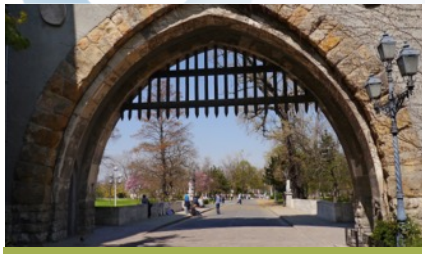
HAEi Newsletter



IN THIS NEWSLETTER

A Message from the President

Dear HAEi Friends,

This newsletter - our fourth so far this year - includes a bonus feature over and above our usual comprehensive coverage of news from the global HAE patient community and press releases from pharmaceutical companies. We are delighted to include highlights of the 9th International C1-INH Deficiency Workshop that took place in Budapest, Hungary, 28 -31 May 2015. This biennial workshop provides clinicians and researchers with an extraordinary opportunity to share experiences, findings, and ideas. In addition, the meeting is unique because the organizers - Drs. Farkas and Varga - have always welcomed and encouraged patient participation. The value of what transpired at this year's conference will become readily apparent as you read about the 2015 Workshop.

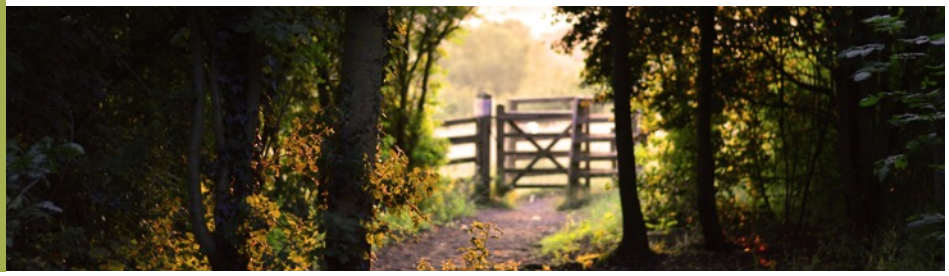
The launch of HAEi's Global Access Program (GAP) represents a significant first step forward in HAEi's quest to broaden the global availability of HAE medicines. As noted in this newsletter, the HAEi GAP offers a regulatory compliant mechanism for delivering desperately needed therapy in countries where modern HAE treatment is not currently available. HAEi GAP provides us with a tangible platform for pursuing one of our primary aims - expanding access to life saving medicine.

Finally, I would like to once again stress the importance of participating in clinical trials that are open in your country. Clinical trials are the path to better treatments and improved quality of life.
It is a credit to our unified global advocacy movement, that HAE has the good fortune of attracting significant pharmaceutical company investment in exciting new medicines. Our patient community has always recognized that clinical research is the only path to improving our lives and graciously made the sacrifices required to participate.

With the potential for great strides in HAE care looming, there is no doubt we will once again step up and do what it takes to get clinical trials completed.

My sincere warm regards,

Anthony J. Castaldo
President, HAEi



Unique Global Access Program launched

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.

"Driven by HAEi, the new program is the first Global Access Program in HAE. The program brings the opportunity of access to HAE medications in countries where innovative effective therapies are otherwise unavailable," said Henrik Balle Boysen, Executive Director, HAEi. "This is the first program of its kind in HAE, and we believe the first time this type of program has been initiated by a patient organization."

To realize the program, HAEi has partnered with Clinigen Group plc's Global Access Programs business/division to manage the distribution and logistics for medications in the HAEi GAP. The first HAE therapy available through the program is the human recombinant C1-inhibitor Ruconest® (conestat alfa) manufactured by Pharming Group N.V.

"HAEi is committed to securing access to HAE medications for patients across the globe", said Anthony J. Castaldo, President of HAEi. "We are extremely proud to have established HAEi GAP with our current partners and will continue to work with other manufacturers with the hope of expanding the program in the future."

HAEi GAP follows ethical and regulatory compliant mechanisms and enables patients to gain access to Ruconest through a Named Patient Program (where Ruconest is currently not commercially available). Individuals with a confirmed diagnosis of HAE may be eligible for HAEi GAP. Their doctors can apply to HAEi GAP via Clinigen customer services.

"It is a desperate situation for patients in countries without access to licensed HAE therapies. We hear of patients resorting to the black market or international pharmacy websites to try and access medicine", advised Henrik Balle Boysen. "HAEi GAP offers legitimate access to effective medicine for eligible patients with the security of an established logistics and supply chain to ensure the right medicine reaches the right patient whenever, and wherever they need it".

Sijmen de Vries, CEO, Pharming said: "We are delighted to be the first partners of HAEi and to initiate this program by providing access to RUCONEST, a recombinant human C1-inhibitor, approved by EMA and FDA for the treatment of acute attacks of HAE. In this way we can help to improve the lives of those HAE patients that otherwise would continue suffering from this debilitating and unpredictable disease."

Simon Estcourt, Managing Director, Managed Access Programs, Clinigen said: "HAEi's ground-breaking program will ensure that HAE sufferers worldwide can gain access to effective and potentially life-saving treatment. Our secure supply chain and regulatory expertise will enable us to work closely with Pharming to supply patients with RUCONEST ethically and legitimately, removing the need and the risk for patients to resort to other less reliable or even illegal sources of the drug. We look forward to working with both HAEi and Pharming on this unique project."

HAEi GAP expects to go live in a matter of weeks.

As part of the launch of the HAEi GAP Deborah Corcoran has joined HAEi as Project Manager. With a background in chemistry, she worked in healthcare communications agencies for over 10 years before starting her own freelance consultancy. Over the last five years, Deborah Corcoran has worked with HAEi on several individual projects and is now focusing on HAEi GAP.

You can follow the latest updates in the HAEi Global Access Program directly on haei.org/hae/global_access_program.

Highlights from the 9th C1-INH workshop in Budapest, Hungary

The 9th international C1-INH deficiency workshop - taking place every second year since 1999 - was held in Budapest, Hungary 28-31 May 2015. The workshop constitutes an international forum for professionals involved in the research and management of bradykinin-mediated angioedema, as well as for the representatives of patients - and naturally HAEi attended the event. Attracting some 250 participants from more than 30 countries worldwide the conference focused on HAE due to C1-INH deficiency as well as HAE with normal C1-INH level and acquired angioedema resulting from C1-INH deficiency.

The following pages are dedicated to some highlights from more than 40 oral lectures and over 40 poster presentations.

Tom Bowen, University of Calgary, Canada: Through independent data base registries and research programs we can improve on prevention and treatment programs for HAE. We must provide robust independent data on the pharmacoeconomics and quality of life justifications of our HAE management algorithms. It can be done - it must be done for the sake of our patients.

Jacob Giehm Mikkelsen, Aarhus University, Denmark: Novel genetic engineering techniques facilitate studies of the cellular pathology of HAE. As gene therapy is coming of age, insight info the cellular disease mechanisms may pave the way for genetic intervention as a possible treatment modality.

Erik Hack, University Medical Center, Utrecht, The Netherlands: Several observations in HAE patients are difficult to explain from a pathological model claiming a local activation process at the site of the angioedema attack. Therefore, we postulate an alternative model, which assumes a systemic, fluid-phase activation of the contact system to generate bradykinin and breakdown products. Interactions af these peptides with endothelial receptors explains that such a systemic activation process results in local manifestations of an attack.

Lilian Varga, Semmelweis University, Hungary: Better elucidation of the interactions of C1-INH would improve our understanding of the pathomechanism of bradikynin-mediated angiodemas and could take us closer to developing individualized and targeted therapies further.

Nathália Cagini, Federal University of Sao Paolo, Brazil: The results show a wide range of alterations in the SERPING1 gene responsible to the HAE symptoms in Brazilian patients.

Anette Bygum, Odense University Hospital, Denmark: Patients referred with a diagnosis of angioedema may suffer from other diseases and physicians at angioedema centers need to be aware of possible differential diagnoses.

Ruchira Engel, Sanquin Reseach and University of Amsterdam, The Netherlands: We have developed a robust, specific and semi-quantative assay to detect the neutralization capacity of plasma samples containing anti-C1-INH antibodies. This assay can be an important tool for the study of clinical implications af anti-C1-INH neutralizing antibodies.

