MARCH 2017

Global perspectives:

HAEi MAGAZINE · ISSUE 2

Patient story

Raquel Martins

Helping others has given me another perspective

New HAEi Regional Patient Advocate for Latin America

Javier Santana will take over the RPA responsibilities in Latin America after Alejandra Menéndez who for over a decade and a half, selflessly and most capably have helped patients all over Latin America.

Website hosting
– come to us!

A growing number of national HAE organizations have their own websites with their own individual hosting solution. However, some of them would like to change hosting or altogether change the look and content of their websites. And others would like to just have a website at all.

"In order to accommodate any such national HAE organization we have established a 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", says HAEi Executive Director, Henrik Balle Boysen.

At this point national websites have been launched for Iceland, Greece, Kenya, Macedonia, Serbia, Spain, and Turkey – and most recently Hungary.

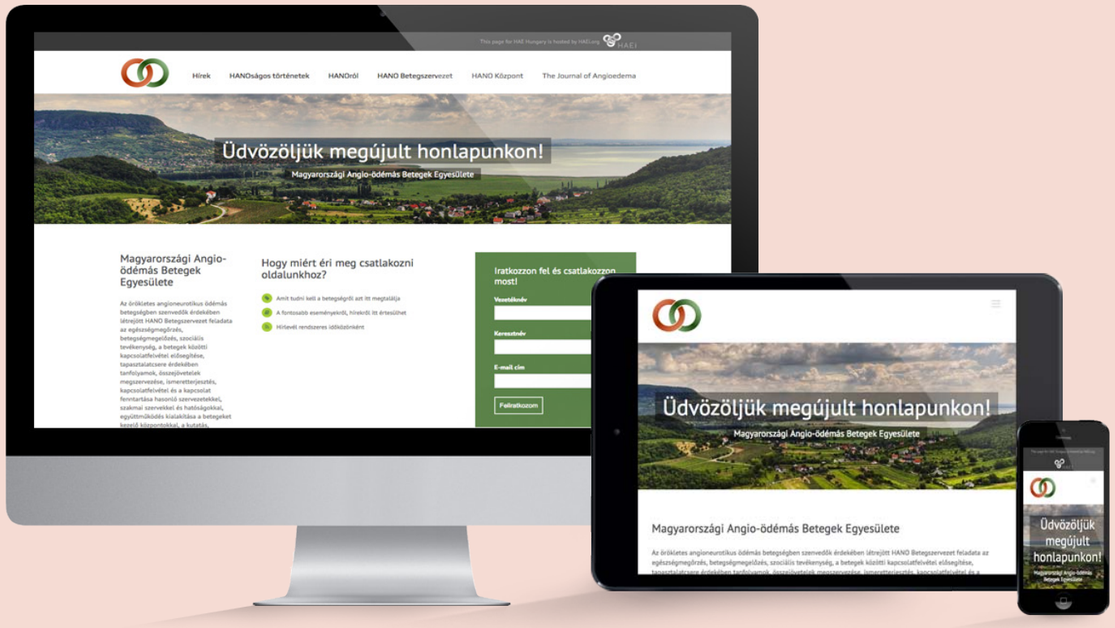
"We are preparing a few more at the moment and hopefully both Ireland and Poland will be launched within the next few months", says Henrik.

At **www.haei.org/haei_countries** you'll find an overview of all 55 countries registered with HAEi.

Link to national website hosted by HAEi

Link to national website

The national flags on the page link to the HAEi information on the specific country (national organization, care centers, hospitals, available medication etc.)



Dear HAEi Friends,

Welcome to Global Perspectives, the HAEi quarterly magazine dedicated to providing the HAE patient community with a comprehensive overview of what is happening in the world of HAE.

As patients with a rare disease that significantly impacts individual and family quality of life, we share a passion for raising HAE awareness and disseminating vital information that breaks the awful cycle of misdiagnosis and inappropriate therapy. For Raquel Martins from Brazil – the patient whose story is featured this edition – her HAE diagnosis served as a call to action. Raquel's longstanding devoted efforts have resulted in a patient organization that has a membership of over 1,300.

The situation in Brazil, however, offers a real world example of the challenges patients face in the battle to win access to and reimbursement for HAE medicines. Despite years of impressive advocacy efforts, HAE patients in Brazil can only get treatment after suing the government and waiting for as long as a year as each individual case gets adjudicated. The Brazilian HAE group, now led by Raquel's daughter Renata, is working feverishly to change the system so patients no longer have to go through a lengthy legal appeal to gain access to life saving HAE therapy.

Also in this issue, HAEi is pleased to introduce Javier Santana who is taking over as the HAEi Regional Patient Advocate for Latin America. Javier is assuming the duties formerly handled by Alejandra Menendez, a true HAE champion who has selflessly helped HAE patients in Latin America for over a decade and a half.

HAEi is here to help our member organizations meet their goals. Please do not hesitate to call or write your Regional Patient Advocacy (see pages 7-11) for any of your HAE related needs.

Warm regards to all HAEi friends,

Anthony J. Castaldo
President, HAEi

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Cover photo
Raquel Martins, Brazil. You can read her story on page 17 in this issue of Global Perspectives

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HAEi is registered as a non-profit organization in Switzerland

HAEi

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

In this issue

In this issue of Global Perspectives

New HAEi Regional Patient Advocate for Latin America

Unfortunately, due to other pressing commitments, Alejandra Menéndez no longer has sufficient time in her schedule to accommodate her role as HAEi Regional Patient Advocate (RPA) for Latin America.

Alejandra has, for over a decade and a half, selflessly and most capably helped patients all over Latin America. She is irreplaceable. Nevertheless, HAEi had to come up with a solution that maintains our regional presence in Latin America.

"HAEi has identified a person – Javier Santana – who we believe has the experience and ability to handle the RPA responsibilities in Latin America. Based on extensive talks with Javier, we are very impressed with his background, capabilities, and enthusiasm for representing HAEi in the region. He has a good understanding of the task at hand because he has worked to help his wife Michelle create HAEA Puerto Rico from nothing other than a list of a few patients and physicians", says HAEi President Anthony J. Castaldo.

Javier, who is fluent in both Spanish and English, has a wide-ranging background that includes political advocacy, organizing and running governor level election campaigns, working with government health officials, marketing, and Public Relations. Also, he is working in the fight to raise disease awareness in Puerto Rico and lobby the government for access to and reimbursement for HAE medicines.

Javier will be contacting member organizations in Latin America to introduce himself and explore how he can continue the longstanding commitment of Alejandra to patients in the region.

The Regional Patient Advocates

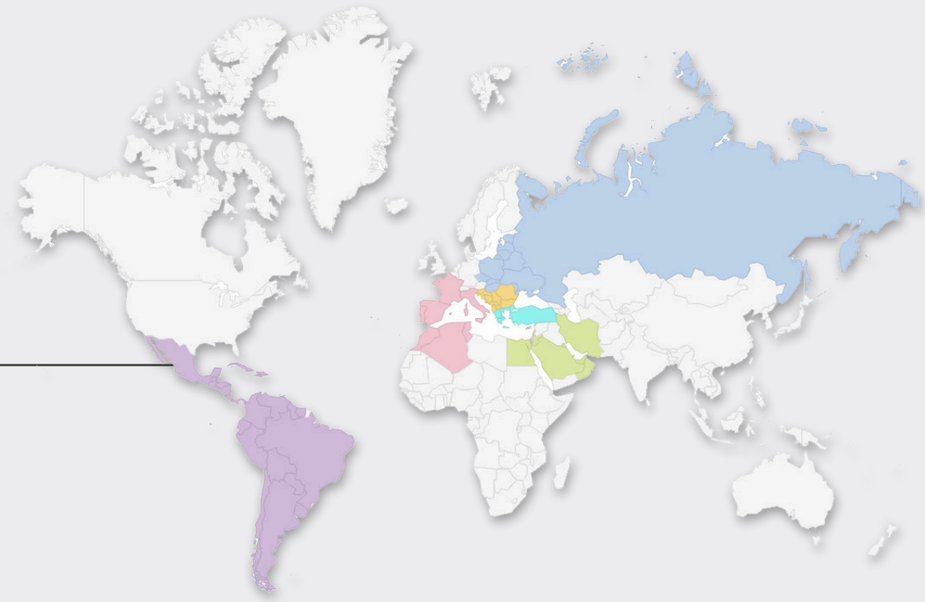
- **Michal Rutkowski;** Central and Eastern Europe
- **Maria Ferron Smith;** Mediterranean
- **Natasa Angjeleska;** South East Europe/Balkans
- **Javier Santana;** Latin America
- **Rashad Matraji;** Gulf Region and Middle East
- **Maria Ferron and Natasa Angjeleska**

News from the Regional Patient Advocates

Last year HAEi was delighted to introduce the first five Regional Patient Advocates (RPA). Throughout 2016, the dedicated group of HAE patient advocates worked with existing member organizations in their respective regions, and in addition, provided support and guidance in countries with no established member organization. In this way they have helped local patients establish a formal patient group and connect with the international community, working towards improving knowledge and care of HAE in their countries.

At the start of this year, the RPAs and the HAEi management met in Vienna, Austria, to discuss future plans and new initiatives for 2017. The meeting emphasized the impact the RPAs have already had in their regions within the first year, but also provided an insight as to how HAEi can continue to support the global HAE community.

The RPAs have continued to carry on their hard work. On the following pages you will find a couple of updates per region with highlight on countries not featured before.



Javier Santana
Latin America

IN GENERAL

Javier started in the role of RPA in February 2017 and has been making contact with a number of key healthcare professionals, patients and HAE member organizations.

MEXICO

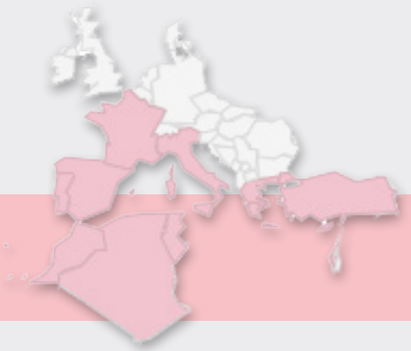
Contact has been made with Dr. Sandra Nieto regarding a future webpage for HAE patients and also to ascertain the contact details for knowledgeable HAE physicians to add to the HAEi world map.

URUGUAY

Following discussions with an active patient in Uruguay, contact has been initiated with an expert physician who sees HAE patients regularly, to establish how HAEi can support advocacy efforts through the Latin American RPA.

"Javier Santana – our new RPA in Latin America – has worked to help his wife Michelle create HAEA Puerto Rico from nothing other than a list of a few patients and physicians. He also has a wide-ranging background that includes political advocacy, working with government health officials and fighting to raise disease awareness in Puerto Rico and lobby the government for access to and reimbursement for HAE medicines."

HAEi President Anthony J. Castaldo



Maria Ferron
Mediterranean

IN GENERAL

Maria has continued to correspond with contacts made throughout 2016 and sought to expand the network of patients and member organizations in the region. She has also been promoting the HAEi/AEDAF Camino Walk 2017 and the May C1-INH conference in Budapest, Hungary to those in the area.

MALTA

Following the last update on the lack of access to self-treatment at home for patients in Malta, HAEi is happy to announce that a request for patient access to self-treatment when travelling has been granted. Hopefully this is the first step towards self-treatment for all patients in Malta. There has also been progress on bringing additional treatment options to Malta and patients should soon have access to subcutaneous medication.

PORTUGAL

Following the Portuguese conference held in January, HAEi will provide support in communications with the Portuguese Ministry of Health regarding the problems facing many patients accessing treatment. The Portuguese Member Organization (ADAH) has expressed interest in having their website hosted through HAEi, and the initial steps for this process are already underway.

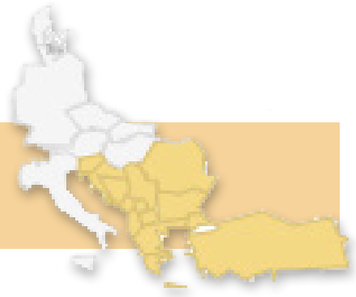
ISRAEL

The Israeli HAE member organization (EDEMA) have held a very successful workshop in Sheba Medical Center, and have promises from other medical centers to have workshops as well, but so far with no specific dates.

ALGERIA, MOROCCO AND TUNISIA

Working with Rashad Matraji, the RPA for the Gulf region, Maria will be continuing to establish communication with physicians in Tunisia, Morocco and Algeria to gain a better understanding of the HAE situation in these countries, and establish next steps to set up more formal patient groups there.

