HAE Registry**

– recruiting in France.

**Determination of Specific Biomarkers of Acute Attack of Angioedema Within Pediatric Population**

– recruiting in France.

**Epidemiological Analysis for HAE Disease**

– recruiting in Germany, Poland, and the United Kingdom.

**Firazyr Patient Registry (Icatibant Outcome Survey - IOS)**

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

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

– recruiting in Italy.

**Pathophysiological study for autoimmune dysregulation of HAE**

– recruiting in Japan.

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

– recruiting in the United States of America.





**National Institutes of Health**  
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#### **Study of BCX7353 as a Treatment for Attacks of HAE**

– recruiting in Austria, Denmark, France, Germany, Hungary, Israel, Italy, North Macedonia, Poland, Romania, Switzerland, and the United Kingdom.

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

– recruiting in the United States of America.

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#### **Study to Evaluate the Efficacy and Safety of BCX7353 as an Oral Treatment for the Prevention of HAE Attacks in Japan**

– recruiting in Japan.

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#### **Study to Evaluate the Real-world Effectiveness of Lanadelumab in Participants With HAE**

– will be recruiting in the United States of America.

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#### **The Role of the Coagulation Pathways in Recurrent Angioedema**

– recruiting in France.

Read more about these and other clinical trials at <https://clinicaltrials.gov> and <http://apps.who.int/trialsearch>.

# News from the Industry

6 January 2019

“In December we filed with regulatory authorities to begin our Phase 2 study of KVD900 as a potential oral acute treatment for HAE. This enlarged study is expected to provide data in late 2019. We continue to be excited by the potential for KVD900 to provide a safe, oral on-demand option for HAE patients to more conveniently and effectively manage their disease,” says Andrew Crockett, CEO of **KalVista Pharmaceuticals, Inc.** “We are also pleased to announce that we made the regulatory filings for our next oral plasma kallikrein inhibitor, KVD824, and expect to begin dosing that first-in-human trial soon. We expect to provide a further update on KVD824 around mid-year.”

Following the necessary regulatory approvals, the Phase 2 trial evaluating KVD900 as an on-demand treatment for HAE attacks will begin dosing in approximately 50 patients at over 10 European clinical sites. The study will recruit type 1 and 2 HAE patients who have had three attacks in 90 days prior to enrollment. During the first part of this two-part study patients will receive a single 600 mg dose of KVD900 to explore pharmacokinetic and pharmacodynamic properties. All patients will then enter part two of the study, which is a crossover investigation in which the efficacy of KVD900 will be assessed versus placebo across two attacks. Patients experiencing an attack will take a single dose of 600 mg of KVD900 or placebo within one hour of the start of the attack. The second attack will be dosed with the other treatment. For all attacks, symptom severity will be monitored and additional data points will be collected for at least 24 hours. Patients will use their normal, on-demand treatment as required.

(Source: KalVista)



10 January 2019

**Takeda Pharmaceutical Company Limited** has completed its acquisition of Shire plc, becoming a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan.

Takeda now has an attractive, expanded geographic footprint and leading position in Japan and the U.S., bringing its highly-innovative medicines to approximately 80 countries/regions with dedicated employees worldwide. Takeda's R&D efforts are focused on its four therapeutic areas of Oncology, Gastroenterology, Neuroscience and Rare Diseases, with targeted R&D investment also committed to Plasma-Derived Therapies and Vaccines. Takeda's strengthened, highly innovative R&D engine enables the company to have a more global, robust and modality-diverse pipeline as well as to focus on breakthrough innovation.

“We are delighted that the acquisition was approved by an overwhelming majority of our shareholders at Takeda's extraordinary general meeting. We are also pleased to have completed the acquisition several months earlier than expected, which was enabled through the hard work of our respective organizations and the smooth receipt of regulatory clearances,” said Christophe Weber, President and CEO of Takeda. “We appreciate the support of our employees, partners and shareholders throughout the process. This marks a significant moment in Takeda's history and is an exciting step forward as we accelerate our transformation journey to deliver highly-innovative medicines to patients around the world with expanded scale and geographical footprint.”

