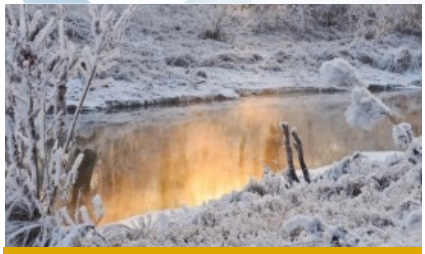
HAEi Newsletter



IN THIS NEWSLETTER

A Message from the President

Dear HAE Friends,

On behalf of the HAEi Executive Committee, I would like to wish everyone a very happy holiday season.

This is the time of the year when families joyfully gather in celebration and all of us begin looking ahead to a new year of promise and progress.

2015 will be another very busy year for HAEi as we continue focusing on a broad range of core activities that serve the global HAE community. We will continue our efforts to help establish patient groups in a growing list of countries and look forward with great excitement to helping member organizations set up creative activities to honor **hae day :-**) 2015.

In addition, throughout 2015, HAEi will focus on a variety of activities designed to raise awareness and accelerate the pace of global advocacy efforts aimed at achieving broader access to modern HAE therapies. These include:

--Establishing HAEi ***"Standards of Care"*** for the global HAE community.

--Preparing a ***"Global State of HAE Management Report"*** that will help us better assess the treatment and diagnosis landscape throughout the world.

--***Regional Workshops***. HAEi will organize workshops in areas where there are newer HAEi members. The objective of the workshops will be to bring together patients, physicians/researchers and industry to establish working relationships and action plans. We plan to hold meetings in the following regions: Balkans, Latin American, Eastern Europe, and China.

--Creating a ***"Global Access Program"***. In October 2014, our Executive Committee approved further exploration of a program that we hope will provide a mechanism for bringing medicines to patients in countries where HAE therapies are not registered. The details are currently being worked out and we will soon approach our pharmaceutical company stakeholders for their input.

With warm regards and best wishes for a happy and healthy new year!

Anthony J. Castaldo
President, HAEi

Executive Committee meeting fall 2014

The HAEi Executive Committee met in Frankfurt am Main, Germany Friday 31 October to Sunday 2 November 2014. All afternoon Friday was spent at the Hämophilie-Zentrum Rhein Main (HZRM) with a interesting tour of the clinic as well as insight into the development of treatments for HAE patients from a German point of view followed by training in self-administration. Dr. Inmaculada Martinez Saguer and Dr. Carmen Escuriola Ettingshausen took care of the first part of the program, while nurse Karin Andritschke gave practical training in self-administration and told about supervision of HAE patients from the perspective of a nurse.

Saturday began under the heading "HAEi driven early access and named patient programs". The Executive Committee had a very fruitful discussion on how HAEi could improve access in countries where medication currently is not registered.

Training in self-administration at the Hämophilie-Zentrum Rhein Main (HZRM)

HAEi has had a longstanding interest in establishing a program that would allow manufacturers to either donate or otherwise provide access to HAE medicines in countries where these products are currently not registered. Recently the HAEi President and Executive Director met with a company based in Birmingham, United Kingdom. This company has the expertise to help HAEi design and implement a legally sound and regulatory compliant global program to broaden the availability of HAE medicines and the Executive Committee approved further discussions regarding a possible innovative approach to widen access to these rare disease medicines.

The program for Saturday continued with a number of sessions with most of the pharmaceutical company giving an insight into their views on innovation, advocacy and access. The Executive Committee members had good discussions with Senior Global Product Manager Hanno Waldhauser and Senior Director Commercial Development Georg Henkel from CSL Behring, followed by CEO Sijmen de Vries and Global Vice President Marketing and Sales Paul Janssen from Pharming Group NV

(left and centre on the photo above). Then came Vice President Medical Affairs Andreas Maetzel from BioCryst Pharmaceuticals, and Head of Global Patient Advocacy Communications & Public Affairs Tom Croce, Global Marketing Lead Angioedema Theodora Karasarides and Global Medical Director Irmgard Andresen from Shire concluded this part of the afternoon program.

The last item on the agenda of this indeed full day was a discussion on how HAEi can further strengthen its position in the social media and raise awareness. A few specific ideas were discussed and HAEi expect to be able to roll at least one of them out well in advance of **hae day :-**) 2015.

On the final meeting day the HAEi Executive Committee discussed a number of topics including the funding situation for the upcoming year, the 2016 HAE Global Conference, HAEi projects such as newsletters, basic research programs and a resource center on www.haei.org. Also, the Executive Committee agreed to a relaunch of the haei.org website during the first half of 2015.

The committee also discussed the strategic initiatives for 2015, among other things geographical focus areas, early access programs and named patient programs, expanding the boundaries for HAEi, the establishment of a Patient Advocacy Forum as well as a Global Advisory Board and new awareness activities.

Present at the meeting were the HAEi Executive Committee members Mr. Anthony J. Castaldo, President (USA), Mr. Michal Rutkowski, Vice-President (Poland), Mrs. Alejandra Menendez, Secretary (Argentina), Mrs. Fiona Wardman, Treasurer (Australia), Mrs. Sarah Smith Foltz (Spain), Mr. Jørn Schultz-Boysen (Denmark), Mrs. Beverley Yamamoto (Japan), and Mrs. Natasha Jovanovska (Macedonia), while Mr. Peter Hermeling (Germany) and Mrs. Rachel Annals (United Kingdom) were unable to attend.