Iris Leibovich, Sheba Medical Center, Israel: This preliminary retrospective study indicates that prodromes and attacks are correlated in severity, location and degree of dysfunction.

Delphine Gobert, Hopital Saint-Antoine, France: Our results confirm the association of acquired angioedema with indolent lymphoma and monoclonal gammapathy of undetermined significance. The benefit of rituximab, used alone or combined with chemotherapy, seems promising.

Urs C. Steiner, Spitalnetz Bern Tiefenau/Ziegler, Switzerland: As clinics are very individual an individualized therapy is required and women need a closer attendance.

Inmaculada Martinez-Saguer, HZRM Hemophilia Center Rhine Main, Germany: Monozygotic twins with the same HAE specific mutation have inter-individual variations in symptom expression in terms of frequency and location of attacks.

Daniela Riveno, Hospital La Paz, Spain: Fertilization therapies might cause an aggravation of angioedema in patients with HAE-C1-INH, which could be managed by on-demand and intermittent long-term potentiation with plasma derived C1-INH concentrate.

Kinga Viktória Kóhalmi, Semmelweis University, Hungary: The prevalence of erythrocytosis is not significantly higher in C1-INH-HAE patients after treatment with danazol. Nevertheless, erythrocytosis may occur as a rare adverse effect of danazol and hence, periodic monitoring of hematological parameters is necessary.

Teresa Caballero, Hospital La Paz, Spain: The HAE activity scale is a short, valid, reliable and psychometrically sound measure of disease activity for C1-INH-HAE, which may be very useful for further research and clinical studies. Further studies are needed to assess the scale's sensitivity to change.

Zsuzsanna Zotter, Semmelweis University, Hungary: Increase incidence of edema was associated with bacteriuria. This emphasizes the triggering role of bacteriuria in the occurrence of edematous episodes.

Anne Aabom, Odense University Hospital, Denmark: Childhood complement measurements are problematic. Consequently, we have changed our diagnostic approach to newborns from HAE families. First choice is early genetic testing if the mutation of the affected parent is known. Cord blood is useful. Second choice is complement measurements at the age 6 months and after 12 months. Cord blood sampling is not worthwhile.

Atsuko Hisada, Juntendo University, Japan: Early onset of angioedema, positive family history, recurrent angioedema in the extremities and gastrointestinal tract, and suffocation are distinctive characteristics of HAE. A low serum of C4 is a useful marker for making differential diagnosis of HAE.

Alban Deroux, Interal Medicine Grenoble, France: D-dimers are promising for the diagnosis of bradykinin-mediated angioedema attacks, especially in abdominal forms.

Andrea Zanichelli, Università degli Studi di Milano, Italy: 50 % of patients with HAE type I/II have previously been misdiagnosed, most commonly with allergic angioedema or appendicitis.

Stefania Loffredo, University of Naples Federico II, Italy: Increased levels of angiogenic and lymphangiogenic factor might reflect a susceptibility of endothelium to vascular permeability and vasoditating mediators.

Erika Kajdácsi, Semmelweis University, Hungary: Vascular regulation during HAE attacks is affected by vasoactive peptides. Our results suggest that the cooperation of several vasoactive peptides may be necessary to counterbalance the actions of excess bradykinin and to terminate the attacks.

Ibolya Czaller, Semmelweis University, Hungary: It is reasonable to expect that the cessation of smoking may result in the mitigation of the symptoms of HAE.

Anete S. Grumach, Faculty of Medicine ABC, Brazil: Each pregnancy and postpartum period had diverse characterization in comparison to pre-pregnancy period. Abdominal symptoms and articular pain was more accentuated during pregnancy and postpartum periods. Abortions were more frequent in comparison to non carriers of HAE.

Ana Alvez Liste, Hospital La Paz, Spain: The frequency of angioedema attacks increased during pregnancy. Plasma derived C1-INH concentrate was effective and safe for the treatment of HAE during pregnancy.

Grzegorz Porebski, Jagiellonian University Medical College, Poland: Both recombinant and plasma derived C1-INH are safe in pregnancy. No impact on the frequency of attacks was observed after switching from recombinant C1-INH to plasma derived C1-INH.

Ferah Genel, Dr. Behcet Uz Children's Hospital, Turkey: HAE must be considered in differential diagnosis of cases in which a partial response in obtaining from Familial Mediterranean Fever (FMF) treatment, particularly in countries where FMF is frequently encountered, because early diagnosis of HAE can facilitate prevention of life-threatening complications, such a upper airway obstruction.

Teresa Caballero, Hospital La Paz, Spain: These analyses support the effectiveness of icatibant for the treatment of laryngeal attacks. Most laryngeal HAE type I/II attacks were successfully treated with a single icatibant injection.

Nóra Veszeli, Semmelweis University, Hungary: Home treatment with recombinant C1-INH is an effective and well-tolerated therapy for al types of HAE attacks. Early treatment of attacks result in better outcomes.

Kinga Viktória Kóhalmi, Semmelweis University, Hungary: Treatment with the lowest effective doses of danazol is not associated with any abnormality with a significant effect on growth in childhood.

Karin Andritschke, HZRM Hemophilia Center Rhine Main, Germany: With the new volume-reduced plasma derived C1-INH concentrate formulation, not only the number of infusions is minimized but also time to treatment of acute, potentially life-threatening HAE attacks can be reduced. This is due to reduced complexity of having to reconstitute several vials and reduced intravenous infusion times because of a much lower infusion volume.

Karen Lindsay, Auckland City Hospital, New Zealand: Data from patients with HAE will provide invaluable information for future service planning.

Following the very successful HAE conferences in Copenhagen, Denmark in 2012 and Washington D.C., USA in 2014, HAEi will be holding the third HAE Global Conference in Madrid, Spain in May 2016.

Attendees can expect a wide variety of important information and learning opportunities that include HAE fundamentals, the most recent clinical advances and consensus treatment recommendations, and advocacy strategies/techniques for gaining or broadening access to HAE medicines. There will be a separate track for young patients that will enable peer group interaction and sharing of insights on how to cope with HAE. Health care professionals will also be an integral part of the conference. Additionally, HAE physician/researchers from throughout the globe will gather to present abstracts and discuss future research opportunities. The 2016 HAE Global Conference will also feature a nurses educational and experience exchange track to further energize the cooperation with HAE nurses around the world.

HAEi expects the conference to be attended by 550-600 delegates - including patients, care givers, nurses, physician/researchers, other healthcare professionals, and industry representatives - from all over the world.

The dates for the HAE Global Conference in Madrid are 19-22 May 2016.

HAEi Executive Director Henrik Balle Boysen expects to be able to go into more details about the HAE Global Conference 2016 in the fall of 2015.

Ask the doctors

The US HAE Association recently implemented a new process for answering patient's 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.

Here is one of the questions - and an extract of the answer from the expert physicians, Dr. Sandra Christiansen, Dr. Marc Riedl, and Dr. Bruce Zuraw.

Question:
Are African Americans less likely to have HAE? Is race a factor?

Answer:
Dr C: As best we know, all ethnic groups are affected by HAE type 1&II. The C1 inhibitor gene appears to be particularly vulnerable to a variety of mutations; however the specific mutation does not seem to affect the severity of disease. I do not believe that we have a complete understanding however regarding interaction of race with disease expression.

Dr R: HAE affects people of many ethnicities including those of African, Asian, European, and Native American descent and we see patients from all of these backgrounds in our clinical practice. Much of the epidemiologic, genetic, and scientific data we currently have is from European populations because large HAE research centers have existed there for many years. We only have accurate prevalence estimates from a few countries in the world - so far these haven't shown any dramatic differences in prevalence rates of HAE between various ethnic groups. We also know that unique C1INH gene mutations have been found in many parts of the world suggesting that ethnic background is not a major predictor of who is affected by C1INH deficiency. But at the moment I don't think we have enough data to give a solid answer to this question.

Dr C: Yes, we are still gathering data from around the world on HAE I&II and are just beginning to scratch the surface on HAE with normal C1 inhibitor. There was a report in Chinese subjects that the disease had a later onset (age 21) and lower incidence of abdominal attacks than prior European series.