Natasa Angjeleska
South East Europe/Balkans



IN GENERAL

So far in 2017, Natasa has had frequent communication with patients and doctors via e-mail, and patients via social media thanks to the Facebook group set up last year. This communication helped in announcing contacts for physician and hospitals in various countries in the region, which will help patients and doctors continue to increasingly connect with one another and raise the profile of HAE.

TURKEY

HAE Turkey's collaboration with a PR agency to create patient stories and visual resources has been extremely positive, and has already assisted in reaching new patients who were living without knowledge about their condition. There have also been continued discussions with the Ministry of Health in Turkey.

SERBIA

There has been an intensive media campaign in Serbia to continue driving public awareness of HAE, and a mass initiative, 'Letter to the Ministry', to request access to treatments for patients. The Ministry will soon announce the decisions for new therapies on the list of medications covered by the health insurance fund and hopefully HAE medications will be included. These efforts were supported by additional efforts from the vice-president of HAE Macedonia assisting with lobbying and fighting for better medication in the country. This was a fantastic example of how member organizations can work together to improve the awareness and access to treatment for HAE patients.

CROATIA

A leading physician in Croatia has recently published a paper on HAE in a specialist newspaper targeted at all physicians in Croatia, along with a useful poster that helps health professionals identify potential HAE patients. Some patients have already received correct diagnosis and treatment for HAE thanks to this activity throughout Croatia.

ALBANIA

A national HAE expert is negotiating with insurance funds to hopefully secure terms for reimbursement of HAE medications for patients in Albania.

BOSNIA & HERZEGOVINA

Two potential HAE patients have been identified by a leading HAE physician, however access and funding for diagnostic testing is a challenge. There has been communication with a leading physician in Slovenia to share information and experience and with any luck this could lead to a cooperation which might make funding/ paying for testing less of a challenge.

Rashad Matraji
Gulf Region and Middle East

IN GENERAL

The challenges in this region are great as there are no HAE patient groups in any of the countries that Rashad supports. He continues to work with doctors and interested patients across the region on a number of awareness and support activities.

In addition to the WhatsApp group a Facebook page has also been set up. Rashad and a leading physician in the region will be meeting with representatives from the Haemophilia patient association in the region to exchange ideas and learn from their experiences. Leading physicians in the region are discussing the possibility of developing HAE guidelines, either for the region or for individual countries, based on WAO guidelines. The contact details for the HAE doctors in this region have been collated and should be live on the HAEi world map very soon.

UNITED ARAB EMIRATES

A new HAE patient has been identified and she is now part of the group of active patients in this country. Patient events are being organized for March and April, and through these it is hoped that awareness of HAE will be raised.

Roles of the Regional Patient Advocates

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

HAEi/AEDAF Camino Walk 2017

After the very successful HAEi/AEDAF Camino Walk on the legendary Camino de Santiago in Galicia (Spain) in May 2016, we have decided to organize yet another Camino Walk – this time to commemorate the global hae day :-) in 2017

At the moment there are 30+ participants in the 2017 version of the Camino Walk, coming from Argentina, Denmark, Malta, Mexico, South Africa, Spain, and United States.

"We plan to meet in Madrid Airport Saturday 13 May in the morning and go by bus via Leon, Astorga, and la Cruz de Ferro on the way to Galicia. Sunday 14 May we will set out on the first day of walking, taking us from Sarria to Portomarín, and Monday we will walk from Portomarín to Palas de Rei. The third day of walking is **hae day :-)** where we will go from Palas de Rei to Ribadixo da Baixo. All these states are less than 20 km each – and we will end our Camino Walk Wednesday 17 May with a very short walk from Monte do Gozo to Santiago de Compostela and order to attend the pilgrims' mass in the cathedral before going back to Madrid by bus", says the President of HAE Spain (AEDAF), Sarah Smith Foltz.

Returning to Madrid 17 May 2017 there will be ample time for those who plan to attend the 10th C1 Deficiency Workshop in Budapest, Hungary before the beginning of the event.

There is still room for a few more walkers – if you want to join please have a look at www.haei.org/camino-walk-2017-sign-up.

Step by Step

THE HAE GLOBAL WALK 2017 HELPS RAISE AWARENESS STEP BY STEP

Raising HAE Awareness
Step by Step

On and around **hae day :-)** 2017 a group of HAE patients, care givers, doctors, industry representatives, and people from HAE organizations will walk three stages of the Camino in northern Spain together.

"We know of many people who would like to take part in the walk in Spain but for some reason or other are not able to do so. Therefore we have set up a website for a HAE Global Walk 2017 – and we encourage everyone interested to participate in the event", says HAEi Communications Manager, Steen Bjerre:

"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 our website. We will then add these steps to those taken by the people walking the Camino."

The HAE Global Walk was first launched in 2016 – and from late April and all through May 2016 HAEi registered more than 12,000,000 steps taken by individuals as well as groups wanting to be part of the global HAE awareness movement.

"On the website you will be able to follow the development day by day – for instance you can see in which countries the steps are walked, how many kilometers or miles have been walked, and how many people have participated. And most importantly: You can add your own steps and thus help the HAEi steps campaign on its way. Please make sure to visit the website and add whenever you walk as every step counts", says Steen.

Your HAE steps can be entered at www.haeday.org.

Every year, policymakers, regulators, industry leaders, physicians, scientists, and patient representatives from around the world come together for the plasma protein therapeutics industry's premier European event, the International Plasma Protein Congress (IPPC). The most recent congress took place in Prague, Czech Republic, in March 2017.

Professor Henriette Farkas, winner of the 2017 Hilfenhaus Award, and Dr. Oliver Schmitt, Chairman of the PPTA Europe Board of Directors.

The Hilfenhaus Award to Professor Farkas

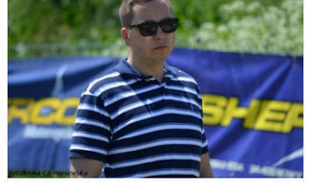
During IPPC 2017, the Hilfenhaus Award of this year was bestowed to Professor Henriette Farkas, MD, Ph.D., DSc, for her work related to treating those suffering from HAE and working to improve treatments and patients' quality of life.

Henriette Farkas is professor of allergology and clinical immunology at the Hungarian Angioedema Center at Semmelweis University in Budapest, Hungary. Besides, Prof. Farkas was the first one to start the treatment of HAE in Hungary. Her commitment earned her several awards and recognitions, for instance the "Jendrassik Ernő" Medal and Award of Semmelweis University in 2005, the "L'Oréal-UNESCO Awards for Women in Science" in 2013, and the "For HAE Patients" award of the International HAE Working Group in 2013.

She is also member of many important bodies, such as the Committee of the Hungarian Allergology and Clinical Immunology Society, the Hungarian Professional College of Immunology & Allergology, the Medical Advisory Board of HAEi, the International HAE Working Group, and the World Allergy Organization Steering Committee for Angioedema.

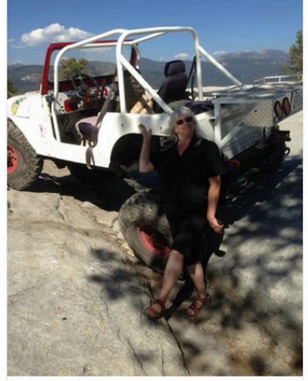
During the ceremony, Prof. Farkas gave a very clear overview of HAE, outlining the symptoms, the life-threatening consequences, the mechanism of activation of HAE and different treatment options. She then reported how access to care developed throughout the years in Hungary, evolving from a very stringent approach in the 1980s, to a mere hospital use in the following decade and finally to self-administration in 2011.

Prof. Farkas also presented the diverse activities carried out in the Hungarian Angioedema Center; it is the core of the regional HAE Network project, which aims at accelerating the proliferation of such centers in neighboring countries, as well as providing workshops and training courses. She finally presented some remarks on efficacy and safety of the therapy with plasma derived C1-inhibitor, both in the short and in the long-term prophylaxis, specifically in pediatric and female patients.



Michal Rutkowski, Poland (1980)

When he was a teenager, basketball meant almost everything to Michal Rutkowski. He spent hours practicing and game time was the most important of the week. It happened often that during that particular day he had an HAE attack, but somehow he was able to convince the body to pause with the edema, at least during game time.



Lois Perry, USA (1958)

Raquel de Oliveira Martins, Brazil (1945)

Raquel de Oliveira Martins overcame her rare disease and founded an association of patients in order to spread information to doctors and the general public.

Patient stories

At www.haei.org HAE patients from Australia, Belarus, Brazil, Denmark, Hungary, Norway, Poland, Russia, the United Arab Emirates, the United Kingdom, and the United States tell their touching and motivating stories.

Here you can read about the HAE lives of a diverse group of patients that include a university lecturer, a truck driver, a retired nurse, an operations manager, an architect, and a cattle farmer.

Ann Price, United Kingdom (1944)

The story of HAE in the family of Ann Price started with much ignorance, fear, pain, and mismanagement, but now she and her HAE relatives have confidence and enough control over the situation to live full and active lives.

Arianna Kitzinger, Hungary (1964)

After a childhood full of mysteriousness and misery, Arianna Kitzinger now leads a relatively serene life with manageable HAE attacks. For a long time, she did not know how to face or handle her condition but fortunately met the right doctor just as she was on the verge of giving up hope. "It's never too late", she confirms when recalling the memories of a rare life with a rare disease.

One of the HAEi patient stories is about Raquel Martins, Brazil.
She overcame her rare disease and founded an association of patients
in order to spread information to doctors and the general public.

Raquel's story in brief

Born 1945 in Sao Paulo; living in São Paulo, Brazil. Widow; mother of Renata and Fernanda.

Studied at Faculdade de Saúde Pública, University of São Paulo (1975-76); HR Analyst at CESP (1978-91).

HAE symptoms started at seven or eight; diagnosed in her teens.

Other HAE patients in her family: Grandmother, mother, daughter.

Patient story: Raquel Martins

Helping others has given me another perspective

The first HAE attack I can remember, occurred when I was between seven and eight years old and had an ordinary tooth extraction. This led to a bleeding that lasted for five days and eventually triggered a series of edemas. My attacks used to happen almost every week during my childhood. However, I only had edema to my face this once but I had many others in the whole body and several to the throat. In comparison my daughter Renata had several edemas to her face but never to her throat. Indeed, however rare this disease is, each HAE patient is unique.

Like numerous other patients with a rare disease, you lived for a long period of time with misdiagnosis as well as pointless procedures.

Yes – whenever I had an attack in my hands or in the arms, the verdict of the doctors would be the same, as they could find no apparent reason: It is most likely an allergic reaction of some kind to something that we can unfortunately not determine. During my teenage years it even lead to two unnecessary surgeries: I had my appendix removed at the age of 16 and two years later my tonsils were removed.

And that is how it kept on for years – not knowing what was causing you to swell?

Yes, all the way up to 1973, when I had yet another swelling to my hands and feet. At that time I was working in the Department of Health and luckily enough my boss sent me to the Emergency Room at the Hospital das Clínicas in São Paulo. That led to a five-year long search for an answer and then I finally had the diagnosis of HAE laboratory-proven. However, at that time the disease was unknown to almost every doctor in my country. There are no precise annals, but I may very well have been the first Brazilian to be diagnosed with HAE.

By now you know that HAE runs in your family?

Yes, my mother died when she was only 26. That was due to an edema in the glottis, ultimately preventing her from breathing. I was only seven at that time and my maternal grandmother became my foster mother. She also periodically had some sort of edema, mostly to the skin. So in that sense you can say that the phrase "having the same disease as your mother" has always been with me – and with my mother before that.

It hasn't stopped with you though?

No, I in turn transmitted HAE on to one of my two daughters.

I guess many people would have kept to fighting their own fight but you somehow found the strength to fight for others as well.

You could say that the fight against absence of information has become part of it for me. After I had my diagnosis, I had to explain lots and lots of doctors about HAE and eventually that led to the notion that I might just as well try to spread information on HAE wherever I could. I was able to set up a small network of patients and within a few years we were a group of about 30 people who would discuss our challenges with countrymen with the same condition. Ultimately, that led to the first contact with the global patient organization HAEi and soon after that followed the foundation of the Brazilian Association of Patients with Hereditary Angioedema – in short that is ABRANGHE in Portuguese. Today we have more than 1,300 patients registered, most of them already diagnosed or in the process of being diagnosed with HAE.