HAE Global Conference 2016

The HAEi Executive Committee members have agreed that after Copenhagen, Denmark in 2012 and Washington D.C., USA in 2014 it is time for the conference to return to Europe in 2016.

"We are looking for the right combination of good conference center and hotel facilities, easy access from many locations in the world, and - as the conference will take place around the time of the global awareness day **hae day :-**) 2016 - agreeable weather conditions", says HAEi Executive Director Henrik Balle Boysen.

The venue for the 2016 HAE Global Conference will be published on **hae day :-**) 2015.

Trials recruiting patients

According to the International Clinical Trials Registry Platform under World Health Organization (WHO) the following trials are recruiting at the moment:

- ***12-Week Safety and Efficacy Study of BCX4161 as an Oral Prophylaxis Against HAE Attacks OPuS-2.*** Recruiting in 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

- ***Pathophysiological study for autoimmune dysregulation of HAE.*** Recruiting in Japan. http://www.umin.ac.jp/ctr/index.htm

- ***A Call Center During HAE Attacks (SOS HAE).*** Recruiting in France. http://clinicaltrials.gov/show/NCT01679912

- ***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

- ***A Study to Evaluate the Clinical Efficacy and Safety of Subcutaneously Administered C1-esterase Inhibitor in the Prevention of HAE.*** Recruiting in Australia, Canada, Czech Republic, Hungary, Israel, Italy, Romania, Spain, United Kingdom, and USA. http://clinicaltrials.gov/show/NCT01912456

- ***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

New and upcoming National Patient Groups

The global family of HAE organizations keeps on growing. In September-October a National Patient Group (NPG) was established in Kenya as well as in Russia, and at the moment the first steps to a National Patient Group has been taken in the Philippines.

As mentioned at the HAE Global Conference 2014 in Washington D.C., USA, we are also working on establishing NPG's - and eventually National Member Organizations (NMO's) - in countries like Venezuela, Chile, South Africa, Thailand, Singapore, Taiwan, and South Korea.

In other words: What started with just a good handful of countries in 2004 has now grown into a truly global umbrella organization with NMO's in 27 countries and NPG's in further 12 countries.

No NMO or NPG in *your* country? Please don't hesitate to contact HAEi at info@haei.org and we will gladly help you through the first steps of establishing a national HAE organization.

HAE NEWS FROM AROUND THE GLOBE

From our National Member Organizations

Argentina (www.aehargentina.org)
With over 90 attendees AEH Argentina held a national patient meeting on 15 November 2014 in Buenos Aires. Participants from 10 provinces gathered to enjoy a productive and informative session, which focused on educating the patient community on the current treatments available and how to facilitate access to those life saving therapies. The meeting was highly enriched by the presence of the main HAE reference physicians in Argentina, who aimed at highlighting the importance of intelligent use of modern treatments to improve patients' quality of life. Presentations and guides to self infusion, both intravenous and subcutaneous, were introduced to patients willing to become acquainted with HAE home treatment, whilst a government official from the Ministry of Health was invited to explain the complexity of the county's health system and suggest resourceful tools to navigate through it in order to expedite access to HAE treatments.
AEH Argentina presented data on a survey on "Accessibility and Use of Available Treatments" conducted all over the country during the course of 2013 and the first half of 2014 as well as a summary of the new projects for the upcoming year. ASSIST AEH, a mobile application, specifically developed for HAE patients in Argentina, was also introduced during the meeting. All the information presented blended with the unique opportunity of sharing experiences, reuniting with old friends and welcoming new faces to the group made this yet another unforgettable event.

Australia (www.haeaustralasia.org.au)
T-shirt competition: Until the end of Januar 2015 HAE Australasia is running a design competition: Design a T-Shirt to celebrate **haeday :-)** 2015 and win a Red Balloon voucher for 150 AUD if your entry is chosen. The competition is open to residents of Australia and New Zealand.

2015 Patient Meeting: The next annual patient meeting will take place 16 May 2015 in Sydney.

Brazil (www.abranghe.org.br)
Firazyr in Brazil: On 14 October 2014 the Brazilian Health Surveillance Agency (ANVISA) approved self-administration of Firazyr.

Patient meeting Porto Alegre: A patient meeting was held at the Hospital da Crianca Santo Antonio in Porto Alegre on 29 November 2014. The program included an orientation on diagnostics and treatment (Dr. Giovanni Di Gesu) and news from the Brazil HAE organization (Raquel Martins).

Allergy conference: The WAO International Scientific Conference 2014 (WISC 2014) and the Annual Congress of the Brazilian Association of Allergy and Immunology (ASBAI) was held in Rio de Janeiro 6-9 December 2014. The overall theme of the two events was "Advancing the borders of allergy: From treatment to prevention by targeting the environment, infections and the susceptible patient".

Patient meeting Santo André: A patient meeting took place at the Faculdade de Medicina do ABC in Santo André on 13 December 2014.

Canada (www.haecanada.org)
Patient information events: HAE Canada is inviting the members to a patient information event in Ottawa, Ontario on 31 January 2015. Dr. William Yang, MD, FRCPC, FAAAAI has agreed to be the primary speaker at the event that will be will be the first with webcast, allowing members from all over Canada to participate. Information can be found on www.haecanada.org.