Dr Z: I've been fascinated by the very low reported incidence of HAE in the Japanese population. Looking more carefully at the data, it appears that the Japanese patients diagnosed with HAE are recognized at a older age than typical in the West. This suggests that the real issue may be a problem in recognizing the disease and making the proper diagnosis. Indeed, recent efforts by a group of Japanese physicians working with a Japanese patient group has begun to identify many more HAE patients in Japan than was previously suspected. So, I would agree that we have little evidence of either a predilection for or a protection against HAE among different populations.

Trials recruiting patients

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 are recruiting at the moment:

- ***First-in-Human Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of BCX7353 in Healthy Volunteers.*** Recruiting in United Kingdom. https://clinicaltrials.gov/ct2/show/study/NCT02448264

- ***Pathogenesis of Physical Induced Urticarial Syndromes.*** Recruiting in USA. https://clinicaltrials.gov/ct2/show/NCT00887939

- ***Safety of Ruconest in 2-13 Year Old HAE Patients.*** Recruiting in Germany, Israel, Italy, Macedonia, Poland, and Romania. https://clinicaltrials.gov/ct2/show/NCT01359969

- ***Firazyr® Patient Registry Protocol (Icatibant Outcome Survey - IOS).*** Recruiting in Austria, Brazil, Denmark, France, Germany, Greece, Ireland, Israel, Italy, Spain, Sweden, and United Kingdom. https://clinicaltrials.gov/ct2/show/NCT01034969

- ***Screening Protocol for Genetic Diseases of Mast Cell Homeostasis and Activation.*** Recruiting in United States. https://clinicaltrials.gov/ct2/show/NCT00852943

- ***12-Week Safety and Efficacy Study of BCX4161 as an Oral Prophylaxis Against HAE Attacks OPuS-2.*** Recruiting in Belgium, Canada, France, Germany, Hungary, Italy, United Kingdom, and USA. http://clinicaltrials.gov/show/NCT02303626

- ***Safety and Efficacy Study of CINRYZE for Prevention of Angioedema Attacks in Children Ages 6-11 with HAE.*** Recruiting in Argentina, Germany, Italy, Mexico, Romania, United Kingdom, and USA. http://clinicaltrials.gov/show/NCT02052141

- ***A European Post-Authorisation Observational Study Of Patients With HAE.*** Recruiting in France, Germany, Spain, and United Kingdom. http://clinicaltrials.gov/show/NCT01541423

- ***C1 Inhibitor Registry in the Treatment of HAE Attacks.*** Recruiting in the Netherlands. http://clinicaltrials.gov/show/NCT01397864

- ***A Pharmacokinetic, Tolerability and Safety Study of Icatibant in Children and Adolescents With HAE.*** Recruiting in Argentina, Australia, Austria, Canada, Colombia, Germany, Hungary, Israel, Italy, Spain, and USA. http://clinicaltrials.gov/show/NCT01386658

- ***Study to Assess the Tolerability and Safety of Ecallantide in Children and Adolescents With HAE.*** Recruiting in USA. http://clinicaltrials.gov/show/NCT01832896

- ***Double-Blind, Multiple Ascending Dose Study to Assess Safety, Tolerability and Pharmacokinetics of DX-2930 in HAE Subjects.*** Recruiting in Italy, Jordan, and USA. http://clinicaltrials.gov/show/NCT02093923

- ***A Study to Evaluate the Long-term Clinical Safety and Efficacy of Subcutaneously Administered C1-esterase Inhibitor in the Prevention of HAE.*** Recruiting in USA. https://clinicaltrials.gov/ct2/show/NCT02316353

- ***A Phase 2 HAE Prophylaxis Study With Recombinant Human C1 Inhibitor.*** Recruiting in the Netherlands. https://clinicaltrials.gov/ct2/show/NCT02247739

- ***An Open-Label Study of Icatibant in Japanese Subjects with Acute Attacks of HAE.*** Recruiting in the Japan. http://www.shiretrials.com/sitecore/content/studies/clinicaltrialsen/2015/05/14/06/44/shp-fir-301?sc_lang=en

This trial is not yet recruiting but is expected to be so later on in 2015:

- ***HAE, Neurobiology and Psychopathology.*** Will be recruiting in Italy. https://clinicaltrials.gov/ct2/show/NCT02159430

HAE NEWS FROM AROUND THE GLOBE

Australia and New Zealand (www.haeaustralasia.org.au): ***Patient Meeting:*** The 4th Annual HAE Australasia Patient Meeting was held in Sydney on **hae day :-**) 2015. The 64 attendees were there to share stories, and to learn more about living with HAE.

Professor Connie Katelaris - Medical Advisor for HAE Australasia - presented an overview of HAE and the current treatments available now as well as the possibility of future therapies, including some new drug trials that may get underway shortly. As part of Professor Katelaris' work and research, she conducts studies of patient groups that assess quality of life and improvements to quality of life that new treatments are able to make. Such studies are very important to prove the value of costly treatments for rare patient populations like ours. Patients were given the opportunity to contribute to the latest quality of life survey on the day.

Associate Professor Rohan Ameratunga discussed the genetic side of HAE, including the use of genetic testing to confirm an HAE diagnosis as well as the possibility of utilizing pre-implantation testing to identify affected embryos prior to conception. He also described HAE as a metabolic disorder of the liver and how in the future advances such as liver gene therapy and gene editing could be possible treatments for HAE.

Jarrod Willers shared his experience of living with HAE from both his own perspective as a patient and as a father of two teenage daughters with HAE. Like many other patients he experienced years of symptoms before finally receiving a diagnosis. Jarrod Willers also spoke about the challenges for his two young daughters who also have frequent painful attacks. A reminder of the struggles that can come from living with a rare and painful illness. On a brighter note, Jarrod Willers has found the introduction of Firazyr in Australia has been life changing and has greatly improved his quality of living.

Dr Christopher Basten - a Clinical Psychologist - discussed common issues facing patients with conditions like HAE, the feelings you may have and how to deal with these and other people who may be affected by your HAE. He challenged that patients who were able to accept and adapt to their condition were more focused on what was still good in their life and the things that they could still do despite their condition. He acknowledged that it is completely understandable to sometimes feel isolated, lonely and frustrated as a rare disease patient. Dr Basten believes we as patients can benefit from a willingness to modify our lives and to remember and accept that we still have many assets and strengths to draw on. Feelings of resentment, sadness and 'why me' are inevitable for most patients. Acknowledging these feelings and accepting them is emotionally healthy and understanding your condition is only one part of the whole you, can help. Finally, Dr Basten suggested taking responsibility for your treatment and being assertive and knowledgeable when dealing with healthcare professionals, employers, colleagues and educators as being helpful. When discussing your condition with others, he suggests setting your own tone for the conversation, coming prepared with key messages and information and referring them to additional resources such as the HAE Australasia website for more information.

HAEi's President Anthony J. Castaldo and Executive Director Henrik Balle Boysen focused on the background and history of HAEi and some of the new initiatives, including HAEi Global Access Program and the 2016 HAE Global Conference. They also presented '10 things every patient and care giver should know about HAE', reminded people to keep quality of life of the patients and their families in focus and to continue to further enhance access to the modern life saving therapies for HAE patients. A 'Patient's Bill of Rights' as well as the benefits of self administration were also discussed during their presentation.

All the participants spoke highly of the chance to meet with others that share their story. In many cases it is the first time a HAE sufferer has met someone else with the condition. It is of great benefit to bring your family to meet the family at Patient Meetings. Next year HAE Australasia will be hosting a meeting in Perth, and also one in Auckland for our New Zealand members.

See more Australia and New Zealand on the next page.

Australia and New Zealand (www.haeaustralasia.org.au) - **continued:**

Please contact your MP: Improved treatment options, better HAE management and an improved quality of life can all come about though the establishment of a Patient Registry and other projects. In order to make these things happen we need the support of our governments. Please help us, to help you by letting government hear your voice. Speak to your local MP. Australia and New Zealand are not even close to meeting World Allergy Organisation recommendations for management of HAE. Our governments won't like to hear this as they strive to have 'world best standards' of health care. So we ask you to please make a time to see your local MP and tell them we need a change. Email us at info@haeaustralasia.org.au - we have flyers and resources that you can take with you to help facilitate the discussion.

Young HAEro Award: Ryan Bogoyevitch is the winner of the Young HAEro award, nominated by his sister Jess as a supportive brother that helps and inspires her.