The first few years after your diagnosis you didn't have any medication.

No, I just had to keep a meticulous record of my attacks, their intensity, their frequency and the possible triggers. However, in 1982 I began taking medication. Actually, it wasn't just one kind of medication, as I switched periodically whenever studies indicated the effectiveness of a new medication. I must have been the first patient to gain access to the attenuated androgen Danazol through the Department of Health in São Paulo.

And more and more doctors know about HAE by now?

Well, the number of physicians registered with the Brazilian HAE organization is close to 400 so that has improved quite a lot over just a few years. In other words we have many HAE specialized doctors – the problem is for the patients to reach them as the country is so big and the patients so widespread.

Your daughter Renata – who by the way has taken over your position as President of the Brazilian HAE organization – has told me that patients have had to file a lawsuit against the state in order to get medication. Is that still the case?

Alas, that is still the case, yes. Both Firazyr and Berinert are registered with Anvisa, the Brazilian Health Surveillance Agency. However, they don't have clinical protocol for HAE in Brazil yet – and that has been leading to a pretty special situation: To get the medication the patient must ask his or her doctor to make an individual medical report about the patient and HAE requesting for Firazyr or Berinert. The patient then has to send the medical report and personal documents to a lawyer and provided that the patient pays for the legal assistance, the lawyer will make a lawsuit against the state.

Only after this bureaucratic and laborious process the patient will receive the medicine. To make things just a little easier for the HAE patients in Brazil, we have joined forces with an advocacy organization that makes this process free for patients registered with the Brazilian HAE organization.

Raquel with her daughters Fernanda and Renata

Patient story

Raquel learned to live well with her HAE and over the years found energy to help others also dealing with HAE. Helping others has given Raquel another perspective and kept her focus away from her own disease

And that procedure works?

Well, up until now patients filing lawsuits against the state have won. Once won, the patient receives a certain amount of medicine, depending on the doctor's prescription and the specific needs of the patient. Whenever the medicine is used, the patient will have to turn to the lawyer again. Particularly the first time it is hard because the patients need to attach a lot of documents and a lengthy medical report.

There is one question that keeps coming to my mind: How could you possibly live with a incapacitating disease, bring up two children, have a 9-to-5 job and run a patient organization pretty much at the same time?

It has just been a question of dealing with things day by day, really. The establishment of the Brazilian HAE organization came at a time when I had learned to live pretty well with my disease and over the years I had gotten used to finding the energy to help others in a similar situation. The responsibility that came with heading the HAE organization helped me even more to control my own situation and I guess you can say that helping others has given me another perspective and kept my focus away from my own disease.

HAE in Brazil

- *Member Organization*
  Established 2010
  www.abranghe.org.br
- *Patients*
  1,300+ diagnosed patients registered with ABRANGHE by January 2017
- *Care centers*
  10 – São Paulo (4), Rio de Janeiro, Minas Gerais, Bahia, Federal District, Espírito Santo, and Paraná
- *Hospitals*
  27 – São Paulo (14), Rio de Janeiro (5), Rio Grande do Sul, Distrito Federal, Espírito Santo, Paraná, Pernambuco, Bahia, Minas Gerais, and Santa Catarina
- *Available medication*
  Berinert, Firazyr and Danazol are registered for HAE treatment. Oxandrolone, tranexamic acid and Epsilon amino caproic acid are prescribed off label

Raquel and other mainly Latin American participants at the HAE Global Conference 2016 i Madrid, Spain

News from around the Globe

AUSTRALIA AND NEW ZEALAND
www.haeaustralasia.org.au

HAE Patient & Carer Conference: This day long conference is run every second year for the benefit of the HAE Australasia patients, their families and the HAE community in Australia and New Zealand – and next time is 13 May 2017 in Melbourne.

The topic for this year's conference is "Improving the HAE Emergency Experience" and speakers will include Professor Connie Katelaris (HAE Specialist) and Professor Tony Brown (Head of a Hospital Emergency Department). Also, there will be a screening of the HAE documentary "Special Blood" as well as patient stories and other kinds of updates.

HAE Australasia is looking for expressions of interest from conference attendees to take part in a CSL Behring plant tour where plasma products are produced. The tour would either be the day before or after the conference.

The conference is free to attend for HAE Australasia members. To assist patients from out of state and New Zealand to attend, there is a generous travel grant available on a first in, first served basis.

HAE Healthy Minds Workshops: HAE Australasia continues to partner with Dr. Chris Basten Clinical Psychologist. Dr. Basten presented at the most recent Patient & Carer Conference in Sydney and was so well received that he has designed and facilitated small group workshops with patients and carers on living with HAE. After successful workshops for both adults and adolescents in Sydney, Brisbane and Perth HAE Australasia is continuing to bring these workshops to patients in other cities. The workshops will give the participants an opportunity to discuss HAE related issues and concerns, and be given ways to help deal with these in a supportive and positive way.

Upcoming Workshops will be held in Melbourne 25 March 2017 and in Auckland 1 April 2017. These workshops are kindly supported by and made possible with the help of CSL Behring and Shire Australia.

CANADA
www.haecanada.org

HAE Canada is arranging a patient information event in Kingston, Ontario 1 April 2017. The guest speakers are Dr. Rozita Borici-Mazzi (MD, FRCPC, Allergiat/Immunologist), Loris Aro (RN, Unnimar Strategies), MedicAlert, Steve Sadaka (HAE Patient). The event will also feature and question and answer panel.

FINLAND
www.haefinland.org

Jubilee: HAE Finland is celebrating its 10th anniversary this year. During that time, the organization has influenced the availability of HAE medications in Finland both in hospitals and for home usage. Also, HAE Finland has had strong influence on the diagnostic and improvement of patient treatment. However, there is still a lot of wotk to be done for patients and their relatives.

HAE Finland is celebrating its 10th anniversay in 2017

Meetings: This year HAE Finland will be arranging its yearly spring happening 22-23 April, this time taking place in Lappeenranta. Later on during 2017 the organization will arrange support meetings in three cities across the country. Furthermore, HAE Finland will be organizing a 10-year celebration to take place during autumn. The date hasn't been set yet but the program is expected to include educational lectures for doctors as well as presentations by HAE association members and patients.

HUNGARY
www.haenet.hu

Conference: Four days in May 2017 Budapest will once again be the center of HAE as the 10th C1-INH Deficiency Workshop takes place in the Hungarian capital. This conference focuses on bradykinin-mediated angioedemas, and particularly on the types resulting from C1- inhibitor deficiency. The topics of the event cover a wide range of subjects. These are, among others, the latest achievements in the diagnostics of the disease. They also include the exploration of its hereditary, pathogenetic, and clinical background; as well as the management and follow up of the patients. See the preliminary program at www.2017.haenetworkshop.hu/program.

Website: As far as we know "Üdvözöljük megújult honlapunkon!" is Hungarian for "Welcome to our new website!" – and that is just what it says at the top of the new HAE Hungary website hosted by HAEi. Have a look at http://haei.org/hungary

MACEDONIA
www.haei.org/haemacedonia

HAE Macedonia is one of the founders and has a seat in the Board of Directors in the National Alliance of the Rare Diseases in Macedonia.

On Rare Disease Day a press conference was organized and achievements of the Rare Disease Program were discussed in terms of securing therapies for rare diseases, including HAE, and the patient registry was also explained. However, the Ministry of Health received numerous requests for improving the program for the next period.

The president of the Rare Disease Committee and a representative of the Rare Disease Program from the Ministry of Health addressed the audience, as well as a member of the Macedonian Academy of Science, showing support in cooperation in terms of introducing genetic testing for additional rare diseases in the forthcoming period.

In cooperation with other research institutes in the region HAE Macedonia will explore opportunities for genetic testing for HAE in the coming period, having in mind that it is one of the problems that should be addressed for a number of countries in the South-Eastern European region, that is Macedonia, Albania, Serbia, Kosovo, Bosnia and Herzegovina.

The press conference for the Rare Disease Day was held at the premises of the EU Information Center, since the day is shared through EURORDIS. For Macedonia this year it was decided to mark the day by sharing stories about parents of children with rare diseases. Stories were displayed as a poster exhibition and distributed in the form of brochures.

Two members of HAE Macedonia told their story, Verce Jovanovska Jankovska as a patient herself and a mother of a boy of eight years with HAE, and Natasa Angjeleska, a mother of a teenager with HAE.

The theme of the Rare Disease Day attracted media to ask for interviews, and HAE Macedonia was able to tell more about HAE, the challenges and the quality of life of patients in Macedonia in electronic and print media in Macedonia. HAE stories were also published in the regional media Al Jazeera in Serbian-Croatian language along with two stories of patients with other rare diseases.

SPAIN
www.angioedema-aedaf.org

General Assembly: The 19th General Assembly and Annual Meeting of HAE Spain (AEDAF) will be held on Saturday 1 April 2017 in Hospital Universitario La Paz in Madrid. This year the Spanish organization is pleased to have representatives of HAEi participating: President Anthony Castaldo, Executive Director Henrik Balle Boysen, and Maria Ferron, who is the HAEi Regional Patient Advocate for the Mediterranean countries. AEDAF will also be screening "Special Blood", Natalie Metzger's documentary about HAE.

Workshop: On 19 January 2017 AEDAF held its 11th patient workshop in Cáceres (Extremadura) with an attendance of around 40 people. The workshop was sponsored by Shire.

Camino Walk: AEDAF is also helping to organize the 2nd HAEi/AEDAF Camino Walk, which will take place from 13 May to 17 May 2017.

SERBIA
www.haei.org/rs

The pediatric immunologist Dr. Goran Ristic, a valued member of HAE Serbia Medical Advisory Board, has moved to Barcelona, Spain. HAE Serbia would like to invite all to give a big welcome to the newest member of HAE Serbia Medical Advisory Board, Dr. Dusanka Markovic from Clinical Center of Nis.

SWITZERLAND
www.hae-vereinigung.ch

Patients meeting: HAE Switzerland will be having its 18th HAE patients' meeting 24 Juni 2017 at the Triemli Spital Zürich. On the agenda are items such as an orientation of available HAE drugs and initial experience with the new C1 inhibitor drug Cinryze, results of the medication study BCX7353, and a talk on HAE drugs for children.

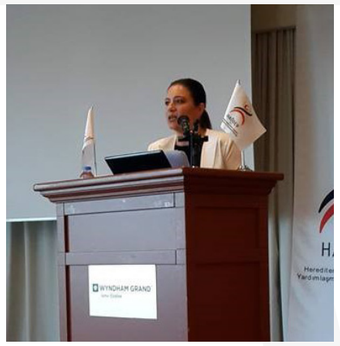
Annual General Meeting: The 16th Annual General Meeting of HAE Switzerland is scheduled for 10 November 2017.

TURKEY
www.haei.org/turkey

From Ersan Sevinç, International Communications Manager of HAE Turkey:

Attending the HAE Global Conference 2016 in Madrid, Spain was a great chance for HAE Turkey to understand how the process goes on and what we can do in our country. With this widened perspective, HAE Turkey has started to work on many ideas and tried to develop them in a proper way. The first step that we learned was establishing good connections with the government and the Ministry of Health. We have managed to get in touch with some officials who would like to help us and as a consequence we started to negotiate with the Ministry of Health and SGK (the General Health Insurance in Turkey).

At the HAE Global Confecence 2016 i Madrid HAE Turkey learned a lot about how a local patient organisation can keep developing and now HAE Turkey works on many ideas. The first steps has led to a close relationship with the Ministry of Health and SGK (the General Health Insurance in Turkey). HAE Turkey presented the new ideas a national patient meeting in Izmir, Turkey.



While going on with these negotiations, we organized a national patient meeting, which was held 22 October 2016 and took place in İzmir, Turkey. At this meeting we presented the things that we learned so far and we talked about a path, which we must all follow in order to improve the conditions in Turkey. Participation of Natasa Angjeleska from HAE Macedonia – and also one of the HAEi Regional Patient Advocates covering Turkey – had a positive impact on patients in terms of learning how HAE exists all around the world and what the opportunities are for patients.

During the visits to the Ministry of Health we decided that media is a key to success in order to raise awareness and attract public attention. We therefore started creating materials for the newspapers and online media tools. Over a short period of time we had the chance of publishing our news in some of the well-known Turkish newspapers such as NTV and Habertürk. This really helped us to achieve some results and to meet many new patients around the country. Hopefully the media attention will also help us to express ourselves better in front of the Ministry of Health in order to have better conditions for HAE patients.