Patient events in 2015 are also being planned for Toronto (May), Edmonton (June), and Calgary (September).

Strategic plan: HAE Canada has recently completed work on a five year strategic plan. The plan can be viewed on the recently revitalized website at www.haecanada.org. The primary goals associated with the plan are:

- *Organizational Effectiveness* – Improve the ability to achieve the mission and goals by engaging and empowering the members; developing the board; training the volunteers; and by collaborating with stakeholders and partners.
- *Equipping Patients & Health Care Providers* – Equip patients, caregivers, family and health care providers with the information, tools and resources needed to ensure those with HAE and other related angioedema live healthy and productive lives.
- *Building the Community* – Convey relevant information, about HAE and other related angioedema, to those in the community.
- *Advocacy* – Enhance the ability to advocate for the members by communicating the mission; lobbying and influencing governments; by educating people; and by promoting awareness of the issues faced daily by those with HAE and other related angioedema.

Guideline: The HAE Canada strategic partner CHAEN has released the 2014 guideline on diagnosis and treatment of HAE. It has been published in the Journal of the Canadian Society of Allergy and Clinical Immunology and can be downloaded from www.aacijournal.com/content/10/1/50.

Firazyr in Canada: The Ministry of Health Services in British Columbia is considering Firazyr for PharmaCare coverage. Under the PharmaCare program, the ministry seeks to provide coverage for drugs that support the health and well-being of British Columbians and provide value for money. Before a drug can be included in the PharmaCare formulary, it undergoes a review taking place in three stages: Health Canada review, Common Drug Review, and Ministry of Health Services Drug Review. In British Columbia the ministry conducts its own review before making its coverage decision. The ministry has implemented a process that lets patients, caregivers and patient advocacy groups submit input on specific drug reviews. The deadline for input was 19 November 2014 and HAE Canada is now waiting for the decision of the ministry.

For the French speaking Canadians: Due to language barriers in the country, HAE Canada has make an association with the APIQ (Association des Patients Immunodéficients du Québec). Jacques Coulombe in Montréal is the APIQ HAE committee director and coordinating with HAE Canada. According to Mr. Coulombe there will soon be information on HAE at www.cipo-apiq.ca - in the meantime feel free to contact him on (514) 432-8594 or at coulombejacques@mac.com.

France (www.amsao.fr)
The next patient meeting will be held 14 March 2015 at Hôpital Cochin in Paris.

Hungary (www.haenet.hu)
The 9th C1-Inhibitor Deficiency Workshop in Budapest is schedules for 28-31 May 2015. The conference focuses on bradykinin-mediated angioedemas, and particularly on the types resulting from C1-inhibitor deficiency. The topics covered by the four-day long event are, among others, the latest achievements in the diagnostics of the disease, exploration of its hereditary, pathogenetic, and clinical background as well as the management and follow up of the patients. See more on the conference at www.haenet2015.hu.

Japan (info@haej.org)
Patient advocacy meeting: HAE Japan is having an international patient advocacy meeting on 12 January 2015 in conjunction with HAEi. Keynote speakers will be Dr Bruce Zuraw, HAEi President Anthony J. Castaldo, and HAEi Executive Director Henrik Balle Boysen. Further details are up on the new bilingual website at www.haej.org.

The day before there will be a meeting between HAEi and HAE Japan patient advocacy leaders and key physicians, including Dr Zuraw, Dr Ohsawa, Dr Hide and Dr Honda. Dr Zuraw will be giving a talk entitled "HAE - a scientific overview and prospects for clinical practice". This will be followed by a discussion focusing on current international consensus regards treatment guidelines and clinical practice.

Strategy: HAE Japan is moving ahead with its strategy to gain authorization and remuneration for self-possession and self-infusion of HAE treatments. At the moment HAE patients in Japan can only access treatments in a few designated hospitals making travel for work or leisure extremely difficult and in some cases dangerous for patients. HAE Japan has petitioned the Ministry of Health Labour and Welfare and is currently waiting for a response.

Macedonia (www.haemacedonia.mk)
HAE caravan: During half of October and all November 2014 HAE Macedonia took an educational caravan around the country with the purpose of raising awareness of HAE among the general public - but also in order to identify potential patients, help them enter the HAE network and provide them with guidance. Another purpose of the caravan was to intensively teach MD's on how to recognize the disease and to refer patients to adequate facilities to have them tested. The caravan covered seven cities throughout Macedonia and lectures were given by Prof. Vesna Grivcheva-Panovska, PhD.

Dancing for HAE: On 30 November 2014 HAE Macedonia held the event "Dancing for HAE". A professional dancing studio performed a flash mob in one of the biggest city malls in Skopje, with the aim to attract the attention of the bystanders for the event. HAE Macedonia gave a short presentation about HAE and handed out informative brochures and balloons. The city of Skopje donated money for the event.

HAE workshop: The biannual South Eastern European HAE workshop will be held on 3 April 2015 in Skopje. The organizers have invited participants from Serbia, Croatia, Slovenia, Montenegro, Bosnia, Albania, Kosovo, and Bulgaria as well as prominent international opinion makers in the field of HAE. The aim of the workshop is to establish sustainable and applicable practice for HAE treatment in South Eastern Europe.