Chile (www.facebook.com/angioedema.hereditariochile):
For **hae day :-)** 2015 Lorena Merino and her 12 year old son Diego (who is a HAE patient) publicized two videos on Facebook and they had a chance to go on television to tell about HAE.

The patient group in Chile is working on becoming a formal organization - and at the same time there are negotiations to join a national organization for rare diseases.

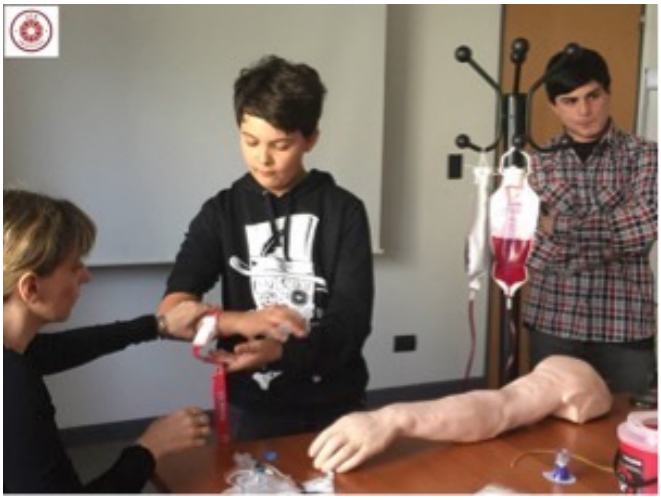
Also, together with other rare disease groups HAE Chile has participated in a meeting with the president of Chile, Mrs. Michelle Bachelet Jeria (in pink).

As Chile has no HAE specialists patients are treated by dermatologists, gastroenterologists, and general practitioners. HAE is still an unknown disease to physicians and only a very few emergency departments can help patients properly. However, this month two health care professionals will begin work on a survey on HAE.

CSL Behring is expected to soon start paperwork in order to get Berinert to the patients in Chile.

Argentina (www.aehargentina.org):
Social Media Campaign: During the three weeks leading to **hae day :-)** AEH Argentina organized a social media campaign through its different social platforms: Facebook page and Twitter account: www.facebook.com/AEHArgentina and www.twitter.com/AEHArgentina.

The campaign included specifically designed educational content so as to promote awareness of HAE. The campaign proved to be very successful: The stats for counted for over 8,200 people visiting the Facebook page on 16 May only from Argentina and almost 9,000 hits from 44 countries around the world. AEH Argentina sends a heartfelt thanks to the patient community for its amazing commitment and participation.



First Self-infusion Workshop for Children and Young Adults: Under the motto 'Patients need to be their own best advocate' AEH Argentina held its first self-infusion workshop for children and youngsters on 11 May 2015. With the help of a professional training-team from the Haemophilia Foundation, the young members were able to share a fun afternoon with their peers while learning to self-infuse.

The opportunity turned out to an incredibly enriching experience for everyone taking part. Nothing could have been more rewarding and motivating than providing the young members with one of the key tools that will help them gain freedom and have a much better quality of life. Congratulations to the amazing kids!

United Kingdom (www.haeuk.org):
Supporting patients: HAE UK is developing it's role supporting HAE patients in HAE clinics. The organization has visited clinics in Birmingham and in Liverpool's Alder Hey Children's Hospital and met up with HAE patients and their families. HAE UK also had a stand at the Immunology and Allergy Nurses Conference in May, and this provided helpful opportunities to meet with the specialist HAE nurses.

Raising awareness: To raise awareness of HAE one of the HAE UK members was featured in a television documentary (not yet aired), and hopefully another television documentary will be produced later this year.
Several of the HAE UK members did fundraising and awareness events to mark **hae day :-)** 2015, sharing stories via Facebook and Twitter, holding coffee events and dress down days at work. One 9 year old girl with severe HAE, with the help of her mother, organized a sponsored walk with a few of her close family and friends to raise awareness - and she raised an amazing 1,238.73 GBP for HAE UK. Read more about Ruby and her walk in this newsletter.

Patient day: HAE UK will be having the annual Patient Day in Birmingham on 7 November, focusing on 'HAE through all the stages of life'.

Hungary (www.haenet.hu):
Five percent of all Hungarian HAE patients (9 out of 158) attended the first self-injection training session. Six patients were accompanied by a supporter, who also learned the technique of self-infusion. After the first session more patients would like to learn this technique. Therefore, the Hungarian HAE association intends to organize more training sessions in the near future, and hopes that all patients will take advantage of this opportunity.

Germany (www.angiooedem.de):
On 12 June 2015 HAE Germany, Healthcare at Home and the HAE Team from Charité Berlin once again joined forces in setting up a Patient Day. Among the topics were the future of HAE and HAE patients, HAE in children, and HAE studies taking place at the moment.

USA (www.haea.org):
HAE app: The US HAEA is excited to announce that the myACT app (Access to Continued Therapy) is now available to help patients easily store information needed to successfully manage their HAE. The myACT app is ready now for the android base operating system. An iOS version of the app is currently in development - please see the US HAEA website for information regarding release date.

HAEA Scholarship Program: Sherry Porter from the HAEA Patient Services Team awarding HAE patient Kelsie Neahring with the HAEA Scholarship Program. The HAEA is dedicated to helping the American patient community achieve their lifelong goals and aspirations. The Scholarship Program will provide financial support for HAE patients seeking to improve their lives through academic achievement.

Large scale study: The US HAEA Angioedema Center is initiating a large-scale project to study HAE with normal C1 inhibitor. Further details about the project and how to participate will be forthcoming over the next several months.

2015 Patient Summit: The next US HAEA National Patient Summit will be held at the Denver Marriott Tech Center in Denver, Colorado on 9-11 October 2015. The summit is a great opportunity to meet new and old HAE friends at a fun and supportive gathering of patients and families, to learn about the latest in angioedema research and treatments, and to have HAE questions answered by expert HAE physicians/scientists. Also, the summit is a chance to speak to insurance and reimbursement specialists as well as to participate in research that will be published in medical journals.

Spain (www.angioedema-aedaf.org):
In addition to its 17th General Assembly and Annual Meeting held in Madrid on 17 April 2015, AEDAF has resumed its 'School for Patients', a series of regional workshops being held around the country that began in 2014. The 5th one took place in Talavera de la Reina (Toledo) on 3 June 2015, for patients and their families from the autonomous regions of Castilla-La Mancha and Extremadura, and the 6th in Oviedo (Asturias) for patients and families from Asturias and Cantabria. It plans to hold at least two more next autumn, one in the Canary Islands and another in northern Spain.
AEDAF was also represented in the 9th C1-Inhibitor Deficiency Workshop held in Budapest 28-31 May.

Of course AEDAF will be devoting a lot of time and effort in the year to come to helping with the organization of the 3rd HAE Global Conference to be held in May 2016 in Madrid and planning something exciting for **hae day :-)** a few days before the conference.

Japan (www.haej.org):
Patient meeting: HAE Japan held a meeting in Tokyo for **hae day :-**) 2015. There were 21 participants, including four new faces – three patients and one family member – who have now become the newest members. Dr Michihiro Hide gave a detailed talk on the changes to the law that controls reimbursement for rare disease patients, including HAE patients. As a result of the effective advocacy of Dr Hide and other doctors, C1 Deficiency is now entered separately as a condition for reimbursement under the PID listing. Previously, it had been incorporated within a larger category and easy for doctors to miss if they were not familiar with HAE. Mr Akio Masuzawa also gave an incredible talk on his experiences as an undiagnosed patient and then more recently the change in his life since diagnosis. Having experienced three laryngeal attacks that required a tracheotomy just before and soon after being diagnosed, his story was uncomfortable is many ways to hear. His important message was that no one can predict the severity of an attack until it is over, so all attacks should be treated.