One of the other successful things that have happened lately is that the C1-Inhibitor Cetor has been substituted with Cinryze. However, it is still not allowed to use it for home treatment. Cinryze is only for use in hospital with full reimbursement for both acute and prophylactic therapy for adults. We are still fighting for home treatment and while doing this, we are trying to create awareness of home treatment as the optimal solution for every case of daily life. With the help of patients' will and our coordination, we hope that we can solve this matter as soon as possible.

To summarize, attending the global conference has really changed our perception and taught us a great lesson. Participating in Drei-Länder Treffen in Munich, Germany and the Balkan conference in Skopje, Macedonia we have also learned a lot from all of our international friends. We all put our hearts into working for HAE Turkey and we are happy that we are starting to see results.

UNITED KINGDOM
www.haeuk.org

From Laura Szutowicz, CEO of HAE UK:

2016 kicked off with incredible Rick Talbot braving the icy seas off Llandudno to raise money for Lions and HAE UK (yes, alright it was Boxing Day 2015 but nearly 2016….).

Rick and his wife Pam went on to raise a huge amount of money for HAE UK with the proceeds of his birthday party and Pam's year as President of the local Lions.

To ensure that we were functioning correctly as a Charity, we had to design a lot of policies such as Child Protection, Fundraising and so on to suit ourselves and to comply with Charities Commission rules. Our thanks to John Price who coordinated all of this.

To align ourselves with HAEi, we decided we must elect a Youth Ambassador and after working our way through a fabulous shortlist we (and the Trustees) eventually selected Alex Graham as our 'VICTOR'. Alex, her sister and her mother all have acute problems with their HAE but all three of them have been incredibly brave and proactive in managing their HAE.

May saw the HAE Global Conference. It was the most illuminating experience, such fun to meet people I had only heard of and to actually feel part of the whole organization. The greatest news was that my indispensable 'right hand' Rachel Annals was re-elected onto the Executive Committee. We also were fortunate that our Youth Ambassador was able to attend and join in with the young persons' track, which was the first time this had been trialed. Such a success and will be repeated!

I had spent much of the spring working with NHS England and the Immunology and Allergy CRG to produce the new guidelines for use of C1-INH as prophylaxis. I also alerted NHS England to the problems surrounding the withdrawal of Stanozolol for those of our community who cannot tolerate Danazol. Thanks to help from the CRG a policy was formulated to recommend Oxandrolone where patients cannot tolerate Danazol.

This was eventually released formally in July, along with the new NHS 'Clinical Commissioning Policy for Plasma Derived C1-Esterase Inhibitor for Prophylactic Treatment of Hereditary Angioedema (HAE) Types I and II' to give it its full title. What was exciting about this new policy was that it recognized that peripheral attacks are disabling and should be treated, whereas the old policy was only for acute attacks or prophylaxis before dentistry, surgery etc. information.)

Along with the work on the various policies, HAE UK had recruited two new Trustees: Tim Crouch, already on the Medical Advisory Panel, and Tom Pickering who is a lawyer with a particular interest in Charity law. We are incredibly fortunate that Tom and his firm Travers Smith are prepared to give us the benefit of their expertise pro bono. We are also fortunate that two more top class medical people were prepared to join our Medical Advisory Panel. Dr. Scott Hackett (Birmingham), paediatric immunologist, and Dr. Tariq el Shanawanny (Cardiff) both have particular interest in HAE and were very welcome participants in our Bristol Patient Day in the autumn.

The (first ever) Scottish Patient Day was at the Salutation Hotel in Perth where we made a lot of new friends, with some 40 attendees, and excellent speakers.

Time galloping on, we found ourselves in Bristol for the Patient Day! We were very fortunate that the hotel we chose suggested that they would let us have a room free of charge for a reception the evening before for people travelling down the night before 'the Day' itself. This was a really good evening and definitely to be repeated. Less to be repeated is the sleepless night poor Rachel had worrying about the AV which although booked had not turned up. Rachel was up at 5 the next morning to try to sort it but we were still let down. The theme of the Patient Day was "Empowerment", and we did wonder how this was going to work. But the fantastic presenters and presentations made it all come true and we got so many comments afterwards about how 'energized', 'hopeful', 'optimistic' and 'inspired' people felt. So it seemed to have worked!

The rest of us tucked in to an excellent breakfast and the day started with a brief introduction from me about the format to come. For the first time, we were able to welcome delegates over age 12, and there were over 100 members plus the various pharma and other charity representatives. Our first presenter was Dr. Tariq el Shanawany, who gave a fascinating insight to new treatments for HAE, giving many listeners new hope of things to come – and not too far in the future, either. He was followed by Dr. Mark Gompels on Sport and HAE which was an inspirational look at how to manage HAE and still lead a full life.

Just before the coffee break Dr. Hilary Longhurst introduced the premiere of the film 'Peripheral Attacks and Me'. This was developed by CSL Behring and their partner Pegasus following on from the interviews people gave at their booth in 2015 and subsequent follow up. We all had a chance to spot our local film stars (all of whom were present at Patient Day 2016!). CSL have used these interviews and the film to develop a whole campaign around encouraging patients and clinicians to recognize how disabling peripheral attacks are and how they must be treated efficiently and quickly. The film and other information can be accessed on http://peripheralattacks.co.uk.

Our patient story after coffee was Paul Carroll, our very own Iron Man! His description of how he morphed from 'couch potato' to super fit was a testament to a very special determination. We were very fortunate that Henrik Balle Boysen could join us to give the HAEi perspective and 'HAE around the World'. This was very inspirational and very humbling when we realize just how poorly served many HAE patients in the world still are. Dana Shapiro was our next patient presenter and her tale of being determined to climb Mt Kilimanjaro (and her amazing photos!) was incredible. But like Paul, she started with baby steps – walk home from work, then run a few yards, then walk, gradually run a bit more until you are running seven kilometers to and from work! Plus sleeping with her C1 in her sleeping bag to make sure it didn't freeze.

After a very good lunch we had the pleasure of Pippa Adams presenting her dissertation on the 'Lived Experience of Female HAE Patients', which many of our members were interviewed for. Pippa has produced a really good piece of work which I am sure will be really useful for patients and clinicians.

Dr. Scott Hackett, one of our Medical Advisory Panel, presented on 'HAE and the Family' and then our Youth Ambassador Alex presented a short film she had made of all our 'Haeros'; all our younger members who are determined not to be defined by their HAE. Alex herself is a shining star; she achieves every goal she sets herself, whether it is to be a black belt karate instructor or to get top results in her GCSEs. She and her team of the younger delegates spent time in the afternoon designing 'emergency kits' which will soon be available.

The break out groups were well supported and June Cole was one of our most popular facilitators with her workshop on how to put together your own presentations to give to GP surgeries and A&E departments. We have used her slides to create a generic presentation for everyone to use.

The active part of the day closed with a lively Question and Answer session and then we were able to show the film 'Special Blood' by Natalie Metzger.

As for projects for 2017 our website is undergoing the process of being rebuilt into a more modern, more user-friendly format. Rachel and I have previewed it and it is very exciting, much more interactive and hopefully will be a really useful resource.

We are also working on huddles. Basically, a huddle is a small gathering of HAE UK members in a given locality. Whether you have HAE or are a friend or family member all are welcome to meet over a cup of tea or coffee, chat and catch up, exchange news, views, discuss problems and more importantly solutions. They could be organized in conjunction with an HAE clinic.

We'll be visiting Scotland again in 2017 and then there will be the National Patient Day in November.

We are delighted to have been able to give a small amount of financial help to Pippa Adams, who is now doing her Master's degree with a dissertation on the mental health effects of living with HAE. The finance will enable her to carry out more full research, interviewing more people and to publish the paper more widely.

We are very excited by the opportunity for young people to attend the Youngsters' Camp in Frankfurt, Germany in August and look forward to hearing their experiences. We already have applicants.

The (first ever) Scottish Patient Day was held in Perth. Some 40 people were attending and the participants made a lot of new friends and enjoied the excellent speakers of the day.

Also in Bristol HAE UK had a Patient Day. The event started off with a reception the evening before the actual 'Day' with great success (and promise of repetition). The theme of the Patient Day was 'Empowerment' and participants we fortunate to witness fantastic presenters and presentations.

One project for 2017 is to rebuilt the HAE UK website into a more modern, more user-friendly format.

Another project is wokring on small gatherings where HAE UK memebers can meet over a cup of tea or coffee to chat and catch up, exchange news, views and ideas and discuss different topics of heart.

USA
www.haea.org

From the US HAEA Executive Vice President Janet F. Long:

As we continue to grow together as a community, the HAEA works to continually meet the needs of our members. With this in mind, the HAEA is strengthening its mission through the realignment of our work teams and by developing a more focused approach to Health, Advocacy, Engagement and Advances in Research (HAEA). We are committed to our HAEA community and look forward to helping every HAE patient achieve lifelong health.

Through our four areas of focus, the HAEA will be able to bring specialized programs to our members and a more customized attention to an ever-changing HAE world. As we move forward into the future, we hope to reach important milestones together.

In 2017, the HAEA will Stand Up Strong for: HAE Health, Advocacy, Engagement, and Advances in Research.

Advocating on behalf of patient rights: This year will pose many challenges to patients throughout the United States as the new Government Administration and Congress evaluate changes to the Affordable Care Act (ACA). As repeal and replace discussions take place among policy makers, having an active role and a strong voice will be important in helping us to send a clear and strong message to Washington about patient rights.

The US HAEA has joined over 100 advocacy groups from around the nation to discuss with health policy experts the U.S. legislative agenda for 2017, identify possible changes to existing healthcare policies, and determine how together, we can work to protect patient rights.

The HAEA maintains a strong presence on Capitol Hill and has a prominent role within several important rare disease patient coalitions that are ready to vigorously fight on behalf of patients when any "access to therapy" public policy challenges arise. Priorities being considered by the 115th Congress that may have an impact on our U.S. patient community include:

- Re-evaluation of the Affordable Care Act (ACA)
- Allowance of purchase of insurance across state lines
- Converting Medicaid to a state block grant
- Changes to the prohibition of health discrimination

Furthermore, the HAEA hosted a live chat with our President, Tony Castaldo, and members of the Health and Medicine Council of Washington (HMCW) to share strategies on how patients can get involved and reach out to local legislators. Since then, several HAEA members have had their personal letters read into the Congressional Record, patients have participated in the ACA Town Hall meetings taking place in numerous states, one patient was invited to meet with her state congressman, while another was invited to the President's State of the Union address.

Advances in Research: The US HAEA Angioedema Center at the University of California San Diego recently celebrated its 3-year anniversary. This international research center is staffed by world class HAE physicians/researchers and provides immeasurable opportunities to better the future of those who suffer from all types of angioedema or swelling. This center also continues to move forward groundbreaking research on all types of HAE. The center provides educational opportunities to physicians, both nationally and internationally and hosts an allergy/immunology Fellow to increase HAE education among the medical community.

The US HAEA Angioedema Center can help with:

- Diagnosis
- Clinical support and guidance for the treating physician
- An individualized management plan for the patient
- Prior authorizations and paper-work for access to HAE medicines
- Information on the latest therapies and clinical trials

American Academy of Asthma Allergy and Immunology: The US HAEA represented patients at the 2017 international meeting of the American Academy of Asthma Allergy and Immunology (AAAAI). Thousands of allergist/ immunologists, allied health and related healthcare professionals gather annually at this meeting to participate in the hundreds of educational offerings, on a variety of topics, including HAE, that take place during the four-day event.

HAEA executive leadership Tony Castaldo, Janet Long, and Lois Perry, along with Patient Advocate John Williamson attended the meeting and hosted an exhibit booth to share information with physicians on HAE and the many programs the HAEA has developed to support US physicians and HAE patients.

HAE-in-Motion: 2017 will be an active year for HAE patients and engagement and awareness will be key in helping to educate the general public about this rare condition.

The HAE-in-Motion 5K races will take place in over a dozen cities across the United States and hundreds of patients, families and friends are expected to participate. The HAE-in-Motion 5K is projected to serve as the HAEA's largest national fundraising event.

At this point US HAEA has booked these events: 1 April Warminster (PA), 9 April DeKalb (IL), 30 April San Juan (PR), 13 May Cullman (AL), 20 May Wheaton (IL), 10 June Omaha (NE), 17 June Danville (IL), 9 September Harrison (OH), 17 September Bloomington (MN), 23 September Cranford (NJ), 7 October Providence (RI), and 22 October Littleton (CO).