Mexico (www.facebook.com/AEH.Mexico?fref=ts)
Legislative forum: On 3 December 2014 a legislative forum on HAE took place at the Cámara de Diputados in Mexico City.

USB bracelet: The Mexican HAE Association has been working on the development of an USB bracelet with capacity enough to hold the patient's medical history as well as scientific information on HAE and videos on how to administer medicine.

New Zealand (www.haeaustralasia.org.au)
Until the end of Januar 2015 HAE Australasia is running a design competition: Design a T-Shirt to celebrate **haeday :-**) 2015 and win a Red Balloon voucher for 150 AUD if your entry is chosen. The competition is open to residents of Australia and New Zealand.

Norway (www.haescan.org)
The first Norwegian information meetings of the new Scandinavian HAE organization took place 29 November 2014 in Bodø and 30 November 2014 in Oslo.

Sweden (www.haescan.org)
The new Scandinavian HAE organization held its first Swedish information meetings on 15 November 2014 in Stockholm followed by Malmö on 16 November 2014.

Switzerland (www.hae-vereinigung.ch)
The annual meeting of HAE Switzerland was held on 7 November 2014 at Restaurant Arlecchino in Olten.

United Kingdom (www.haeuk.org)
NHS policy: In April 2013 NHS England published its policy for treatment of acute attacks of HAE. It is quite long and not easy to access. However, in November 2014 NHS England approved a short Patient Summary of the policy, outlining the basic service specifications that have been centrally commissioned, and that every HAE patient should be able to access. Patients can use this policy summary when they talk with their consultant about home therapy. You can download it from www.haeuk.org/wp-content/uploads/2014/11/IACRG_CPol-Summ_HAE_FINAL-2.pdf.

National Patient Day: This years' patient day took place on 6 December 2014 at Addenbrookes Hospital in Cambridge. Speakers included Dr Hillary Longhurst, Dr Bill Egner and Specialist Immunology Nurses John Dempster and Christine Symons. The meeting was open for all HAE patients and their immediate family members (over 16 years of age).

Patient Meeting in North West England: Patients in the North West of England had their own primary immunodeficiency and HAE patient day at the Haydock Park Racecourse in November 2014. The meeting was hosted by the North West Immunology Centres for patients who attend their clinics.

USA (www.haea.org)
ACAAI Annual Scientific Meeting: The 71st ACAAI Annual Scientific Meeting took place in Atlanta, Georgia 6-10 November 2014 under the heading "Faces and Facets of Allergy & Immunology".

National Patient Summits: US HAEA is planning the next two National Patient Summits for the fall of 2015. The upcoming events will offer patients opportunities to participate in HAE research, talk to reimbursement specialists, and interact with HAE friends.

AAAAI Annual Meeting: Houston, Texas will be hosting the 2015 AAAAI Annual Meeting 20-24 February 2015. Thousands of allergist/immunologists, health and healthcare professionals will get together for five days with hundreds of educational offerings on a variety of topics such as allergic disease, asthma, immunotherapy, food allergy, skin disease, practice management, new technologies, and health care reform.

From our National Patient Groups

Belarus (www.hereditary-angioedema.org)
Workshop: Mr. Viktar Lebedz, former member of the HAEi Executive Committee, is presently working on setting up a HAE workshop in Minsk, Belarus.

Special patient: As mentioned in the HAEi newsletter #5/2014 Mr. Lebedz is also the person behind the very special Belarusian HAE advocate, Nadia. Earlier in 2014 she was introduced on the Internet - she even has her own homepage at www.haedoll.org.

As it says on the website: "We have an agreement with the doll master to fix the swollen Nadia's arm as soon as the effective HAE medication is registered in Belarus. We are sure that Nadia will be cured!"

Kenya
We are happy to announce our newest National Patient Group, formed in Kenya on the African continent. The contact person is Ms. Patricia Karani in Nairobi (frepashe@yahoo.com).

Ukraine
As you might know the political situation in Ukraine is quite unstable at the moment. In the words of an HAEi contact in Ukraine: "It was hard before, but now with all the mess in the country it is much harder."

United Arab Emirates
Mr. Rashad Matraji, the HAEi Gulf Region representative, has established a cooperative agreement with the United Arab Emirates Genetic Disease Association (GDA). HAEi and GDA arranged a workshop for physicians from all over the Gulf Region in Dubai, UAE. This conference, taking place 11-13 December 2014, was focusing on raising awareness and increasing diagnosis.

Patient stories from all over the world

For some months now HAEi has been working on the first of a series of HAE patient stories from around the globe.

"It more or less began with a book issued by the Danish HAE organization a couple of years back. This book - containing seven very different patient stories - was quite well received but due to the choice of language it was fairly limited who outside Denmark could make real use of the book. That lead to the translation of a few of the Danish patient stories - but more importantly to the work on a collection of stories aimed at an international audience", says the HAEi Communications Manager, Steen Bjerre.

"We start out with the stories of Ann Price from the United Kingdom, Rashad Matraji from the United Arab Emirates, and Cindy Hughes from Australia. Another three stories have just been approved and will be launched shortly - and over the next few months we expect to publish more stories bringing us to a total of at least 12 before **haeday :-**) 2015. Then more stories will follow and it is our aim to have some 20 patient stories literally covering the globe before the end of the year."

The first stories can be downloaded as pdf documents from www.haeday.org (choose "Press" and "HAE stories").