HAEi Newsletter -Issue7 January 2015
HAE ジャパン日本語訳版

HAEi 理事長 Anthony J. Castaldo からのご挨拶

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親愛なる HAEi 関係者の皆様へ

近年医学会の機関誌にも HAE の治療や管理を提唱する多くの情報が HAE 専門医師や研究者により発行されております。これらの医学専門情報は症例を診る機会がない医師達にとっての貴重な情報源です。実際にそれらのガイドラインや症例報告がとても有効的であると HAE のアメリカ団体

全ての HAE 患者の権利
- HAE 専門の医師と連携して最適な治療を受けることができる
- HAE 治療プランの決定と日々の対処法管理はあくまでも患者の意思を尊重したものであること
- 治療は患者が日常生活を支障なく行う手助けを目的とする

Newsletters: During the meeting HAE Japan distributed the first edition of the a newsletter, which for the moment is only available in Japanese. HAE Japan also distributed a Japanese translation of key parts of the HAEi January 2015 newsletter - and will continue with this translation work for future newsletters. HAE Japan is grateful to Keiko Kishida for undertaking this translation work. Both newsletters will be uploaded to the website.

Prior to the meeting HAE Japan held it's first ever General Meeting as an NPO. The organization was one-year old in April and reflected during the meeting on all that has been achieved and what the members want to achieve in the future. To have a core group of patients, friends and family members of patients, and doctors all working together to further HAE advocacy in Japan is a huge achievement of itself. HAE Japan also offered a special thanks to those who have acted as supporting members from industry providing the organization with a working budget as well as a lot of expertise over the past year.

Meetings with ministry: HAE Japan had a '30 minute' hearing at the Ministry of Health, Labour and Welfare on 2 June 2015 to

discuss three items: the necessity of authorizing self-possession and self-administration of available HAE treatments under the health insurance system; the need to include HAE as a topic in the medical licensing exam for doctors and in professional development training for qualified doctors; and ways to increase access throughout Japan to effective treatments. Beverley Yamamoto attended the meeting as President of HAE Japan, along with Dr Hiroaki Azukizawa and Dr Michihiro Hide, as members of HAEJ Board (Dr Azukizawa) and the HAE Medical Advisory Board. Six officers from the Ministry representing three departments (Health Insurance, Medical Policy, Health) attended and the 30 minute scheduled meeting ended up lasting more than an hour. HAE Japan then spent another 30 minutes or so talking to one official after the meeting and no doubt made an impression. HAE Japan came away with some clear ideas of how to move the organization's agenda ahead on the three issues that were taken to the meeting. Dr Isao Ohsawa was unable to make the meeting, but his careful drafting of HAE Japan's second, evidenced-based, petition clearly was very important.

Patient study: In April Dr Ohsawa and Dr Daisuke Honda, along with other authors, published the results of an important study on HAE patients in Japan: 'Clinical manifestations, diagnosis, and treatment of hereditary angioedema: survey data from 94 physicians in Japan, Annals of Allergy, Asthma, and Immunology, 04/14/2015'. Data was collected from 171 patients via 94 treating physicians. This month, Drs Ohsawa and Honda have been presenting their findings at the European Academy of Allergy and Clinical Immunology conference in Barcelona. We are now looking to moving ahead with an HAEJ funded study of patient experiences.

Important study: The final piece of news is that in April Dr Ohsawa and Dr Daisuke Honda, along with other authors, published the results of an important study on HAE patients in Japan: 'Clinical manifestations, diagnosis, and treatment of hereditary angioedema: survey data from 94 physicians in Japan, Annals of Allergy, Asthma, and Immunology, 04/14/2015'. Data was collected from 171 patients via 94 treating physicians. In June Drs Ohsawa and Honda presented their findings at the European Academy of Allergy and Clinical Immunology conference in Barcelona, Spain. HAE Japan is now looking to moving ahead with a study of patient experiences funded by the organization.

Canada (www.haecanada.org):
Patient Event: HAE Canada will be holding the next patient event in Calgary 17 October 2015. The guest speaker is Dr. Tom Bowen MD, FRCPC (Calgary). For more information or to RSVP, please contact John Sloat at jsloat@haecanada.org.

Reduced volume vial format: Berinert is now available in a new 1500 IU "reduced volume" vial format, reconstituted with 3 ml of Sterile Water for Injection (Diluent). In Canada, Berinert is indicated for the treatment of acute abdominal, facial, or laryngeal attacks of HAE of moderate to severe intensity.

"It is part of our commitment to the HAE community to continuously bring innovative improvements and provide more treatment options to patients in Canada" said Philippe Hebert, General Manager of CSL Behring Canada.

The existing vial size and formulation (Berinert 500 IU reconstituted with 10 ml Sterile Water for Injection) will continue to be available.

Denmark, Norway and Sweden (www.haescan.org):
Patient conference: The first Scandinavian HAE conference will take place on 6-8 November 2015. The venue will be in Nyborg, Denmark.

New website: HAE Scandinavia is working on an improved website, hopefully ready for launch within a few months.

Brazil (www.abranghe.org.br):
1st LATAM Forum: The First HAE Forum LATAM was held in São Paulo, Brazil 23-24 June 2015.
The objective of the meeting was to foster deeper integration of the LATAM experts on HAE and discuss a number of HAE related issues. With participation of around 50 physicians from all over Latin America - many of them clinicians and/or researches with at least an average knowledge and experience in HAE - it was two days of much education and update.

Renata Martins from Abranghe (HAE Brazil) and Alejandra Menendez from HAE Argentina spoke on living with HAE. Among the other speakers and topics were Dr Cicardi ('Suspicion and Accurate Diagnosing of HAE'), Dr Rozenfeld ('HAE Diagnostic Testing – Experience in setting up an specialized Lab'), Dr Grimace ('How to shorten time to diagnosis – Our Challenges & Opportunities'), Dr. Bailleau ('Overview of Clinical Management'), and Dr Bianchi ('HAE Treatment: Review of International Guidelines').

President Raquel de Oliveira Martins (HAE Brazil), President Alejandra Menendez (HAE Argentina) and Renata Martins (HAE Brazil)

In the words of Renata Martins: 'It was a pleasure to share information and learn more about others Latin American countries.'

1st HAE workshop: The 1st Brazilian HAE workshop promoted by GEBRAEH - a group of HAE doctors in Brazil - took place 2 July 2015 in São Paulo, Brazil. Among the topics and speakers were 'Diagnosis and Therapy of HAE: A look into the future' (Dr Zuraw), 'Disease Activity and Quality of Life in Angioedema Patients' (Dr Magerl), 'Pathogenesis of angioedema made simple' (Dr Kaplan), 'HAE in Brazil and Latin America' (Dr Grumach), and 'Classification of HAE in Brazil' (Dr. Giavina-Bianchi). Also, President Raquel de Oliveira Martins of the Brazilian HAE organization gave an insight from the patients' point of view.

Kenya (https://www.facebook.com/100009028142543):
Patricia Karani, the National Patient Representative in Kenya, writes that the postings about Kenya in this newsletter has made the first person contact her inquiring about HAE in the country. Ms. Karani writes:

"Kenya is really an uphill task from physicians who are not as knowledgeable about the disease to the fact that there are no

prophylaxis or anaphylaxis medicines in this country. I have searched for some form of medication for the past six months and I discovered Danazol 200mg in only one pharmacist in Nairobi. Danazol is rare and it has run out of stock in the country. In Kenya we have to beg doctors to listen and show interest. It is really very difficult. It is my prayer that a teleconference with the participation of a doctor from Aga Khan Hospital in Nairobi, representatives of HAEi and US HAEA and myself will be the first great step to help our medical fraternity take up some form of interest for this condition and the beginning towards finding other patients in Nairobi and Kenya."

Russia (www.fondpodsolnuh.ru):
The National Patient Group in Russia had a great **hae day :-**) 2015 in Moscow, holding the first Russian meeting of patients and doctors. Even though patients are facing many difficulties, on 16 May 2015 they took a very important step showing that they are together and ready to actively defend their interests.

Venezuela (Angioedema-Hereditario-De-Venezuela/1475867039316898):
Ruconest is on its way to the patients in the South American country: In May Pharming Group NV entered into an exclusive distribution agreement with Cytobioteck S.A.S., a privately owned Bogota, Colombia based specialty healthcare company, for the distribution of Ruconest for the treatment of acute attacks of HAE in Colombia and Venezuela. Soon after the drug was tested on an intensive care patient with very positive results - and most recently CEO Osvaldo Piñeros from Cytobioteck, Regulatory Affairs Manager Carlos Zorrilla from Netmedical and Ms. Mary Bocaranda from HAE Venezuela met in order to discuss a work plan for the acquisition of drugs nationwide in Venezuela through the Social Security Institute.