See much more at http://5k.haea.org.

Special Blood documentary heading overseas: The U.S. documentary film "Special Blood" by filmmaker Natalie Metzger that follows four patients with a dramatic, rare disease fighting to live normal lives will soon be available to audiences overseas.

"Special Blood" is an intimate look into the personal lives and struggles of rare disease patients in America.

Natalie Metzger uncovers stories of inspiration, struggle, and death come too early. As she enters the community which they have created around their shared disease, she shows us how these brave underdogs are changing the future for rare disease patients on a global scale.

The film has been recognized with numerous film awards.

Read more about screenings here: specialblood.com/screenings.html

The 2017 US HAEA Summit: The US HAEA is excited to announce our upcoming National Patient Summit on 15-17 September 2017 in Minneapolis, MN.

US HAEA 2017 NATIONAL PATIENT SUMMIT STAND UP STRONG

The meeting will be held for the entire US HAEA community and will feature educational lectures, one-on-one learning opportunities with HAE expert physician/researchers, the chance to participate in on-site HAE research, a fun evening that includes dinner and entertainment to enjoy with members of your HAE community, another exciting HAE-in-Motion 5K walk/run, and much more.

This year's theme, Stand Up Strong, calls our community to action and highlights the work and participation of our HAE champions who make a difference every day by getting involved and helping to raise HAE awareness within their own communities.

New sponsors: On 24 March 2017, US HAEA held a reception to thank Pharming NV and Ionis for their generous donations to the US HAEA Angioedema Center at the University of California at San Diego. These funds will support research and the top notch care of angioedema patients provided by the compassionate expert physicians and staff at the center.

Ask the Doctors

In 2015 the US HAE Association implemented a process for answering patients' questions about HAE. Physician/Scientists at the US HAEA Angioedema Center at the University of California San Diego field questions and the answers are posted on Facebook pages for Angioedema Center Facebook Page and the US HAEA. Dr. Sandra Christiansen, Dr. Marc Riedl, and Dr. Bruce Zuraw answer a recently asked question.

"A US and international update on the pediatric guidelines for HAE care"

Dr. Christiansen: There have been two recent articles published on this topic. The first was a collaborative effort by the HAEA medical advisory board (MAB) led by Michael Frank. "Management of Children With Hereditary Angioedema Due to C1 Inhibitor Deficiency" published in the journal Pediatrics. This document comprehensively summarized the available treatment options for HAE with regard to prophylactic and on demand care. Consensus opinion was given regarding their use in children. As is the case with adults, emphasis was placed on early treatment of attacks. Also underscored was the importance of access to an expert physician as well as detailed treatment plans and immediately accessible documents regarding the child's health condition and specific guidance for administration of medication. Coordination of care was also addressed which is of particular importance for children. The article gave practical advice for measures to be taken at school or when there are caregivers outside of the family responsible for the child's health. An exciting development in the wake of this publication was the US approval of plasma derived C1 inhibitor, (Berinert), for use in children. Prior to this we were certainly using this therapy however it is nice to have this 'official'. The article also alluded to ongoing trials with additional therapies. Currently the lowest approved age for use other than Berinert is for Kalbitor (Ecallantide) at age 12.

The second article is "International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency", an effort led by Dr. Farkas from Hungary on behalf of HAWK – an international consortium of expert physicians – appearing in the journal Allergy. While in many ways mirroring the MAB US document there are interesting nuances, which reflect some of the differences between the US and other parts of the world with regard to drug availability. All of us participated in each of these efforts.

Dr. Zuraw: I'It is widely recognized that HAE tends to be less severe in children than in adults; and that the average age that patients begin to experience swelling symptoms is around 10 years. Despite these facts, it is crucial to understand that HAE is an autosomal dominant genetic disease, meaning that patients are born with the disease-causing mutation, and have the disease for their entire life. Furthermore, while it is true that patients begin to swell on average at around 10 years of age, individual patients may begin swelling before they are two years old. Finally, the case of a 6-year-old child who died from an HAE attack has been reported in the literature. Putting these facts together, we can make several conclusions: first, that it is imperative that all children of an affected parent be tested for HAE; second, that treatment must be available to treat affected children; and third, that there be a management plan in place for all affected children.

Testing children of an affected parent is an essential first step that should be done as soon after birth as reasonable. In general, the current tests are interpretable in children by one year of age, and possibly even as early as six months of age. Genetic testing can be done at any age if the parent's mutation is known. While parents may hope that their children do not inherit the disorder, hope is not a plan. All parents should know that the absence of a known HAE diagnosis puts that patient at a much higher risk of a bad outcome. Approximately 25% of HAE patients have a new mutation that was not present in either of their parents. In these cases, we obviously cannot do the testing until the child begins to swell. To deal with this, it is important that pediatricians recognize that unexplained angioedema (including abdominal pain) may represent HAE.

The next problem involves which medicines are able to be used for HAE. Among the four on-demand medications that are approved to treat HAE attacks in the United States, one is licensed for all children and adults (plasma-derived C1INH, Berinert), one is licensed for children 12 years of age or older (ecallantide, Kalbitor), one is labeled for use in adolescents (recombinant human C1INH, Ruconest) and one is licensed for children 18 years of age or older (icatibant, Firazyr). The failure to license three of these medicines in younger children is unfortunate but does not mean that they would not be effective or safe in children. Rather it reflects the reality that sufficient proof of their efficacy and safety have not yet been established. In general, this is a consequence of the difficulty in doing clinical studies in children.

There are three major medicines used for HAE prophylaxis currently: plasma-derived C1INH (Cinryze), danazol, and tranexamic acid. Cinryze is approved for use in adolescents and above. Danazol does appears to be

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effective in children but is generally not recommended because of safety concerns. Tranexamic acid may be effective in children but there is limited data.

It is important that children with HAE have a management plan in place. The types of management plans used for children are similar to those used for adults. Like adults, children need access to on-demand medications for when they have an attack. Also like adults, home or self-administration is preferred since this shortens the delay until treatment. Long-term prophylactic treatment options for children are clearly suboptimal.

Overall, there is an urgent need for additional clinical trials of HAE medicines to be done in children. In general, new medicines should be studied first in adults. Once a medicine has been shown to be safe and effective in adults, a follow-up study in children should be done to permit licensing and the option for use in the pediatric HAE population.

Dr. Christiansen: I concur, hope is not a plan – please have all of your children tested. It is always best to know and be prepared.

Dr. Riedl: When comparing the US and international consensus documents on pediatric HAE, there are certainly more similarities than differences. Both documents highlight several important management themes:

- The importance of C1INH testing for the children of parents with a known history of HAE. The documents agree that testing is most reliable after the age of one year.
- Children affected by HAE benefit from seeing an HAE specialist to help establish and coordinate an optimal management plan. Patient and family educational opportunities are highlighted as an essential part of optimal HAE care.
- Children with HAE should have reliable access to effective HAE medication to treat angioedema attacks. Both publications highlight the fact that we have substantially less data on the safety and efficacy of HAE medications in children compared to adults. However, a plasma-derived C1INH product is approved for children in many parts of the world including the US, and some reassuring data exists for other medications. In some countries, such as the US, additional medications are approved for adolescents (12 and older) such as ecallantide and recombinant C1INH.
- Long-term prophylactic therapy can be considered for children when necessary.
- Both documents emphasize the use of home-treatment and self-administration whenever possible to facilitate early treatment of symptoms and improve quality of life.
- Both publications recognize the need for additional studies in pediatric HAE to determine the safest, most effective treatment strategies for children.
- A couple of notable differences between the two publications:
- Differences exist regarding the recommended HAE medications for long-term prophylaxis in children. The US consensus document more strongly advises against the use of androgen therapy in kids. US experts do not recommend the use of androgens in children due to the considerable risk of serious side effects and the availability of other treatment options. The international consensus publication states androgens are not usually considered in children before the age of sexual maturation, but androgens can be considered as a treatment option in older children with close monitoring. The international group recommends antifibrinolytics (amicar, tranexamic acid) as a preferred prophylactic medication in children, whereas the US guidelines are less enthusiastic about these drugs noting substantial adverse effects reported in some children. Both groups agree that pdC1INH is the most preferred prophylactic agent in children when available.
- The international guidelines recommend that children with HAE avoid vigorous physical activities that are known to trigger HAE attacks, such as participating in certain sports. The US guidelines do not include such recommendations as the authors considered it important for children to pursue normal desired physical activities and sports whenever possible.

2017 HAEi Youngsters Summer Camp

The Youngster Track at the 2016 HAE Global Conference in Madrid, Spain was a great success and led to many new connections between HAE youngsters from a number of countries around the globe.

"Since May 2016 a large group of youngsters have kept in touch via social media. It is wonderful to see how they enjoy the opportunity of having a truly global network of fellow HAE patients, with whom they can share experiences and ideas. The Executive Committee of HAEi has therefore unanimously decided to arrange a HAEi Youngster's Summer Camp in early August 2017 to further encourage our young patients in the global HAE community", says HAEi Executive Director Henrik Balle Boysen.

The first HAEi Youngster's Summer Camp will take place 3 August to 6 August 2017 in Frankfurt, Germany. Henrik explains:

"We have space available for a maximum of 100 campers and have asked the HAEi Member Organizations to recruit youngsters between 12 and 25 years old to attend the camp. There will be a registration fee of 75 EUR per participant but other than that HAEi will pay for flight tickets for the youngsters from their home airport to Frankfurt and back as well as transfer from Frankfurt Airport to the venue, accommodation at NH Hoteles in Mörfelden/Walldorf and all meals during the stay at the hotel. Also all activities during the Camp period are included."

While we are still working on the final program for the Summer Camp, the overall theme is, "Living with HAE". There will be plenty of time for our youngsters to network and create new friendships – and HAE Expert Physicians will be in attendance.

More information on the 2017 HAEi Youngsters Summer Camp can be found at www.trippus.net/HAEi-YoungsterCamp2017.

2017
HAEi Youngster's
Summer Camp

Global Advocacy Work

Global Advocacy Work

Recent events

6 – 8 January: HAEi had its second workshop for the Regional Patient Advocates in Vienna, Austria.

11 – 14 January: HAEi participated in the Platform of Plasma Protein Users (PLUS) Consensus Conference 2017 in Estoril, Portugal. While in Portugal HAEi met with the Portuguese member organization.

13 – 16 January: HAEi met with patients, physicians, and the Philippine Society for Rare Disorders to in Manila to establish a member organization in the Philippines.

23 – 24 January: HAEi met in San Juan, Puerto Rico with a group that established HAE Puerto Rico (on behalf of the US HAEA) and has developed significant experience in HAE advocacy. The meeting resulted in getting Mr. Javier Santana on board as the Regional Patient Advocate for Latin America.

8 – 10 February: HAEi met with the Medical Advisory Panel Co-Chairs in Milan.

20 – 22 February: HAEi conducted site visits with two of the possible future partners for the HAEi Global Access Program.

27 – 28 February: HAEi had a very positive first site inspection at the venue for the 2018 HAE Global Conference. The whole conference area at the hotel will be blocked for the HAE event. The venue for the next conference will be revealed 16 May 2017.

3 – 5 March: HAEi participated in the American Academy of Asthma, Allergy and Clinical Immunology (AAAAI) Annual Meeting in Atlanta, USA.

16 – 18 March: HAEi conducted an advocacy workshop with patient leaders and physicians in Bangkok, Thailand. The workshop focused on creative ways to speed up the process of winning access to medicines in Thailand and to arrange a HAE patient/physician workshop in Thailand at a later stage.