Weber continued, “The execution of our integration begins today, and we are confident in our ability to execute a smooth integration under the leadership of our experienced and diverse Takeda Executive Team with a strong track record. The Operating Model we established in September last year has set a clear framework for our integration plans, and we have a highly skilled and dedicated integration team leading the process.”

(Source: Takeda)





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22 January 2019

**Attune Pharmaceuticals** announces the positive results from the first in human studies evaluating ATN-249, a novel orally administered plasma kallikrein inhibitor for the treatment of HAE. The data were presented by Ira Kalfus, M.D., chief medical officer of Attune, as a poster presentation at the Western Society of Allergy, Asthma and Immunology (WSAAI) 2019 Annual Scientific Session.

“We are very pleased that our first-in-human study showed orally administered ATN-249 achieves high blood plasma levels, with dose-dependent pharmacokinetics and a favorable safety profile,” said Andrew McDonald, Ph.D., CEO of Attune Pharmaceuticals. “We expect to complete the multiple ascending dose trial shortly and plan to rapidly advance the program to a Phase 2 trial.”

The randomized, placebo-controlled, Phase 1 single ascending dose clinical trial of ATN-249 in healthy volunteers successfully met all its objectives in assessing safety, tolerability and pharmacokinetics (PK) with results supporting further development as an oral plasma kallikrein inhibitor for the prophylactic treatment of HAE. Plasma levels of ATN-249 increased in approximate proportion to dose, and drug exposure was not affected by dosing with food. Once-daily dosing of ATN-249 was safe and well tolerated at all studied doses (50mg to 800 mg) in healthy volunteers. There were no moderate or severe adverse events with all adverse effects being mild and deemed not related to the drug, as well as no dose limiting toxicities.

Ira Kalfus, M.D., said, “The positive outcome of this Phase 1 trial is an important milestone in the development of ATN-249 for the treatment of HAE, a rare and potentially life-threatening disease. Current treatment options for HAE are limited to intravenous and subcutaneous options and are often associated with adverse events. ATN-249, as a potential effective and well-tolerated oral treatment, has the potential to significantly improve disease management and patient quality of life.”

The first in human study of ATN-249 was a double blind, placebo-controlled safety, tolerability, and pharmacokinetic single ascending dose study in 48 healthy volunteers. A total of 30 subjects received a single dose of ATN-249 ranging from 50 mg to 800 mg and 12 subjects received placebo. In the food-effect pharmacokinetic study, 6 subjects in the 100 mg cohort received ATN-249 under fasted conditions (period 1) and after a 7-day washout received a second 100mg dose 30 minutes after the start of a high fat, high caloric meal (period 2).

(Source: Attune Pharmaceuticals)





## 23 Janary 2019

Following the presentation of two abstracts at the Western Society of Allergy, Asthma and Immunology (WSAAI) in Maui, Hawaii, USA, the **Pharming Group N.V.** COO Bruno Giannetti (MD, PhD) said:

“This real-world evidence demonstrates that Ruconest continues to serve an important role in the management of HAE despite the availability of other therapeutic options.”

The presentations are:

- Impact of Hereditary Angioedema Prophylaxis With Recombinant Human C1 Esterase Inhibitor on Burden of Emergency Department Visits by Dr Douglas Jones, Rocky Mountain Allergy, Asthma and Immunology:

The authors report a patient on plasma-derived C1-INH prophylaxis who was still experiencing HAE attacks and required numerous visits to the emergency department (ED). The patient was switched to Ruconest prophylaxis, and the number of attacks requiring acute treatment decreased significantly (1 attack over a 15 month period) along with visits to the ED.

- Recombinant Human C1 Esterase Inhibitor as Routine Short-Term Prophylaxis for Hereditary Angioedema Inadequately Controlled With Long-Term Prophylaxis During Menses by Dr Andrew Smith, Allergy Associates of Utah:

The authors report a patient suboptimally controlled with plasma-derived C1-INH prophylaxis, initially delivered intravenously and then switched to the subcutaneous route of administration. Because of frequent breakthrough attacks especially during menses, Ruconest was added to her regimen as a short-term prophylactic therapy. This resulted in a substantial reduction of her HAE symptoms, and the patient did not require any acute therapy since beginning Ruconest.