Poland (www.hae.org.pl):
Reimbursement of Firazyr: Michal Rutkowski, the president of HAE Poland, writes:

"We have been waiting for over six years but now the Ministry of Health has approved submission for another HAE product. From 1 July 2015 Polish HAE patients will have full access and reimbursement of Ikatibant (Firazyr) - subcutaneous injection medication from Shire! What a significant live quality improvement we will have! Now that we have gotten to the goal, what is next? Cynrize?!"

National patient meeting: HAE Poland will be holding its next national patient meeting in Warsaw 3-4 October 2015.

Romania (www.haenet.ro):
Dr. Dumitru Moldovan from the Romanian Network for HAE writes about the recent achievements in the emergency management of HAE attacks in Romania:

"In the past eight years a pilot centre was built up and patients confirmed with C1-INH were included in a national register of HAE. An HAE patients association was founded two years ago. In the past two years a sustained effort was made to put together experts on HAE, patients' representatives, emergency department leaders and authorities in Romania to start the first program of emergency care of HAE attacks. Interviews with states secretaries responsible for the emergency medical care from Ministry of Health and Ministry of Internal Affairs were planned.

As of March 2015, the Registry of HAE patients includes 91 patients from 31 families. In the past year, these patients have recorded 920 peripheral, 770 abdominal, 170 facial, and 80 upper respiratory attacks.

Since summer 2013 a gradual positive attitude of the Ministry of Health was noted regarding the reimbursements of new drugs approved for treatment of HAE attacks. Data from the Romanian Registry of HAE patients were provided and direct costs of treatment of facial, upper respiratory and abdominal attacks were evaluated. Elaboration of a protocol for treatment of HAE attacks is ongoing. A 24/7 telephone HAE expert consultancy is offered.

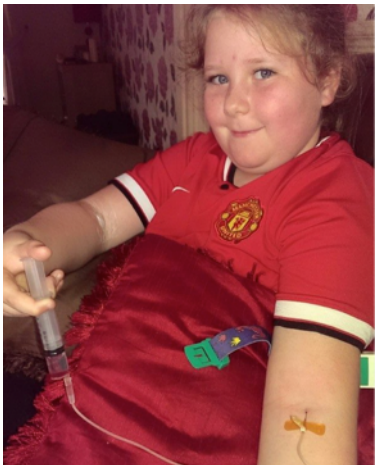
Ruconest meets legal requirements for reimbursement - acquisition has been started and the first vials were administered.

The recent developments on the cooperation between patients' organization, HAE experts, emergency departments and authorities enable us to hope a new era is coming to HAE patients in Romania."

Ruby's sponsored walk

To celebrate **hae day :-**) 2015, Ruby - a nine year old HAE patient living in the United Kingdom - wanted to do something to help raise awareness of HAE. And her family also thought it would be a good idea to raise some funds for HAE UK at the same time. Her mother, Faye Hesford, writes:

A sponsored walk seemed like a great idea. Ruby, her dad and I spent the run up to **hae day :-**) bombarding Facebook with simple facts about HAE. I also posted photographs of Ruby whilst she was experiencing HAE swells. Most of the photographs were taken as evidence for doctors and not intended for posting on a social networking site. I think that the visual shock of seeing Ruby looking so sick in contrast to her usual happy self was enough to generate great interest. I received numerous private inbox messages and mobile text messages from people offering support and making comments like 'I knew that Ruby had an illness but I had no idea how poorly it made her - no-one would ever guess if they saw her happy face'. I received one message from an old school friend who is now a paramedic. She read all the information I gave about HAE and then did some investigations of her own and she made sure that all her colleagues were aware of HAE. I also have many other friends who work in hospitals and many who work in schools who all shown great interest and shared HAE posts to help raise awareness and funds. The donations on the 'Just Giving' page came flooding in. Although the project was titled 'Ruby's Walk for HAE', we had lots of help from friends, family and HAE UK. Dozens of people walked with us making it a thoroughly enjoyable day. Ruby's classmate, Sienna, also has HAE and she, along with her mum and one of her sisters also walked with us, as did a wonderful young family from Bolton who read about the event on Facebook. We generated lots of interest en route and collected over 170 GBP whilst walking. We set a target of 200 GBP but that was smashed within the first few days. The total of the donations currently stands at over 1,281.73 GBP - which is a massive 640% of the target initially set. The total continues to rise and we have promises of several more donations. We have received an on-line certificate from 'Just Giving' as out of 65,838 fundraisers in the UK, Ruby was in the top 3% of fundraisers in the UK during May.



Regarding Ruby's life with HAE her mother writes:

Like many HAE patients with no known family history, Ruby suffered tremendously before her diagnosis, with swells and stomach problems from being a toddler. By the time she was five, she was spending more and more time off school due to sickness and the visits to GP and hospital began. Luckily for Ruby, we had heard of HAE as, ironically, her classmate suffers from the disease. Ruby's symptoms and those of her friend's were very similar and this was how we finally got the correct diagnosis, not too long after Ruby's 6th birthday. Ruby is very severely affected by HAE, experiencing swells every few days without treatment. Due to the frequency and severity of Ruby's swells, her consultant decided that she would benefit from home therapy, just two months after her diagnosis. I was trained how to infuse her with 500u Berinert twice per week. This initially worked, however, after a year she started to have more breakthrough swells so the dosage was doubled. This worked for a while but recently Ruby had to have the dose increased to 1000u three times per week. Ruby's diagnosis has also led to my own diagnosis of the illness in November 2014, aged 45. I too had many 'mystery' illnesses during my childhood.

Ruby has a fantastic outlook on life. Although she is shy by nature, she is happy, loving, very caring and loves to win! She is a football fanatic and an avid Manchester United fan. Despite mine and her dad's concerns, Ruby was adamant that HAE would not stop her from participating in sport. She has recently won a certificate for swimming and has received numerous awards for football - most recently from Stockport County FC who have sent her a complimentary family ticket for receiving player of the season award during after school football coaching. Excitement is Ruby's main trigger for HAE attacks, so we have to try and time her infusions to coincide with football matches, swimming day and any other events she is excited about such as birthday parties, sleepovers, trips out. Ruby also insisted on attending all of her school's educational visits off site. The school was very concerned as to what they would do if Ruby had an HAE swell during an outside visit. To eliminate as much risk as possible and to ensure Ruby can attend all trips, I go with them and take Berinert with me. Ruby is excelling at school and has surpassed all targets set, apart from attendance. Unfortunately, due to HAE her attendance falls below the national average. Ruby does try to do everything that every other nine year old child would do and when HAE knocks her down, she gets straight back up and gets on with living and enjoying life. Last week I was contacted by school who told me that her face was swelling at an alarming rate. They asked me to collect her immediately. I was able to do so and infuse her within 40 minutes of the phone call. Ruby insisted on going straight back to school as soon as the swelling started to subside.

Ruby is eager to learn how to administer her own C1. She already knows how to prepare the mix and has inserted the butterfly needle in my arm on several occasions. Although Ruby is very young, I feel that the knowledge alone that she could perform her own infusions would give her so much more freedom and peace of mind.

Global Advocacy Work

Recent activities

This is a brief overview of some of HAEi's activities in the recent months:

15-17 May HAEi took part in the national HAE Australasia meeting in ***Sydney, Australia.*** It was a very well organized meeting by our friends down under. There still are mountains of work to do in Australia and New Zealand to secure newer and safer therapies for all patients suffering from HAE.

At the end of May HAEi was represented at the 9th C1-inhibitor workshop in ***Budapest, Hungary.*** This is the longest running (the inaugural meeting took place in 1999) and most important scientific meeting solely dedicated to HAE.

7-10 June HAEi was in ***Barcelona, Spain*** participating in this years EAACI conference. The event was a great opportunity to catch up both with healthcare professionals and industry.

25-26 June HAEi took part in a Pharming Advisory Board meeting in ***Berlin, Germany.***

2-3 July HAEi met with Clinigen Group in ***London, United Kingdom*** to get an overview of the Global Access Program and status for final launch.

Future activities

16-17 September HAEi will participate in and host a round-table discussion on patients' access to medication at the Orphan Drug Summit 2016 in ***Copenhagen, Denmark.***

2-4 October HAEi will participate in the annual patient meeting of our Polish member organization. This year the meeting will take place in ***Warsaw, Poland.***

9-11 October HAEi will participate in the US HAEA National Patient Summit 2015 in ***Denver, Colorado, USA***. This summit is expected to attract 6-700 delegates.