Upcoming events

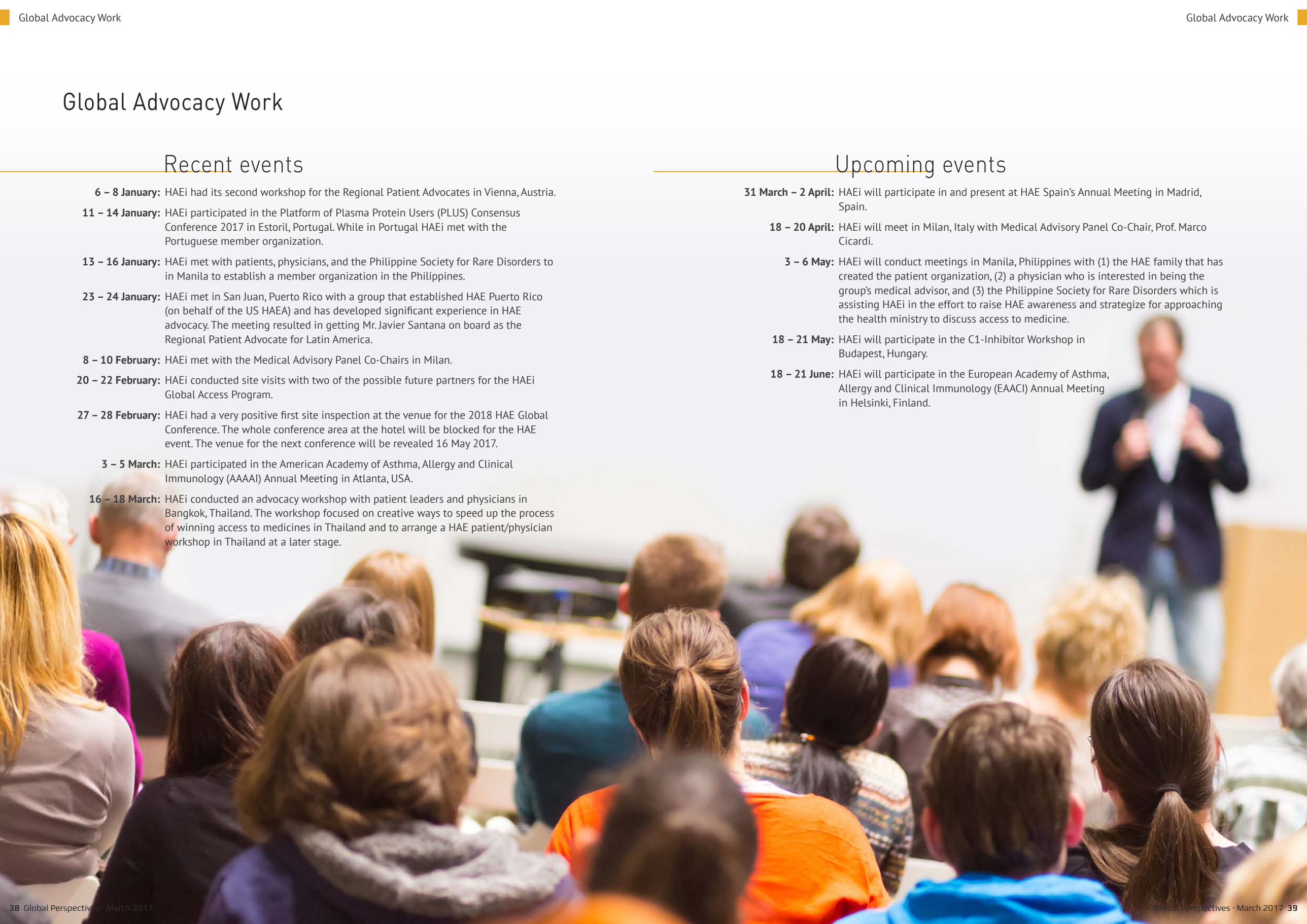
31 March – 2 April: HAEi will participate in and present at HAE Spain's Annual Meeting in Madrid, Spain.

18 – 20 April: HAEi will meet in Milan, Italy with Medical Advisory Panel Co-Chair, Prof. Marco Cicardi.

3 – 6 May: HAEi will conduct meetings in Manila, Philippines with (1) the HAE family that has created the patient organization, (2) a physician who is interested in being the group's medical advisor, and (3) the Philippine Society for Rare Disorders which is assisting HAEi in the effort to raise HAE awareness and strategize for approaching the health ministry to discuss access to medicine.

18 – 21 May: HAEi will participate in the C1-Inhibitor Workshop in Budapest, Hungary.

18 – 21 June: HAEi will participate in the European Academy of Asthma, Allergy and Clinical Immunology (EAACI) Annual Meeting in Helsinki, Finland.



Clinical Trials

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:

Biomarker for HAE Disease Type 1 (BioHAE)

– will be recruiting in Germany.

https://clinicaltrials.gov/ct2/show/NCT03029728?term=hereditary+angioedema&recr=Open&rank=1

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

– recruiting in USA.

https://clinicaltrials.gov/ct2/show/NCT01832896?term=hereditary+angioedema&recr=Open&rank=2

C1 Inhibitor Registry in the Treatment of HAE Attacks

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

https://clinicaltrials.gov/ct2/show/NCT01397864?term=hereditary+angioedema&recr=Open&rank=3

Efficacy and Safety of BCX7353 to Prevent Angioedema Attacks in Subjects With HAE (APeX-1)

– recruiting in Australia, Austria, Canada, Denmark, Germany, Hungary, Italy, Macedonia, Spain, Switzerland, and United Kingdom.

https://clinicaltrials.gov/ct2/show/NCT02870972?term=hereditary+angioedema&recr=Open&rank=4

Safety of Ruconest in 2-13 Year Old HAE Patients

– recruiting in Czech Republic, Germany, Hungary, Israel, Italy, Macedonia, Poland, Romania, and Slovakia.

https://clinicaltrials.gov/ct2/show/NCT01359969?term=hereditary+angioedema&recr=Open&rank=5

Study of C1 Inhibitor (Human) for the Prevention of Angioedema Attacks and Treatment of Breakthrough Attacks in Japanese Subjects With HAE

– recruiting in Japan.

https://clinicaltrials.gov/ct2/show/NCT02865720?term=hereditary+angioedema&recr=Open&rank=6

Firazyr Patient Registry Protocol (Icatibant Outcome Survey - IOS)

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

https://clinicaltrials.gov/ct2/show/NCT01034969?term=hereditary+angioedema&recr=Open&rank=7

Determination of Specific Biomarkers of Acute Attack of Angioedema Within Pediatric Population (BRADYKID)

– recruiting in France.

https://clinicaltrials.gov/ct2/show/NCT02854397?term=hereditary+angioedema&recr=Open&rank=8

The Role of the Coagulation Pathways in Recurrent Angioedema (Angiocoag)

– recruiting in France.

https://clinicaltrials.gov/ct2/show/NCT02892682?term=hereditary+angioedema&recr=Open&rank=9

Determination of Specific Biomarkers of Angioneurotic Crisis (BIOBRAD)

– recruiting in France.

https://clinicaltrials.gov/ct2/show/NCT02833675?term=hereditary+angioedema&recr=Open&rank=11

Long-term efficacy and safety study to evaluate DX-2930 in preventing angioedema attacks in patients with Type I and Type II HAE

– recruiting in Canada, Germany, Italy, Jordan, United Kingdom, and United States.

https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2015-005255-27

BCX7353 for the prevention of HAE attacks

– recruiting in Australia, Austria, Canada, German, Hungary, Macedonia, Spain, Switzerland, and United Kingdom.

https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2016-001272-29

Study to determine the efficacy and safety of C1 Esterase Inhibitor liquid for injection compared to placebo in the prevention of Angioedema attacks in adolescents and adults with HAE

– recruiting in Canada, Germany, Hungary, Israel, Romania, Spain, and United States.

https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2015-002478-19

A placebo controlled trial of three doses of BCX7353 to evaluate the safety and efficacy in the prevention of attacks in patients with HAE

– recruiting in Canada, Germany, Hungary, and United Kingdom.

https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2015-003923-74

A study to evaluate the long-term clinical safety and efficacy of subcutaneously administered C1-esterase inhibitor in the prevention of HAE

– recruiting in Australia, Canada, Czech Republic, Germany, Hungary, Israel, Italy, Spain, United Kingdom, and United States.

https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2014-001054-42

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 Germany, Mexico, Romania, United Kingdom, and United States.

https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2013-002453-29

Pathophysiological study for autoimmune dysregulation of HAE

– recruiting in Japan.

https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000012021

Medical Papers

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

Clinical characteristics and real-life diagnostic approaches in all Danish children with HAE *– by A. Aabom, Odense University Hospital, Denmark, et al.:*

With a potentially early onset, HAE requires special knowledge also in infancy and early childhood. In children from families with HAE, the diagnosis should be confirmed or refuted early, which can be difficult. Studies of childhood HAE and the diagnostic approaches are limited. The aim was to investigate the entire Danish cohort of children with HAE and non-HAE children of HAE patients for diagnostic approaches and clinical characteristics. Conclusions: The rate of home therapy was high and androgens had been avoided. Complement values were often equivocal, especially in cord blood samples. Consequently, we have changed diagnostic practice to early genetic testing in children where the family mutation is known. *Orphanet J Rare Dis., March 2017.*

Sustained response of recombinant human C1 esterase inhibitor for acute treatment of HAE attacks *– by J.A. Bernstein, University of Cincinnati, USA, et al.:*

Symptoms of HAE attacks can recur soon after initial treatment; the durability of response for recombinant human C1 esterase inhibitor (rhC1INH) treatment is unknown. Data were analyzed for 127 patients treated with 50 U/kg of rhC1INH in two studies. Most attacks (90.7%) responded within four hours. The median time to the beginning of symptom relief was 75.0 minutes. No relapse occurred during 24 hours for attacks that initially responded. This analysis supports the efficacy of rhC1INH for treatment of acute HAE across multiple attacks, with a sustained response for at least three days. *Ann Allergy Asthma Immunol., March 2017*

Anabolic androgen use in the management of HAE: Not so cheap after all *– by K.Y. Tse, Kaiser Permanente Medical Center, San Diego, USA, et al.:*

Despite the emergence of targeted therapies for HAE, continued anabolic androgen use has been driven in part by their low cost. Patients with HAE were identified in the Southern California Kaiser Permanente database using clinical and laboratory findings compatible with HAE. These patients were stratified into anabolic androgen exposed and nonexposed groups. Matched controls were selected from the Kaiser database that did not have HAE or anabolic androgen exposure. Patients with HAE exposed to anabolic androgens had a 28% increase in non-HAE comorbidities when compared with their matched (nonexposed) controls. With each gram per month increase in exposure, a 12% increase in non-HAE comorbidities is observed. The most commonly occurring non-HAE comorbidities were psychiatric, muscle cramps, obesity, and hyperlipidemia. The data suggest that long-term anabolic androgen use enhances the risk of developing comorbid health conditions, thus amplifying the cost of care. The report provides additional support for the preferred use of newer, targeted therapies for the management of HAE. *Ann Allergy Asthma Immunol., March 2017*

Health-Related Quality of Life among Children with HAE *– by B. Engel-Yeger, University of Haifa, Israel, et al.:*

Children with symptomatic C1-INH-HAE demonstrate impaired health-related quality of life compared with healthy controls. Health-related quality of life was affected by the frequency and site of C1-INH-HAE attacks and mostly in the school and physical domains. *Pediatr Allergy Immunol., March 2017*

Mutational spectrum of the SERPING1 gene in Swiss patients with HAE *– by U.C. Steiner, University Hospital Zurich, Switzerland, et al.:*

Compared to HAE cohorts in other countries the genetic background of the Swiss HAE patients has not been elucidated yet. This study investigates the mutational spectrum of the SERPING1 gene in 19 patients of 9 unrelated Swiss families. The families comprise a total of 111 HAE-affected subjects, corresponding to approx. 70% of all HAE-affected patients living in Switzerland. Three of the identified mutations are newly described. Members of one family with a nucleotide duplication as genetic background seem to have a more intense disease manifestation with a higher attack frequency compared to the other families. Newly designed genetic screening tests allow a fast and cost efficient testing for HAE in other family members. *Clin Exp Immunol., February 2017*

Screening for HAE at 13 emergency centers in Osaka, Japan: A prospective observational study *– by T. Hirose, Osaka University, Japan, et al.:*

This 3-year prospective observational screening study involves 13 urban tertiary emergency centers in Osaka prefecture, Japan. C1-INH activity and C4 level were measured at the time of emergency department admission. The study comprised 66 patients with a median age of 54 years. Three patients were newly diagnosed as having HAE, and one patient had already been diagnosed as having HAE. C1-INH activity levels of the patients with HAE were below the detection limit (<25%), whereas those of non-HAE patients were 106% (normal range, 70-130%). The median level of C4 was significantly lower in the patients with HAE compared with those without HAE. Three patients were diagnosed as having HAE in the emergency department. *Medicine (Baltimore), February 2017*

Novel usage of fresh frozen plasma in HAE *– by N. Hanizah, Universiti Sains Islam Malaysia, et al.:*

New disease specific treatment including plasma derived or recombinant C1-INH, ecallantide and icatibant have recently emerged and its appropriate use can reduce HAE-associated mortality and morbidity. However, due to its costs, these disease specific treatments have yet to reach Malaysia. Despite that no randomized clinical trial on fresh frozen plasma has been performed, its efficacy in treating acute attacks of HAE is only demonstrated in case studies. *Clin Ter., November-December 2016*

Experimental protocol of dental procedures in patients with HAE: the role of anxiety and the use of nitrogen oxide *– by A. Rosa, University of Rome, Italy, et al.:*

As episodes of HAE can be triggered by anxiety, invasive procedures and trauma, this disease is a major problem in oral and maxillofacial surgery, ENT, endoscopy, emergency medicine, and anesthesia because even simple procedures can cause laryngeal edema. The recommendations on the management of HAE include long- and short-term prophylaxis and treatment for acute attacks, however, the importance of anxiety control during the operating phases is undervalued. An experimental protocol for the surgery management of HAE patients with the help of nitrous oxide is suggested. *Oral Implantol (Rome), November 2016*

News from the Industry

17 January 2017

Following the positive opinion of the Committee for Medicinal Products for Human Use (CHMP), the European Commission has adopted the Commission Implementing Decision to amend the marketing authorization for Ruconest to include self-administration using the Ruconest Administration Kit.