Our family has been very privileged
Ann Price

I am stronger than my disease
Rashad Matraji

This really gives you a whole different perspective on life
Cindy Hughes

Global Advocacy Work

Recent activities

HAEi is invited to participate in a variety of international meetings. This is a brief overview of some of the activities in the recent months:

Early October HAEi met with Cynthia K. Magdaraog, President of the Philippine Society for Orphan Disorders (PSOD) to continue discussions on a HAEi – PSOD collaboration to form a HAE National Patient Group (NPG) in ***the Philippines***. HAEi also met with Dr Silvia Estrada, Director of the National Institutes of Health Office of Genetics and Dr Jovilia Abong, President of the Philippines Allergy and Immunology Society. Drs Estrada and Abong pledged their support for the collaboration between PSOD and HAEi and they agreed to explore programs to raise awareness among doctors and physicians as well as opportunities to establish a diagnostic reference laboratory in Manila. Ms. Magdaraog requested that HAEi return in February to continue work in establishing the Filipino NPG.

In October HAEi took part in a number of activities in ***USA.*** Firstly HAEi participated in the National Organization for Rare Diseases (NORD) annual meeting, among other things talking with representatives from a variety of international patient organizations to share insights and strategies on raising awareness and broadening access to life saving medicines. Then the Global Patient Advocacy and Communication Team from Shire invited HAEi to speak at their annual meeting, providing an overview of HAEi's activities and feedback on what Shire can do to assist the worldwide effort to improve the lives of HAE patients. Thirdly HAEi was present at the first HAE-specific NIH sponsored international scientific conference. And finally HAEi spoke at the "launch meeting" for Ruconest in ***USA*** and also met with Pharming's CEO and other executives.

3 November 2014 HAEi Executive Director Henrik Balle Boysen participated in a discussion panel at BIO-Europe in ***Frankfurt, Germany.*** The topic for discussion was Global Access Programs and the other panelists were Mark Corbett from Clinigen, Steve Bates from UK BioIndustry Association, Dr Markus Kosch from Pfizer, and Luc Dochez from Prosensa.

11-12 November 2014 HAEi was invited to participate in the investigator meeting for the second clinical trial for BioCryst OPuS-2 in ***Nice, France.***

13-15 November 2014 HAEi spoke at Shire's Global HAE meeting in ***London, United Kingdom***. HAEi President Tony J. Castaldo addressed the global assessment survey data that was presented at the 2014 HAE Global Conference in Washington D.C.

19-21 November 2014 HAEi was invited by Prof. Konrad Bork to speak about the Burden of Illness and the Patient Perspective during the annual German Dermatological Conference in ***Mainz, Germany.*** In conjunction with the meeting in Mainz, HAEi spoke at a meeting in ***Aalesund, Norway.*** Hematologist and HAE expert Robert Brudevold invited a group of Norwegian physicians to talk about the importance of Quality of Life in HAE patients and their families.

HAEi, together with the UAE Genetic Disease Association, conducted a workshop for Gulf Region physicians in ***Dubai, UAE*** 11-13 December 2014.

Future activities

10-13 January 2015 HAEi will participate in the first patient/physician meeting since HAE Japan became a recognized NGO in Japan. The event takes place in ***Tokyo, Japan.***

At the end of January 2015 HAEi is invited to the long awaited official opening of the US HAEA Angioedema Center in ***San Diego, California, USA.***

In the second half of February 2015 HAEi will be participating at the annual meeting of American Association of Asthma, Allergy and Immunology (AAAAI). This meeting features HAE related presentations by physician/scientists from throughout the world and therefore provides HAEi a unique opportunity to interact the medical community and representatives from industry. This year's meeting will take place in ***Houston, Texas, USA.***

In March 2015 HAEi will participate in the annual conference "International Plasma Protein Conference – IPPC 2015". This time the conference is held in ***Rome, Italy.***

NEW PAPERS ON HAE

Here are summaries of some of the HAE related scientific papers published since our last newsletter:

Contact System Activation on Endothelial Cells - *by S. de Maat et al., University Medical Center Utrecht, The Netherlands:*
Besides its role in blood coagulation in vitro, the contact system is responsible for the production of bradykinin. This inflammatory peptide is involved in episodes of pathological tissue swelling in HAE, but potentially also in the physiological regulation of vascular permeability. A body of evidence indicates that contact system factors are recruited to the surface of activated endothelial cells, where locally released proteins can activate them. Clinical and biochemical studies indicate that plasmin can evoke contact system activation. This auxiliary role for plasmin may so far not have been fully appreciated in pathophysiology. We propose a complementary model for contact system activation on the endothelial cell surface that is initiated by plasmin activity. *(Semin Thromb Hemost. Nov 2014)*

Presence of c1-inhibitor polymers in a subset of patients suffering from HAE - *by D.E. Madsen, University of Southern Denmark et al.:*
Analyzing 31 Danish HAE families we found that plasma samples from three genotypically distinct HAE type I families contained C1-inh polymers. Identical C1-inh polymerization phenotypes were observed in four affected family members from one of these families. Genotyping of the families revealed that the polymerogenic mutations of two families were located in proximity to the reactive center loop insertion site in C1-inh, and one mutation affected helix C. We demonstrate that C1-inh polymers are present in the plasma of a subgroup of HAE type I patients. *(PLoS One, Nov 2014)*