(Source: Pharming)



## 25 January 2019

**Attune Pharmaceuticals, Inc.** announces the completion of a \$23 million Series B financing with the proceeds to be used to advance a pipeline including the ongoing clinical development of ATN-249, a novel orally-administered plasma kallikrein inhibitor for the treatment of HAE.

Andrew McDonald, Ph.D., CEO of Attune, said, “This financing brings together a syndicate of investors with a deep understanding and long history of supporting companies that develop novel HAE therapeutics. Building upon our recently announced positive Phase 1 data, the Series B enables Attune to rapidly advance our lead clinical program through Phase 2 while also providing capital for our other pre-clinical discovery programs.”

ATN-249 is an oral, novel small molecule kallikrein inhibitor that was optimized for potency and pharmacokinetics. ATN-249 has been tested in phase 1 studies, where 249 achieved high blood levels and was shown to be safe and well-tolerated. In the phase 1 study, ATN-249 was shown to inhibit plasma kallikrein in vivo at levels that are expected to result in inhibition of HAE episodes.

(Source: Attune)



24 February 2019

**BioCryst Pharmaceuticals, Inc.** reports additional topline data from the Phase 2 ZENITH-1 trial, including new data from the 250 mg and 500 mg dose cohorts. Data from the now complete trial confirm previously reported results showing a single dose of oral 750 mg BCX7353 was well-tolerated and superior to placebo ( $p < 0.05$ ) against the majority of efficacy endpoints evaluated in HAE patients suffering an acute attack, and demonstrate a clear dose response across the three dose levels.

Based on the results of ZENITH-1, the company plans to meet with the U.S. Food and Drug Administration (FDA) in the second quarter, and to commence a Phase 3 trial with the 750 mg dose of oral BCX7353 in the summer of 2019.

“The results of ZENITH-1, with onset of action within one hour, duration of effect of a single dose over 24 hours, and a robust efficacy dose response across all dose levels are very exciting for patients who have an urgent need for an oral treatment option for acute attacks,” said Dr. William Sheridan, chief medical officer of BioCryst.

“Based on these excellent results, we plan to quickly advance 750 mg oral BCX7353 into a Phase 3 trial that will be designed to support approval in the U.S. and European Union,” Sheridan added.

Efficacy and tolerability data for the 750 mg dose cohort were previously reported by the company in a September 4, 2018 press release. With the 750 mg dose, compared to placebo, improvement in symptoms and Visual Analog Scale (VAS) scores was seen as early as one hour after oral BCX7353 dosing, and was sustained through 24 hours. Through 24 hours, standard of care (SOC) medication use was reduced by 31.6 percent after BCX7353 compared with placebo ( $p = 0.0029$ ), and no or mild symptoms were reported in 64.1 percent of attacks treated with BCX7353 compared with 32.3 percent of attacks treated with placebo ( $p = 0.0038$ ).

In the additional data reported today at the AAAAI annual meeting, a clear dose response was observed across the 250 mg to 750 mg range. Across dose levels, BCX7353 was generally safe and well-tolerated with no notable differentiation from the adverse event profile of placebo.

(Source: BioCryst)



26 February 2019

In conjunction with the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting 2019 in San Francisco **KalVista Pharmaceuticals, Inc.** CEO Andrew Crockett said:

“We are pleased to provide additional data on KVD900, showcasing a potentially ideal profile for oral on-demand treatment of HAE. Both formulations tested were rapidly and highly absorbed, driving a very fast onset of plasma kallikrein inhibition. The tablet formulation we plan to use commercially showed even faster uptake, with high levels of plasma kallikrein inhibition maintained for a long period and KVD900 was generally safe and well tolerated. Our Phase 2 study of KVD900 in HAE patients is expected to provide data late this year.”