This decision allows for self-administration of Ruconest for acute HAE attacks by adolescents and adults with a new custom-designed Ruconest Administration Kit in the comfort and privacy of their own homes or at any other place they choose, without the necessity of a healthcare professional (HCP) being present.

The Administration Kit will become available for use in the various EU markets, following approval of the Educational Materials by the local authorities, expected over the coming one to three months.

Prof. Bruno Giannetti, the COO of **Pharming Group N.V.**, comments:

"This EU label change is yet another testament to Ruconest's well-established and favorable safety profile. Over 28,000 post-approval vials of Ruconest to treat HAE attacks have now been prescribed, making it a convenient, safe and effective way to stop these attacks. With approval of this administration kit, it will now be as convenient to use Ruconest in the EU as it already is in the US."

Self-administration (at home or without a HCP present) was granted immediately upon approval in the US as a result of more safety data being available at the time of the Biologics License Application (BLA) and subsequent approval in July 2014.

Detailed recommendations for the use of this product will be described in the updated summary of product characteristics (SmPC), which will be published in the revised European public assessment report (EPAR) in all official European Union languages on the EMA website.

(Source: Pharming)

23 February 2017

The New England Journal of Medicine has just published the results from the Phase 1b study of lanadelumab (SHP643; formerly DX-2930) from **Shire plc**.

Lanadelumab is a subcutaneously administered, human monoclonal antibody that specifically binds and inhibits plasma kallikrein, and it is being investigated for the prevention of angioedema attacks in patients with HAE.

"In this Phase 1b study, no serious adverse events or discontinuations due to adverse events were observed at all doses studied. Pre-specified efficacy analyses in patients with at least 2 attacks in the 3 months prior to enrolment demonstrated that from day 8 to day 50, the administration of two doses of lanadelumab (300 or 400 mg) 14 days apart, reduced the rate of attacks by 100% and 88% respectively, when compared with placebo. In addition, all subjects were attack-free in the 300 mg group and 82% were attack-free in the 400 mg group, compared to 27% in the placebo group," said Dr. Aleena Banerji, Associate Professor, Massachusetts General Hospital, Boston.

"The overall results of this study are encouraging; it should be noted that while the duration of treatment was relatively short and only a small number of patients were investigated, the results supported further Phase 3 investigations, which are currently ongoing," added Dr. Paula Busse, Associate Professor, Mount Sinai Hospital, New York.

"Despite improvements in the management of HAE in recent years, there is still a need for long-acting prophylactic treatment options. At Shire we are proud of our history in HAE and ongoing commitment to the clinical development of lanadelumab, an investigational prophylactic therapy for this rare genetic disease," said Philip J. Vickers, Ph.D., Global Head of Research and Development at Shire.

A pivotal Phase 3 trial evaluating the safety and efficacy of lanadelumab as a long-acting prophylactic treatment for HAE is currently underway.

With the clinical development of lanadelumab, Shire is building on its legacy in HAE and as the world leader in rare diseases.

The multicenter, randomized, double-blind, placebo-controlled, multiple-ascending dose study enrolled a total of 37 patients randomized to receive lanadelumab or placebo across four different dosing groups of 30, 100, 300, or 400 mg. Each subject received two doses of lanadelumab or placebo, separated by 14 days, and was followed for 120 days post-dose. The primary objective of the study was to assess the safety and tolerability of multiple subcutaneous administrations of lanadelumab at different dose levels in HAE patients. Secondary and tertiary objectives included characterization of the pharmacokinetics and pharmacodynamics of lanadelumab, evaluation of immunogenicity, and assessments of HAE attack frequency and use of acute attack therapy.

There were no serious adverse events or discontinuations due to adverse events reported in patients treated with lanadelumab. A total of 29% of the patients who received lanadelumab and 38% of those who received placebo had an adverse event that was considered by trial investigators, who were unaware of the trial-group assignments, to be treatment-related. The most common treatment-related adverse events were injection site pain (25% lanadelumab, 23% placebo) and headache (8% lanadelumab, 15% placebo).

In HAE patients, the pharmacokinetic profile of lanadelumab is linear, dose-dependent, and exhibits a half-life of approximately 14 days, typical of a human monoclonal antibody. The pharmacodynamic profile of lanadelumab was assessed by plasma levels of cleaved high molecular weight kininogen (cHMWK). Pharmacodynamic results confirm plasma kallikrein inhibition in a dose and time-dependent manner, and suggest doses of 300 mg or greater have the potential to normalize cHMWK levels based on levels of cHMWK approaching that observed in healthy subjects.

(Source: Shire)

27 Februar 2017

BioCryst Pharmaceuticals, Inc. has announced results from an interim analysis of its Phase 2 APeX-1 trial in HAE. APeX-1 is a dose ranging trial designed to evaluate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of orally administered once daily (QD) BCX7353 for 28 days, as a preventative treatment to reduce the frequency of attacks in HAE patients.

"The results of this interim analysis are extraordinarily encouraging," said Dr. Emel Aygören-Pürsün, MD, principal investigator for the APeX-1 trial and Head of Interdisciplinary Competence Center for HAE, and Specialist in Internal Medicine and Hemostaseology Department of Child and Adolescent Medicine, Goethe University Hospital Frankfurt. "Confirmation of the results would lead to a huge step forward in the treatment of HAE, towards an effective, safe and easy to administer prophylaxis for the debilitating attacks connected with this condition."

"We are extremely excited to have such a strong treatment effect in reducing HAE attacks with our once daily oral therapy," said Jon Stonehouse, CEO & President of BioCryst. "What is even more encouraging is the dramatic benefit seen in the reduction of peripheral attacks and mixed peripheral and abdominal attacks. A once daily oral therapy with an 88% reduction in these attacks has the potential to make a huge difference in HAE patients' lives."

Twenty-eight subjects, randomized equally to receive BCX7353 350 mg QD or placebo for 28 days, were included in the interim analysis. The baseline attack rate was approximately 1/week, and average C1 inhibitor levels were less than 20% of the normal mean, indicating a severely affected patient population. Baseline characteristics were generally well balanced between the two groups with the exception of prior androgen use, which was more common in the BCX7353 group (11 of 14 compared with 6 of 14 on placebo). Compliance with study drug dosing was excellent (> 98%).

The pre-specified per-protocol (PP) interim analysis included data on 24 subjects with confirmed Type 1 or Type 2 HAE completing 28 days of treatment (11 treated with BCX7353 and 13 with placebo). The mean rate of independently-adjudicated angioedema attacks for the pre-defined effective dosing period (weeks 2 through 4) in BCX7353-treated subjects was 0.34/week compared to 0.92/week for placebo, a reduction of 0.57/week (63%), p = 0.006. In the intent-to-treat (ITT) population of 28 subjects, the rates of attacks for the effective dosing period for BCX7353 and placebo groups were 0.44/week and 0.91/week, a reduction of 0.47/week (52%), p = 0.035.

A pre-planned analysis of peripheral and abdominal attacks showed reductions of 88% and 24%, respectively, for BCX7353 compared with placebo (PP analysis, weeks 2 through 4). To understand this difference, patient diaries were reviewed and abdominal attacks (n = 9, BCX7353 and n = 14, placebo) were subdivided into two groups: attacks with abdominal symptoms only and attacks with a combination of abdominal and peripheral symptoms (mixed attacks). This post-hoc analysis showed that there were 2, 2 and 7 peripheral, mixed and abdominal-only attacks on BCX7353 compared with 22, 12 and 2 attacks, respectively, for placebo. Based on this distribution, it is likely that subjects recorded transient abdominal adverse events as HAE attack symptoms in their diary.

Steady state BCX7353 plasma levels in HAE subjects were similar to those in healthy subjects administered the same dose in a previously completed Phase 1 trial. Steady state trough drug levels (24 hours after dosing) were 11–32 times the 50% effective concentration (EC50) for plasma kallikrein inhibition.

Daily oral dosing with BCX7353 strongly inhibited plasma kallikrein throughout the 24 hour dosing interval; the degree of inhibition was similar to that seen with this dose in the healthy subject Phase 1 trial.

Oral BCX7353 350 mg once-daily for 28 days was generally safe and well tolerated in subjects with HAE. There were no serious adverse events (AEs) and no related severe AEs. Two subjects in the BCX7353 treatment group discontinued study drug before day 28, one due to an unrelated pre-existing condition, and one due to an adverse event of gastroenteritis associated with elevated liver enzymes. Treatment-emergent adverse events occurring in at least 2 subjects overall, enumerated by treatment group (BCX7353 [n=14] and placebo [n=14]), were: common cold (3, 4); diarrhea (4, 2); flatulence (2, 0); and fatigue.

No clinically significant changes in hematology parameters, renal function tests, electrolytes, or urinalysis were observed. One subject treated with BCX7353, with pre-existing colitis, hepatic steatosis (fatty liver) and more than 20 years of prior androgen use, had an elevation of alanine aminotransferase (ALT) > 3 times the upper limit of normal at the end of treatment, which resolved.

The efficacy, safety and tolerability profile of BCX7353 observed in this interim analysis strongly supports its continued investigation as a prophylactic treatment for HAE. The steady state drug levels observed far exceeded the proposed therapeutic target range of 4–8 times the EC50, supporting evaluation of lower doses. Therefore, the APeX-1 trial has been amended to add a 62.5 mg QD dose level and to increase the number of subjects at the 125 mg QD and 250 mg QD dose levels, in order to more fully characterize dose response.

(Source: BioCryst)

7 March 2017

Attune Pharmaceuticals, a biotechnology company focused on the discovery and development of novel oral small molecule therapeutics for the treatment of rare diseases, has announced the first preclinical data results for ATN-249, a novel orally administered plasma kallikrein inhibitor for the treatment of HAE. The data was presented in a late-breaking poster presentation at the 2017 American Academy of Allergy, Asthma & Immunology Annual Meeting (AAAAI) and highlighted a profile which suggests high potency with a wide therapeutic window and the potential for once daily dosing of ATN-249.

Studies demonstrated ATN-249 was highly selective and potent at plasma kallikrein inhibition in both biochemical inhibition and contact activation assays. "We are pleased with the performance of ATN-249, in particular, the relative activity against C1-INH, the standard of care in the relevant pre-clinical assays for kallikrein inhibition," said Dr. Andrew McDonald, CEO of Attune Pharmaceuticals, "The data we have seen to date indicates that this lead drug candidate may be a potent, safe, orally-administered plasma kallikrein inhibitor for treatment of HAE and we intend to start Phase I in 2017."

The poster outlined the results of several well-established preclinical assays. The studies included evaluation of selectivity by biochemical inhibition on plasma kallikrein relative to other serine proteases, potency by biochemical inhibition and contact activation assays in human plasma, and pharmacokinetic exposure in monkeys after a single oral administration of ATN-249.

Continued on next page ....