20-21 October HAEi is planning on participating in the WHINN (Weak of Health and Innovation) which will take place in ***Odense, Denmark.*** The goal is to gather more information about possibilities in healthcare technology and how HAEi can better utilize technology on a global basis.

28-29 October HAEi is planning on participating in the EURORDIS Council of European Federations meeting in ***Paris, France***.

The HAEi Executive Committee will meet in ***Frankfurt, Germany*** 30 October-1 November.

6 – 8 November HAEi will participate in and speak at the first HAE Scandinavian conference taking place in ***Nyborg, Denmark.***

News from the Industry

7 May 2015

ProMetic Life Sciences Inc. has selected C1-INH as its next plasma-derived drug candidate to be developed. The C1-INH protein is most commonly used for the treatment of HAE. The world market for HAE reached 1.1billion USD in 2014 and has been growing at an average rate of 44% in the last three years, and analysts expect the market to exceed 3 billion USD by 2020.

ProMetic has successfully completed the bioprocess to isolate and purify C1-INH, and has scheduled scale-up and GMP production to occur during the second half of 2015. ProMetic anticipates commencement of C1-INH clinical trial work in H1 2016. C1-INH adds to a pipeline of previously disclosed proteins already scheduled for clinical development, namely: plasminogen, IVIG and alpha-1 antitrypsin.

"As anticipated, our manufacturing platform is demonstrating its ability to produce multiple high-value biopharmaceuticals simultaneously and at yield and purity levels superior to those commercially available", declared Mr. Pierre Laurin, President and Chief Executive Officer of ProMetic. "We will be announcing other proteins in the coming months. Some of these will be developed and marketed with commercial partners and are already, as in the case of C1-INH, in partnering discussions", added Mr. Laurin.

(Source: ProMetic)

13 May 2015

BioCryst Pharmaceuticals, Inc. has announced the initiation of a Phase 1 clinical trial to evaluate the safety, pharmacokinetics and pharmacodynamics of orally administered BCX7353 in healthy volunteers. Discovered by BioCryst, BCX7353 is a novel, selective inhibitor of plasma kallikrein in development for prevention of attacks in patients with HAE. BioCryst has successfully completed nonclinical safety studies, as well as in vitro studies in which BCX7353 exhibited potent and selective inhibition of plasma kallikrein. The pharmacokinetic profile of BCX7353 in preclinical studies indicates its potential for once daily dosing.

"We are pleased to advance BCX7353 into the clinic and look forward to reporting results from this trial during the third quarter 2015. The successful development of a once daily, orally administered prophylactic drug that is safe and efficacious would be a game changer and a convenient treatment alternative for patients suffering from HAE," said Jon P. Stonehouse, President & CEO of BioCryst.

The main goals of the Phase 1 clinical trial are to assess safety, characterize plasma drug levels in healthy volunteers, and estimate the extent of kallikrein inhibition achieved after oral dosing of BCX7353.

(Source: BioCryst)

14 May 2015

Dyax Corp. has appointed Abbie Celniker, Ph.D., to its Board of Directors.

"Abbie brings nearly three decades of business and scientific leadership in the biotechnology and pharmaceutical industries to Dyax, with a proven track record of successfully developing and commercializing life science products," said Henry E. Blair, Chairman of Dyax's Board of Directors. "Her expertise in advancing late-stage protein therapeutic discovery and development programs will provide the Board with a new and valued perspective as we develop DX-2930 and build our internal pipeline. We are delighted to welcome her to Dyax's Board."

Dr. Celniker currently serves as the President and CEO of Eleven Biotherapeutics, where she also serves on its Board of Directors. She holds a B.A. in Biology from the University of California, San Diego, and a Ph.D. in Molecular Biology from the University of Arizona.

(Source: Dyax Corp.)

News from the Industry

15 May 2015

Shire has launched a new educational website as part of its HAE awareness campaign "Me, Not HAE". The interactive site supports the HAE community by enabling the sharing of stories of inspiration and helping raise awareness of the realities of living with HAE. The "Me, Not HAE" campaign, which was initially launched on **hae day :-)** in 2014, focuses on finding innovative ways to share personal stories from people living with HAE to help inspire the community at large while also driving education and awareness of this rare condition.

In conjunction with the campaign and to recognize **hae day :-)** 2015, Shire is inviting all site visitors to share a wish or message of inspiration with the HAE community from 16 to 30 May. Each wish submitted online will add a leaf to a virtual HAE Wish Tree, building a picture of hope for those living with this condition. Wishes can be made at: www.MeNotHAE.com.

"Shire is dedicated to raising awareness of HAE and recognizes the importance of sharing inspirational messages and stories as a way to encourage and show our support for those living with this challenging condition," said Emmanuel Dulac, Head of the Rare Disease Business Unit at Shire. "We are very pleased to launch this new site in support of this rare disease community on the occasion of **hae day :-)** 2015."

"People living with HAE often feel isolated, so sharing personal stories and messages of hope will help unite the community and strengthen its collective voice," said Anthony Castaldo, president of HAEi. "This new site not only offers visitors the chance to learn more about HAE, but to also contribute messages of hope for the community in support of **hae day :-)** 2015."

"We are proud to help unite the global HAE community and to foster increased awareness of the condition on hae day," said Henrik Balle Boysen, executive director of the HAEi. "It is our hope that **hae day :-)** along with supportive initiatives including this new educational website will ultimately help lead to more accurate diagnoses."

(Source: Shire)

15 May 2015

Dyax Corp. and the HAEA have launched the HAE Hope Essay Contest. By drawing from the inspiring stories of individuals with HAE nationwide, the program seeks to underscore the value of hope for those living with this potentially life-threatening condition.

HAEHope.com is asking eligible HAE patients across the country to submit essays that will focus on one of two themes: 1) What I would tell my 12 year old self about living with HAE, or 2) I have HAE, HAE does not have me.

A multi-disciplinary panel consisting of physicians, nurses, patients and advocacy representatives will evaluate each submission. The two winning essay entrants are eligible to receive a cash award and will be recognized at the HAEA Patient Summit taking place October 9-11, 2015 in Denver, Colorado. A matching donation will be given to the HAEA Scholarship Fund in the winners' names. Program submissions will be used to inform the development of support services and educational materials for HAE patients nationwide.

"People with HAE are very generous with one another, especially in their willingness to provide support," said Gustav Christensen, President and CEO of Dyax. "This contest offers a new forum for that support through creativity, self-expression and first-hand insights about living with HAE. At Dyax, we work closely with HAE patients to understand how this condition affects their lives and how we can help meet their unique needs. Every day we hear their stories of hope, courage and survival. Through this essay program, we seek to honor those experiences and share the inspiration that drives us towards a future where HAE no longer limits peoples' lives."

"For over 15 years the HAEA has helped patients and their families overcome challenges associated with HAE and strengthen the HAE community," said Anthony Castaldo, President of the U.S. HAEA. "Each person involved in this contest will be helping to inspire others through their personal stories and raise awareness about this rare and potentially life-threatening disease."

In the spirit of **hae day :-)** 2015, HAEHope.com seeks to raise awareness of this little known condition and honor those individuals living with HAE.

HAE Hope Essay Contest details can be found on www.HAEHope.com, a support website sponsored by Dyax.

(Source: Dyax Corp.)

News from the Industry

18 May 2015

Pharming Group N.V. and ***Clinigen Group plc*** have entered into an international global access collaboration for HAEi. The "HAEi GAP" program will provide access to RUCONEST® (conestat alfa) to eligible patients with HAE, who currently do not have access to effective medication to treat acute attacks of the disease.

HAEi GAP is the first global access program for HAE and the first to be driven by a patient organization. The program enables patients in countries where RUCONEST is not commercially available to gain access to the drug through an ethical and regulatory compliant "Named Patient Program" mechanism.

"HAEi is committed to securing access to HAE medications for patients across the globe," said Anthony J. Castaldo, President of HAEi. "We are extremely proud to have established HAEi GAP with our current partners and will continue to work with other manufacturers with the hope of expanding the program in the future."