Perioperative Management of Tooth Extractions for a Patient With HAE - *by T. Sanuki, Nagasaki University Graduate School of Biomedical Sciences, Japan, et al.:*
Dental treatments and routine oral surgical procedures, such as tooth extraction, can trigger HAE attacks. Several cases of death resulting from HAE attacks have been reported after such procedures. Patients with HAE are of special concern in dentistry and require precautionary preparations before treatment. *(J Oral Maxillofac Surg., Aug 2014)*

Quality of life in patients with HAE receiving therapy for routine prevention of attacks - *by W.R. Lumry et al., Allergy and Asthma Research Associates, Dallas, USA:*
In a clinical trial setting, patients with HAE had significantly better health-related quality of life after 12 weeks of C1 INH-nf for routine prevention compared with acute treatment of individual angioedema attacks in the absence of routine prevention while on placebo. *(Allergy Asthma Proc., Sep 2014)*

Angioedema deaths in USA, 1979-2010 - *by S.J. Kim, Kaiser Permanente Southern California, USA, et al.:*
Angioedema-associated deaths were very rare 1979-2010. HAE deaths became even more so, whereas non-HAE deaths increased. Risks associated with angiotensin-converting enzyme inhibitors were higher in blacks. Lack of specific coding for acquired angioedema most likely explains the observed association between cancer and HAE. In the future, more granular coding systems may help distinguish HAE from acquired angioedema. *(Ann Allergy Asthma Immunol., Sep 2014)*

Clinical and Laboratory Characteristics That Differentiate HAE in 72 Patients - *by I. Ohsawa et al., Juntendo University Faculty of Medicine, Tokyo, 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 level of C4 is a useful marker for making a differential diagnosis of HAE. *(Allergol Int., Sep 2014)*

Management of hereditary angioedema in pregnant women: a review - *by T. Caballero et al., Hospital La Paz, Spain:*
The management of pregnancy in patients with HAE is often a clinical challenge owing to potential worsening of the disease in relation to the physiological increase in estrogens and the limited treatment options. *(Int J Womens Health., Sep 2014)*

Icatibant, an inhibitor of bradykinin receptor 2, for HAE attacks - *by R.A. Campos, Universidade Federal da Bahia, Brazil, et al.:*
HAE type I patients who received icatibant responded promptly; most achieved improved symptom severity within 30 minutes. Local adverse events occurred in 75 % of the patients. *(Sao Paulo Med J., 2014)*

News from the Industry

20 October 2014

In light of the ***AbbVie*** board's decision to change its recommendation and to advise its shareholders to vote against its offer, ***Shire*** believes that there is now no realistic prospect of AbbVie completing its offer. The board of Shire believes that it is in the best interests of its shareholders, employees and other stakeholders to resolve the situation as quickly as possible. Accordingly it has agreed with AbbVie to terminate the cooperation agreement and Shire. The break fee of approximately 1.635 billion USD is now payable by AbbVie to Shire.

Shire is a well-positioned independent business with a focused growth strategy. The business has maintained robust momentum throughout the offer period. Shire's trading since the end of Q2 has remained strong. Susan Kilsby, Chairman of Shire, said:

"Shire has an exceptional track record of delivering value and growth. This growth profile has been accelerated by our new management team executing a clear and focused strategy. Importantly, we have maintained this momentum since July and made material progress across our business. Whilst we are disappointed that the offer will not now complete, we continue to enjoy excellent prospects as we execute our plan to double Shire's product sales to 10 billion USD by 2020."

28 October 2014

Dyax Corp. has announced financial results for Q3 ended 30 September 2014. Highlights includes the completed dosing of the third cohort (300mg) in the Phase 1b study of DX-2930 in October as well as Kalbitor net sales of 20.3 million USD, a 22 % increase over the second quarter 2014 net sales which were 16.6 million USD.

"We have made tremendous progress this year and continue to build on the positive momentum in our key areas," said Gustav Christensen, President and CEO of Dyax. "The Kalbitor business is performing above our expectations and the DX-2930 program is progressing through the clinic with Phase 1b results scheduled to report early next year."

For Kalbitor, revenue fluctuations are primarily due to variability in the rate at which patients utilize Kalbitor to treat attacks (particularly among patients who experience and treat frequent attacks), as well as the timing and amount of distributor demand.

30 October 2014

Pharming Group NV has published its financial report for the nine months ended 30 September 2014. From the financial highlights:

- Operating costs increased by 1.6 million EUR to 10.9 million EUR (9M 2013: 9.3 million EUR) mainly as a result of increasing activities, including the start of a Phase II clinical study of Ruconest for prophylaxis for HAE, and the expenses of the (non-cash) share-based compensation.
- Cash outflows from operations increased by 6.6 million EUR to 13.7 million EUR during 9M 2014 (9M 2013: 7.1 million EUR), mainly as a result of the 7.3 million EUR increase in manufacturing activities for Ruconest, ahead of the anticipated US launch in 4Q 2014.

From the operational highlights:

- US partner Salix Pharmaceuticals Inc. is preparing to launch Ruconest during 4Q 2014 having received approval from the FDA for Ruconest on 16 July 2014.
- A 20 million USD milestone payment from Salix will become payable within 30 days after the first commercial sale of Ruconest in the US or within 90 days since FDA approval.
- A Phase II clinical study of Ruconest for prophylaxis of HAE was announced. Salix and Pharming will equally share the costs of the study. On FDA approval for prophylaxis of HAE an undisclosed milestone will become payable by Salix to Pharming.