... continued

9 March 2017

Study Results:

- SELECTIVITY: ATN-249 was >2000-fold more selective at inhibiting plasma kallikrein versus other closely related serine proteases, including tissue kallikrein 5, plasmin, Factor Xa, Factor VIIa, thrombin, and tissue plasminogen activator (tPA)
- POTENCY: ATN-249 demonstrated ~10-fold greater plasma kallikrein inhibition relative to C1-INH in both biochemical inhibition and contact activation assays — an ex-vivo assay that closely represents clinical pharmacology
  - In biochemical inhibition, ATN-249 had an IC50 of 2.7nM versus 25.4nM for C1-INH
  - In contact activation assays, ATN-249 had an EC50 of 8.2nM versus 92.4nM for C1-INH
- PHARMACOKINETICS: A single oral dose of ATN-249 at 15mg/kg provided 24- hour exposure 30-fold greater than EC50
- SAFETY: No adverse events were observed at the highest dose (300mg/kg) when evaluated in 14-day non-GLP rat and monkey toxicology studies; safety evaluation in 28-day GLP studies are ongoing.

Based on the positive performance and excellent pre-clinical safety profile, Phase 1 clinical studies of ATN-249 are expected to start in the middle of this year to evaluate ATN-249's safety, tolerability and pharmacokinetic profile in healthy volunteers.

Attune Pharmaceuticals is a pre-clinical stage biotechnology focused on the discovery and development of novel oral once-daily small molecule therapeutics for the treatment of rare diseases. Attune Pharmaceuticals is currently developing 2 programs in rare diseases: HAE and complement-mediated diseases. Attune Pharmaceuticals has identified ATN-249 as a lead candidate to treat HAE and will begin clinical testing in 2017.

(Source: Attune Pharmaceuticals)

KalVista Pharmaceuticals, Inc. has appointed Andreas Maetzel, M.D., M.Sc., Ph.D, to the role of Senior Vice President, Medical.

"Andreas Maetzel brings a wealth of experience in HAE and over 25 years of leadership in the pharmaceutical industry, including clinical development, medical and regulatory affairs," said Andrew Crockett, CEO of KalVista. "I am confident that he will help maximize the potential of our oral plasma kallikrein HAE portfolio as we continue to advance multiple programs into clinical development and develop a best-in-class oral therapy for this disease."

Dr. Maetzel was most recently Vice President, Global Medical Affairs at BioCryst Pharmaceuticals. Prior to that, he was Vice President, Clinical Development & Regulatory Affairs at Cornerstone Therapeutics Inc. Previously, Dr. Maetzel held a clinical development role at BioCryst, and also positions in strategy consulting and at Amgen. He is a Visiting Scientist, Faculty of Medicine, University Hospital Zurich and Charité Hospital Berlin, and Adjunct Professor, Institute for Health Policy, Management & Evaluation, University of Toronto. Dr. Maetzel obtained both a Ph.D and M.Sc. in Clinical Epidemiology from the University of Toronto and a Dr. med. at the University of Hannover, Germany.

Dr. Maetzel commented, "I am very excited to join KalVista at this juncture, with the Company advancing a portfolio of oral programs for HAE. I believe that the Company's strategy of taking multiple compounds into clinical development to develop a best-in-class oral therapy for HAE takes full advantage of KalVista's unique strengths in chemistry and biological understanding of plasma kallikrein. I look forward to working with the team to develop oral therapies for HAE."

(Source: KalVista)

10 March 2017

Pharming Group N.V. has presented its (unaudited) financial report for the full year ended 31 December 2016. Sijmen de Vries, CEO and Chairman of the Board of Management, comments:

2016 was a major year for Pharming. During the year we achieved a number of positive milestones that culminated in December in the game-changing re-acquisition of commercialization rights for Ruconest in North America from subsidiaries of Valeant Pharmaceuticals International, Inc.

Early in the year, we expanded our collaboration with Cytobioteck S.A.S. for the exclusive distribution of Ruconest in Latin America by the addition of four countries. Subsequently, we amended our agreement with Swedish Orphan Biovitrum AB, resulting in the return of the commercialization rights for Ruconest in certain Western European, North African and Middle Eastern markets. This accelerated our goal towards becoming a fully integrated specialty pharma company.

In May, the European Medicines Agency (EMA) confirmed that pre-exposure testing was no longer necessary for Ruconest. Later in the year a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) was obtained recommending permission for home treatment with Ruconest, with a custom-designed self-administration kit, which was confirmed by the EMA with the appropriate label adjustment early in 2017. This EU approval of self-administration is further to the US approval received in 2014.

In July, positive clinical and statistically significant results were achieved in our randomized double-blind Phase II clinical trial for Ruconest in prophylaxis of HAE, meeting all primary endpoints. The study showed that Ruconest, used once-weekly, results in a very similar reduction of HAE attack frequency to that obtained with twice-weekly dosing of the only currently approved product for the prophylaxis of HAE (i.e. approximately 50% reduction in attack frequency in approximately 50% of patients). Ruconest dosed twice-weekly achieved an unprecedented response rate (reduction of attack frequency of at least 50%) of 97% and average reduction of attack frequency of 73%. These results demonstrate, yet again, that the appropriate dosing of our C1 inhibitor leads to results that patients can rely on.

In order to continue to improve the convenience of Ruconest administration, our R&D scientists have formulated a highly-concentrated vial of Ruconest, so that we are now looking to enter clinical trials with intra-muscular and/or sub-cutaneous administration of smaller injections of Ruconest within the next twelve months.

Following a preliminary announcement of the conditional deal in August, in December we announced the definitive acquisition of the North American commercialization rights for Ruconest from Valeant. The transition of the sales force that we acquired as part of the deal was smoothly executed, with the team selling Ruconest one day for Valeant and selling Ruconest the next day for Pharming. Immediately after the close of the deal, we initiated our plans to increase awareness and sales of Ruconest in the US market. We have now hired additional experienced HAE/rare disease sales force members, medical science liaison professionals and a very seasoned management team with expertise in marketing, sales, commercial activity and patient support.

As a result of these EU and US transitions, we now operate with an optimal commercial presence in both Western Europe and the US and can focus fully on delivering on our commitment to become an operationally profitable company during 2017.

(Source: Pharming)

10 March 2017

The European Commission has approved a label extension granting three new indications for Cinryze (C1 inhibitor [human]) from **Shire plc**, broadening its use to children with HAE.

Cinryze is now indicated for routine prevention of angioedema attacks in children (ages 6 years and above) with severe and recurrent attacks of HAE who are intolerant to or insufficiently protected by oral preventions treatments, or patients who are inadequately managed with repeated acute treatment. It is the first and only HAE treatment with this indication in paediatric patients. Cinryze is also now approved for the treatment and pre-procedure prevention of angioedema attacks in children (ages 2 years and above) with HAE.

"This paediatric label expansion demonstrates our ongoing commitment to improving the lives of patients of all ages living with HAE," said Philip J. Vickers, Ph.D., Head of R&D, Shire. "We believe the future of HAE means preventing attacks before they happen, and are proud to now be able to offer the first long-term preventative treatment for paediatric patients. As we expand our HAE portfolio, we remain focused on innovative solutions that fulfil unmet needs for people worldwide living with this rare disease."

Cinryze has been approved since 2011 for these indications in adults and adolescents ages 12-17 years with HAE.

Henrik Balle Boysen, Executive Director of HAEi, stated, "Over the years we have encountered many children who suffer from frequent and severe HAE symptoms that often occur spontaneously and without warning. Despite improvements in the management of HAE in recent years, this new long-term prophylaxis indication for alleviating the frequency of HAE symptoms will be a welcome addition for families with HAE in Europe."

Cinryze will be available for use in paediatric patients later in 2017 throughout Member States of the European Union (EU), as well the European Economic Area (EEA) in which Shire currently has a licence in the adult and adolescent population.

(Source: Shire)

22 March 2017

From 7 to 9 March 2017, **CSL Behring** in Bern, Switzerland hosted the First Intercontinental Immunoglobulin and Hereditary Angioedema Academy.

The conference included presentations from 13 international immunodeficiency and HAE specialists, as well as a plant tour at CSL Behring AG. During the meeting, the approximately 90 immunologists from all over the world enjoyed a unique opportunity to increase their knowledge about the pathophysiology and the clinical management of immunodeficiencies and HAE.

"This event is an important proof point that CSL Behring is a worldwide strategic partner in developing educational programs for physicians. We are very much looking forward to contributing to the cooperation and networking among these Health Care Providers," said Lucilla Franchetta Ortelli, Senior Product Manager.

(Source: CSL Behring)

22 March 2017

New England Journal of Medicine (NEJM) has published results from the COMPACT study, a pivotal Phase III study evaluating the safety and efficacy of CSL830 (a novel, investigational, self-administered, subcutaneous C1-Esterase Inhibitor [C1-INH] Human replacement therapy) from **CSL Behring**.

The study met its primary efficacy endpoint, significantly reducing the time-normalized number of HAE attacks. In addition, the study met its secondary endpoints, including the responder rate (patients who had at least a 50% reduction in their attack rate) and the number of rescue medication uses. If approved by the FDA, CSL830 would be the first and only subcutaneous preventative therapy for HAE.

"Subcutaneous C1-INH, as demonstrated in the COMPACT study, addresses an unmet need for patients and has the potential to change the treatment paradigm by adding a new option to prevent HAE attacks with a subcutaneous therapy," said Bruce Zuraw, M.D., of the University of California San Diego School of Medicine, Director of the US HAEA Angioedema Center at UC San Diego, and chairman of the steering committee of the study.

The NEJM paper provides detailed data on the Phase III randomized efficacy study which evaluated type I & type II HAE patients during two 16-week treatment periods. The study looked at the number of attacks experienced by a patient given CSL830 prophylactically and the number of times HAE rescue medication was needed; both were reduced. Depending on the administered dose, HAE attack rates were reduced by a median of 89% and 95% (for the 40 IU/kg and 60 IU/kg dose, respectively). Additionally, 40% of patients on the higher dose were completely free of attacks, and patients, in general, experienced fewer and milder HAE symptoms overall. No patients on 60 IU/kg experienced a laryngeal attack within the study period.

"The study not only demonstrates very robust and dose-dependent efficacy, but also that the subcutaneous self-injection could be managed by all patients and was well tolerated," said Hilary Longhurst, M.D., of Barts Health NHS Trust, London, United Kingdom, first author of the manuscript and member of the steering committee.

"Despite the strides that have been taken to provide current treatment options, there still remains a need for new therapies that prevent symptoms of this debilitating and potentially life-threatening disease," added Andrew Cuthbertson, M.D., Chief Scientific Officer and R&D Director, CSL Limited. "These study results demonstrate the promise of CSL830 and its potential to significantly change the lives of people living with HAE by reliably preventing attacks with a self-administered subcutaneous therapy. CSL Behring thanks all of the patients who participated in this study for their courage and collaboration. Patient and investigating physician partnerships make clinical programs like COMPACT possible and progress could not be made without them."r.

(Source: CSL Behring)

24 March 2017

As of 24 March 2017, Japan's Ministry of Health, Labour and Welfare (MHLW) has approved an extended use of Berinert from **CSL Behring,** a C1-esterase inhibitor (C1-INH) concentrate, for pre-procedure prevention (short-term prophylaxis) of acute episodes of HAE .

Berinert is now indicated for the treatment of acute episodes and for pre-procedure prevention (short-term prophylaxis) of acute episodes of HAE. Berinert as the first and only C1-INH concentrate therapy in Japan has been used for acute episodes of HAE for many years.

This important approval supports further treatment options for the use of C1-INH concentrate as first-line therapy for the prevention of potentially life-threatening HAE attacks triggered by surgical or dental procedures.

Responding to reports of swelling of tongues or larynx triggered by surgical or dental procedures that may become fatal, the Japanese Society of Oral and Maxillofacial Surgeons and the Japanese Dermatological Association petitioned an extended use of C1-INH concentrate for short-term prophylaxis at pre-procedure prevention.

The petition has successfully been supported to apply Public Knowledge-based Application be submitted by "Review Committee on Unapproved Drugs and Indications with High Medical Needs" as to be an indication that can provide significant clinical benefits, and then concluded by the MHLW advisory committee as of November 2016 that efficacy and safety profiles of this product were already well-known medically pharmaceutically.

(Source: CSL Behring K.K.).

CSL Behring

HAEi Global Access Program

With the launch of the HAEi Global Access Program (HAEi GAP) – a first-of-its-kind medication access program – thousands of patients suffering from HAE will have access to medicines for the first time.

See the latest information about the program at www.haei.org.

HAEi around the world

Currently there are HAE member organizations in 55 countries. You will find much more information on the HAE representations around the globe at **www.haei.org** as the world map will provide you with contact information for the member organizations as well as care centers, hospitals, physicians, available medication, and clinical trials.

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