KVD900 was evaluated in a randomized, double-blind, placebo-controlled Phase 1 single ascending dose study. 64 healthy male participants (n=6 active, 2 placebo per cohort, 8 cohorts) were administered single doses of KVD900 5, 10, 20, 40, 80, 160, 300 or 600 mg in a capsule. 8 participants were administered 100 mg KVD900 in a crossover study of the capsule and a tablet formulation. 12 participants were administered 600 mg KVD900 in a food effect crossover study.

- Orally administered KVD900 achieved rapid and dose-dependent plasma exposure over the range of doses tested from 5 mg to 600 mg
- A single 600 mg dose provided >90% plasma kallikrein inhibition and protection of high molecular weight kininogen (HK) cleavage from dextran sulphate-stimulated cleavage shown by capillary-based immunoassay. HK cleavage is the process by which plasma kallikrein is released during the inflammatory cascade that causes HAE attacks.
- The pharmacodynamic effects of KVD900 inhibition of HK cleavage was maintained for over 10 hours at the 600 mg dose level
- All doses of KVD900 over 80 mg provided complete inhibition of plasma kallikrein

(Source: KalVista)



4 March 2019

In its financial results for the full year ended 31 December 2018 the **BioCryst Pharmaceuticals, Inc.** President and CEO Jon Stonehouse said:

“In a year with many transformative milestones for BioCryst, it has been exciting to see so much progress already in the first two months of the year. The strong Phase 2 clinical data from our now-completed ZENITH-1 trial propels our BCX7353 acute program for HAE into Phase 3 development. We remain on track for the readout of our APeX-2 trial next quarter, and an NDA filing of BCX7353 for HAE prophylaxis by the end of the year. We are thoughtfully building our commercial leadership and infrastructure to execute a successful launch that meets the urgent demand for a once-daily oral therapy that will allow HAE patients to live a more normal life.”

#### Upcoming Key Milestones

- Report 24-week safety and efficacy results from the APeX-2 clinical trial (Q2 2019)
- Begin a Phase 3 clinical trial of oral BCX7353 for the acute treatment of HAE (Summer 2019)
- File a new drug application (NDA) for oral BCX7353 for the prevention of HAE attacks with the U.S. Food and Drug Administration (FDA) (Q4 2019)

(Source: BioCryst)







## The HAE Global Walk 2019 – help raise awareness step by step

On and around **hae day :-)** 2019 a group of HAE patients, caregivers, doctors, and people from HAE organizations will walk three stages of the Camino in northern Spain.

“We know that many people would like to take part in this walk but are not able to do so. Therefore we once again arrange the HAE Global Walk 2019, allowing everyone to participate no matter where they are: From 1 April to 31 May 2019 we will be running a campaign in order to raise awareness of the rare disease HAE”, says HAEi Executive Vice President & Chief Operating Officer Henrik Balle Boysen:

“We encourage you to help raise HAE awareness. All you need to do is to walk any distance you would like wherever you feel like it – on your own or together with others – and report the distance walked to [www.haeday.org](http://www.haeday.org). Your steps will then be added to those taken by people walking the Camino as well as all other HAE steps taken around the globe.”

The HAE Global Walk was first launched in 2016 – and from late April and all through May 2016 we registered more than 12,000,000 steps taken by individuals and groups wanting to be part of the global HAE awareness movement. In 2017 the number of steps grew to more than 21,000,000 – and in 2018 we set a new record with over 54,000,000 steps.

“Last year grew into an actual competition between a number of countries so for 2019 we have changed the format a bit. Now we register where people are from – not where they are walking”, says Henrik Balle Boysen.

On [www.haeday.org](http://www.haeday.org) you can follow the development day by day – for instance you can see which countries have walked how much, how many kilometers/miles have been walked in total, and how many people have participated.

Please make sure to visit the website often during the campaign period (1 April to 31 May 2017) – and add all the walks you like. Every step counts.





# HAEi around the world

Currently there are HAE member organizations in **74** countries. You will find much more information on the HAE representations around the globe at **[www.haei.org](http://www.haei.org)** – and the world map will provide you with contact information for the member organizations as well as care centers, hospitals, physicians, and available medication.

The information on **[www.haei.org](http://www.haei.org)** is being updated as soon as HAEi receives fresh data from the national member organizations.