Post-period highlights:

- Pharming and Swedish Orphan Biovitrum amended and extended the Ruconest Distribution Agreement. Pharming is in the process of initiating directly commercialization of Ruconest in Austria, Germany and the sales through such direct commercialization are anticipated to increase the yield of EU sales.

3 November 2014

Dyax Corp. has announced the expansion of its ongoing Phase 1b clinical trial evaluating DX-2930 to include additional patients and dosing cohorts. Dyax is developing DX-2930, an investigational fully human monoclonal antibody inhibitor of plasma kallikrein, as a subcutaneous injection for prevention of HAE attacks.

The ongoing Phase 1b clinical trial is a multi-center, randomized, double-blind, placebo-controlled, multiple ascending dose study designed to assess the safety, tolerability and pharmacokinetics of DX-2930 in HAE patients.

As of 31 October 2014, 21 subjects were enrolled and completed dosing in three ascending dose cohorts (30 mg, 100 mg and 300 mg) of DX-2930 or placebo. Subjects in each cohort were randomized to active drug or placebo in a 2:1 ratio. Each study subject received two doses of study drug or placebo separated by 14 days and will undergo 15 weeks of follow-up after the second dose.

In light of faster than anticipated enrollment rates, Dyax has decided to take the opportunity to further characterize DX-2930 by adding two additional cohorts. Subjects will continue to be randomized to active drug or placebo in a 2:1 ratio and the dosing regimen will remain unchanged. Active drug-treated subjects in the fourth cohort will receive 400 mg of DX-2930. The dose level of the fifth cohort will be decided based upon a review of interim data.

Addition of the new dosing cohorts is in accordance with the provisions included in the original protocol which allows enrollment into additional dose groups and/or additional patients at any dose group. Total enrollment can be increased to as many as 36 patients and data from additional patients will be used to expand the DX-2930 safety database and provide potentially informative pharmacodynamic data.

"Strong investigator support for the Phase 1b trial has allowed the study to progress rapidly and, at this time, the first three dosing cohorts are fully enrolled," said Burt Adelman M.D., Executive Vice President of Research and Development and Chief Medical Officer at Dyax. "These additional cohorts will provide safety, pharmacokinetic and pharmacodynamic data which will further guide future clinical development of DX-2930. Importantly, we remain on track to report data from this study in early 2015, followed by a Phase 2 study which is also currently planned to begin in 2015."

"Developing a prophylactic treatment for HAE patients is a key value driver for Dyax and we are encouraged by the rapid progress we are seeing with this trial," said Gustav Christensen, President and CEO of Dyax. "We believe DX-2930's unique product profile positions it well as a potential preventative treatment for HAE attacks."

3 November 2014

Salix Pharmaceuticals, Ltd. and ***Pharming Group NV*** has announced the launch of Ruconest (C1 Esterase Inhibitor [Recombinant]) 50 IU/kg in USA for the treatment of acute angioedema attacks in adult and adolescent patients with HAE. The announcement follows the July approval of the drug by the Food and Drug Administration.

"We're excited to offer the only recombinant C1 esterase inhibitor therapy for HAE in USA," said Carolyn J. Logan, President and CEO of Salix. "Ruconest treats the root cause of HAE attacks, which has been shown to raise C1 inhibitor levels to within the normal range. Ruconest can be self-administered by appropriately trained patients and is effective at stopping most HAE attacks in one dose."

Ruconest, a recombinant C1 esterase inhibitor, can be administered by the patient after receiving training by a healthcare provider. Ruconest is over 98 % pure, and because it is not made from human plasma, it does not carry any known risk of passing on viruses that can be found in human blood.

"HAE is an especially challenging disease for patients to manage," said Anthony J. Castaldo, President of the Hereditary Angioedema Association (US HAEA). "If left untreated, patients can experience attacks that are incredibly painful and, because of its unpredictability, HAE interferes with daily life. We're pleased HAE patients now have another treatment option available to them."

Ruconest is available by prescription across USA through Ruconest Solutions and comes with comprehensive patient support services. For more information, including an opportunity for a free trial of Ruconest, visit www.ruconest.com or call Ruconest Solutions at (855) 613-4HAE.

Ruconest is manufactured by Pharming Group NV in the Netherlands. Salix has licensed exclusive rights from Pharming to commercialize Ruconest in North America and market Ruconest for the treatment of acute HAE attack symptoms.

"Ruconest's availability in USA marks a significant milestone for Pharming," said Sijmen de Vries, CEO of Pharming. "Ruconest has helped patients in other countries around the world and we look forward to seeing the difference it will make in the lives of HAE patients in USA."

5 November 2014

Pharming Group NV has announced the receipt of a 20 million USD milestone payment from ***Salix Pharmaceuticals***. The milestone was paid according to the terms and conditions of the Ruconest commercialization agreement between Salix and Pharming.