Sijmen de Vries, CEO, Pharming said: "We are delighted to be the first partners of HAEi and to initiate this program by providing access to RUCONEST, a recombinant human C1-inhibitor, approved by EMA and FDA for the treatment of acute attacks of HAE. In this way we can help to improve the lives of those HAE patients that otherwise would continue suffering from this debilitating and unpredictable disease."

Simon Estcourt, Managing Director, Managed Access Programs, Clinigen said: "HAEi's ground-breaking program will ensure that HAE sufferers worldwide can gain access to effective and potentially life-saving treatment. Our secure supply chain and regulatory expertise will enable us to work closely with Pharming to supply patients with RUCONEST ethically and legitimately, removing the need and the risk for patients to resort to other less reliable or even illegal sources of the drug. We look forward to working with both HAEi and Pharming on this unique project."
(Source: Pharming Group)

25 May 2015

Pharming Group NV has entered into an exclusive distribution agreement with Cytobioteck S.A.S., a privately owned Bogota, Colombia based specialty healthcare company, for the distribution of RUCONEST® (recombinant human C1 inhibitor) for the treatment of acute attacks of HAE in Colombia and Venezuela.

Under the agreement, Cytobioteck will drive all regulatory processes and will purchase its commercial supplies of RUCONEST from Pharming at a fixed transfer price.

Sijmen de Vries, Pharming's CEO commented: "We are very pleased that Cytobioteck will be engaged in the distribution of RUCONEST in Colombia and Venezuela, two countries where a considerable number of patients with HAE have been diagnosed."

"This will be the key agreement to bring comfort and relief to patients with HAE in the region", Cytobioteck's CEO Osvaldo Piñeros commented. He also added "Our job is to deliver the best therapies available for our patients, and we will continue to do so with Pharming as a valuable and strategic ally."
(Source: Pharming Group)

8 June 2015

Clinical data from ***Dyax Corp.***'s DX-2930 Phase 1b study was selected as a late-breaking abstract and presented on June 7, 2015 at the European Academy of Allergy and Clinical Immunology (EAACI) Annual Congress in Barcelona, Spain. Discovered by Dyax, DX-2930 is an investigational fully human monoclonal antibody inhibitor of plasma kallikrein being developed for the prevention of HAE attacks.

The late-breaking, oral presentation, titled "Interim Analysis Results of a Phase 1b, Multiple Ascending Dose Study to Evaluate DX-2930, a Fully Human Monoclonal Antibody Inhibitor of Plasma Kallikrein in Development for Long-term Prophylaxis of Hereditary Angioedema," was given by Aleena Banerji, M.D., Assistant Professor of Medicine at Harvard Medical School and attending physician at Massachusetts General Hospital. The oral presentation highlighted results from Dyax's Phase 1b clinical study assessing the safety, tolerability and pharmacokinetics of DX-2930 in HAE patients.

News from the Industry

"The clinical research findings presented at the EAACI Annual Congress continue to expand our understanding of the safety, pharmacokinetics and pharmacodynamics of DX-2930 in patients with HAE," said Dr. Banerji. "Results from this study also provided proof-of-concept efficacy data patients with HAE," said Dr. Banerji. "Results from this study also provided proof-of-concept efficacy data demonstrating statistically significant reductions in attack rate compared to placebo. These results support further clinical investigation of DX-2930 in HAE patients to potentially prevent HAE attacks."

"We are pleased to have our Phase 1b DX-2930 data selected for oral presentation at the EAACI," said Burt Adelman, M.D., Executive Vice President of Research and Development and Chief Medical Officer at Dyax. "These data are significant because they indicate that DX-2930 may be a viable prophylactic treatment option for HAE. The 120-day follow-up period for the final dosing cohort was completed in May, and we look forward to reporting the full study results in the near future."

The Phase 1b study results demonstrated that DX-2930 was well tolerated at all dose levels. There were no deaths or subject discontinuations due to an adverse event. There were no serious adverse events in subjects treated with DX-2930 and no evidence of dose-limiting toxicity. There was no safety signal in treatment-emergent adverse events, clinical laboratory results, vital signs, or electrocardiograms. Subcutaneous injection was well tolerated. The Phase 1b study results demonstrated that DX-2930 was well tolerated at all dose levels. There were no deaths or subject discontinuations due to an adverse event. There were no serious adverse events in subjects treated with DX-2930 and no evidence of dose-limiting toxicity. There was no safety signal in treatment-emergent adverse events, clinical laboratory results, vital signs, or electrocardiograms. Subcutaneous injection was well tolerated. Pharmacokinetic results demonstrated that DX-2930 has linear, dose-dependent exposure and a mean elimination half-life of approximately 14 days. Pharmacodynamic results from two different exploratory biomarker assays confirmed ex vivo plasma kallikrein inhibition in a dose- and time-dependent manner. Primary proof-of-concept efficacy analyses were based on subjects in the 300 mg, 400 mg, and placebo dose groups who reported having at least 2 attacks in the 3 months prior to study entry.

During the pre-specified, primary efficacy interval of 6 weeks (from days 8 to 50; corresponding to peak drug level), the HAE attack rate (adjusted for baseline attacks) was 0 in the 300 mg group and 0.045 attacks per week in the 400 mg group, compared to 0.37 attacks per week in the placebo group. This resulted in a 100% reduction for the 300 mg dose group as compared to placebo ($P < 0.0001$), and an 88% reduction for the 400 mg dose group as compared to placebo ($P=0.005$). During this primary efficacy interval, 100% of subjects in the 300 mg group ($P=0.026$) and 82% of subjects in the 400 mg group ($P=0.030$) were attack-free compared with 27% of subjects in the placebo group.

The Phase 1b study was a multi-center, randomized, double-blind, placebo-controlled, multiple-ascending dose study. A total of 37 subjects were randomized to active drug or placebo in a 2:1 ratio across 4 dosing groups of 30, 100, 300, or 400 mg. Each subject received two doses of DX-2930 or placebo, separated by 14 days, and was followed for 15 weeks after the second dose.

DX-2930 is a novel, fully human monoclonal antibody inhibitor of plasma kallikrein (pKal) which is currently being developed as a subcutaneous injection for the prevention of HAE attacks. Uncontrolled pKal activity leads to excessive generation of bradykinin, a vasodilator thought to be responsible for the localized swelling, inflammation and pain characteristically associated with HAE.
(Source: Dyax)

11 June 2015
Shire plc has appointed Olivier Bohuon to the Board of Directors as a Non-Executive Director. Olivier will also be a member of the Science & Technology Committee of the Shire Board. Olivier has served as Chief Executive Officer of Smith & Nephew plc, a global medical technology company, since 2011. He has extensive international business and leadership experience across a number of pharmaceutical and healthcare companies in Europe, the Middle East and U.S. He also serves as a Non-Executive Director of Virbac Group SA.
(Source: Shire plc)

HAEi around the globe

HAEi is a global network organization dedicated to raising awareness of C1 inhibitor deficiencies around the world.

We serve as an umbrella organization for national HAE patient representations around the globe. Currently you will find national HAE organizations or other kinds of representation in these 46 countries:

- **Africa**: Kenya
- **Asia**: China, India, Japan, Malaysia, Russia, United Arab Emirates
- **Australia**: Australia, New Zealand
- **Europe**: Austria, Belarus, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Israel, Italy, Macedonia, Norway, Poland, Portugal, Romania, Slovenia, Spain, Sweden, Switzerland, The Netherlands, Ukraine, United Kingdom
- **North America**: Canada, Mexico, United States of America
- **South America:** Argentina, Brazil, Chile, Costa Rica, Equador, Peru, Uruguay, Venezuela

You will find much more information on the HAE representations around the globe at www.haei.org. For instance, under each of the countries there is contact data for the national organization/group, information on care centers, hospitals, physicians, trial centers, and pharmaceutical companies as well as a list of available medication in the specific country.

The information on www.haei.org is being updated as soon as we receive fresh data from the national organizations.

Your feedback is very welcome

Please let us know what you believe should be included in future newsletters. You can do that by providing feedback to Executive Director Henrik Balle Boysen or Communications Manager Steen Bjerre. In addition, we invite you to submit articles on any topics that you believe would be of interest to other readers. We look forward to your comments and working with you on future newsletters.

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

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HAEi

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