Sijmen de Vries, Pharming CEO, commented, "The US launch of Ruconest and the receipt of the 20 million USD milestone from Salix, mark what we perceive as the beginning of a new era for Pharming. The payment strengthens our debt-free balance sheet to more than 38 million EUR as of today. From this solid basis, as result of future receipts of 30 % of US net sales, up to 100 million USD annual sales, increasing stepwise up to 40 % for annual US sales in excess of 100 million USD for the supply of Ruconest to Salix and in addition growing revenues from EU sales, both from our own direct commercialization and by Sobi, we are now aiming for our goal of achieving financial sustainability of the company."

6 November 2014

Salix Pharmaceuticals has announced financial and operating results for the third quarter ended 30 September 2014. Extracts from the report:

- On 16 July 2014, the Food and Drug Administration (FDA) approved Ruconest for the treatment of acute angioedema attacks in adult and adolescent patients with HAE.

- Carolyn Logan, President and CEO, stated, "Within an 84-day period, spanning mid-July to early-October, three new products were granted marketing approval by the FDA. This level of success is noteworthy for any pharmaceutical company, and provides additional evidence of Salix's exceptional track record of in-licensing, developing and bringing to market important drugs for patients who need them."

- "These important milestones should enhance our competitive position and expand our market opportunities," said Ms. Logan. "We began field promotion for Ruconest earlier this week."

6 November 2014

BioCryst Pharmaceuticals has announced financial results for the third quarter ended 30 September 2014. Extracts from the report:

"The primary focus continues to be our oral kallikrein inhibitor program for HAE. Preparations are underway for our OPuS-2 clinical trial of BCX4161 and we expect to begin enrolling HAE patients before year end. We continue to make progress with our second generation HAE program and remain on track to enter Phase 1 clinical development in the second quarter of 2015," said Jon P. Stonehouse, President & CEO of BioCryst.

Activities are underway to initiate the (Oral ProphylaxiS-2) OPuS-2 clinical trial of BCX4161 before the end of 2014. OPuS-2 is a 12-week, three-arm, parallel cohort design trial to evaluate the efficacy and safety of two different dose regimens of BCX4161 administered three-times daily, 300 mg and 500 mg, compared with placebo. The trial, to be conducted in USA and selected European countries, is expected to enroll approximately 100 HAE patients whose average historical attack rate is lower than that observed for patients enrolled in OPuS-1. The primary efficacy endpoint for the trial will be the mean angioedema attack rate for each BCX4161 dose group compared to placebo. The OPuS-2 trial will use 100 mg soft-gel capsules that have demonstrated relative bioavailability of approximately 80 % compared with the hard gel capsule formulation used in OPuS-1, which tested 400mg three-times daily.

Non-clinical safety studies for two second generation compounds for the treatment of HAE are progressing as planned, and first-in-human clinical trials are expected to begin during the second quarter of 2015.

18 December 2014

BioCryst Pharmaceuticals has announced that it has dosed the first patient in OPuS-2 (Oral ProphylaxiS-2), a blinded, randomized, placebo-controlled clinical trial of orally-administered BCX4161 in patients with HAE. OPuS-2 is a 12-week, three-arm, parallel cohort design trial to evaluate the efficacy and safety of two doses of BCX4161, 300 mg and 500 mg, administered three-times daily compared with placebo. This trial, to be conducted in the U.S. and selected European countries, is expected to enroll approximately 100 HAE patients. The primary efficacy endpoint for the trial will be the mean angioedema attack rate for each BCX4161 dose group compared to placebo.

"The OPuS-2 trial will provide important information on the efficacy and safety of 12 weeks of oral BCX4161 for prevention of angioedema attacks in HAE patients. OPuS-2 builds on the positive efficacy, safety, tolerability, drug exposure and kallikrein inhibition results from the OPuS-1 4-week study," said Dr. Marc Riedl, M.D., M.S., Associate Clinical Professor at the University of California-San Diego School of Medicine, Clinical Director of the U.S. HAEA Angioedema Center and OPuS-2 Principal Investigator. "OPuS-2 has been designed as an adequate and well-controlled study and represents an important next step toward reaching our goal of improving HAE patients' lives using oral kallikrein inhibitors," added Dr. William P. Sheridan, Chief Medical Officer at BioCryst.

HAEi around the globe

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

Our ***National Member Organizations (NMO)*** are independent associations working for the benefit of patients in the specific country. Currently we have NMO's in 27 countries:

- **Asia**: Japan
- **Australia**: Australia, New Zealand
- **Europe**: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Israel, Italy, Macedonia, Norway, Poland, Portugal, Spain, Sweden, Switzerland, The Netherlands, United Kingdom
- **North America**: Canada, Mexico, USA
- **South America**: Argentina, Brazil

Our ***National Patient Groups (NPG)*** are HAE patient representatives in countries where no formal association has yet been founded or where the process of founding an association is starting up. Presently we have NPG's in 12 countries:

- **Africa**: Kenya
- **Asia**: China, Malaysia, Russia, United Arab Emirates
- **Europe**: Belarus, Bulgaria, Croatia, Ireland, Romania, Slovenia, Ukraine

You will find much more information on the HAEi 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 NMO's or NPG's.

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.

NEWSLETTER STAFF

Mr. Steen Bjerre
Communications Manager
E: s.bjerre@haei.org
P: +45 22 20 46 01

Mr. Henrik Balle Boysen
Executive Director
E: h.boysen@haei.org
P: +45 31 591 591

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If you would like to subscribe to our Newsletter please send an email to info@haei.org or register directly on our website www.haei.org.

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