

February 2013

Dear HAEi friend,

As mentioned in our November 2012 edition we plan to send out the HAEi newsletter on a quarterly basis. We would like to start 2013 by wishing you all a Happy New Year – and sending you the first 2013 issue of the HAEi newsletter.

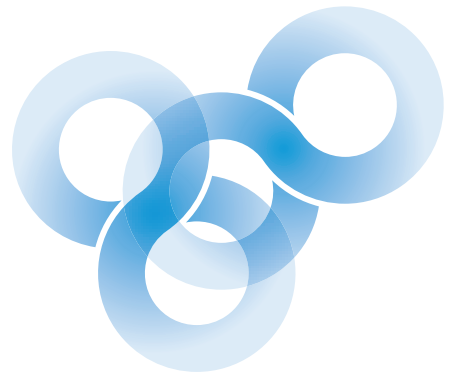
Please let us know what you would like to be included in future newsletters. You can do that by providing feedback to Steen Bjerre at s.bjerre@haei.org or Henrik Balle Boysen at h.boysen@haei.org. In addition, we invite you to submit articles on any topics that you believe would be of interest to other member organizations.

We look forward to your comments and working with you on future newsletters.

HAEi – International Patient Organization for C1 Inhibitor Deficiencies
Steen Bjerre and Henrik Balle Boysen

HAEi Newsletter – February 2013

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Message from the President

Dear HAEi Friends,

As HAE patients, we share a fundamental goal for us and our families – access to a treatment that improves health and well being. While patients in some HAEi member organizations currently have access to a variety of treatments, many still do not. This message is directed to HAEi members who are looking for a path to expand access to HAE medicines in their country.

Clearly, this path leads to the medical establishment and health ministries/insurers who must be convinced to pay for HAE therapies. Unfortunately, the journey will be full of obstacles due to the reality of shrinking health care budgets and the fact that HAE is a rare disease. Nevertheless, nothing will ever happen unless we, as patient advocates, start the process of “clearing the path” by establishing an energetic and well-organized HAE advocacy and awareness effort. You are not alone in this effort because HAEi is ready and able to help anyone, anywhere who is interested in fighting for better patient care.

There are four fundamental building blocks that comprise an effective advocacy and awareness program:

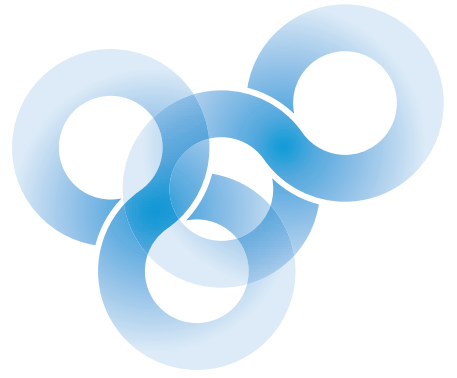
A group of patients who are passionate about improving the lives of HAE patients, and are willing to make a long-term commitment,

A physician or group of physicians who are committed to providing guidance and support to the patient group and educating the country’s medical community,

A pharmaceutical company to provide financial support, collaboration, and assistance to physicians interested in preparing and submitting an HAE paper to a local medical journal or publication,

A coordinated and systematic approach by all stakeholders to engage insurers and/or government health ministries in a discussion on (1) disability, death, and the low quality of life caused by HAE, and (2) the range of therapies available to prevent and treat HAE attacks, and therefore avoid widespread death and disability.

I have first hand experience in the struggle for getting approval for and access to HAE therapies. Our US HAE group worked for over a decade before we finally got access to C1 inhibitor concentrate in late 2008. The path to getting access to this medicine was frustrating because (1) it was far longer than any of us ever imagined, (2) we encountered unexpected thickets of regulatory thorns, and (3) we were confronted by almost insurmountable barriers put up by insurers who initially



denied payment for medicines. The struggle was well worth it and our patient community's quality of life has increased substantially over the past four years.

I encourage HAE friends in countries with inadequate access to therapy to start an advocacy and awareness effort and begin clearing the path so you, your family, and fellow HAE patients can get access to the treatment that you deserve.

Please remember, HAEi is enthusiastic about supporting your advocacy efforts in any way possible.

Warmest regards to all,

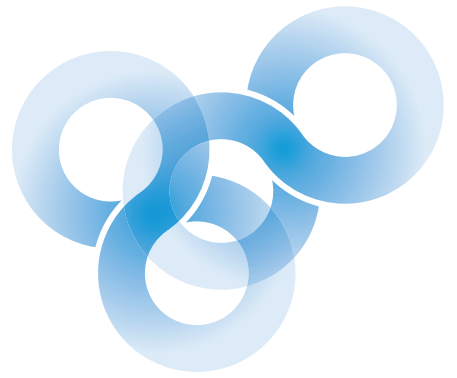
Tony

Anthony J. Castaldo
President, HAEi

HAEi begins efforts to establish a patient group in India

The President of the World Allergy Organization, Dr. Ruby Pawanker, personally invited HAEi to speak at the World Allergy Organization International Scientific Conference in Hyderabad, India. The talk that HAEi delivered addressed HAEi's experience and perspectives on Global Patient Advocacy Initiatives. The event received local press coverage.

During the trip, HAEi worked with Dr. Pawanker to outline a strategy to identify HAE patients in India and hold an initial organizational meeting in late 2013/early 2014. Dr. Pawanker committed to putting out a letter to Indian allergy/immunology practitioners in an initial effort to prepare a map that shows where HAE patients are located. Once that step is completed, HAEi will help Dr. Pawanker organize and conduct an inaugural meeting to include physicians and patients interested in forming a patient organization.



HAEi Working with the Filipino Rare Disease Society to Form an HAE Patient Advocacy Group

HAEi recently met with officials from the Philippine Department of Health and the Philippine Society for Rare Diseases (PSOD). These meetings provided a first step towards organizing a Philippine HAE advocacy group that includes patients and physicians. PSOD—which has been successful in organizing and obtaining treatment for patients with lysosomal storage diseases—is excited about working with HAEi to facilitate the establishing an HAE patient advocacy group.

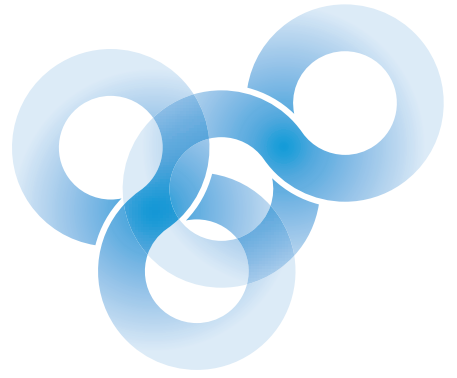
PSOD is also in the process of putting HAEi in contact with other rare disease advocacy groups in the Western Pacific. Our work in the Philippines is a tangible step in pursuing our strategy of reaching out to—and helping—patients in developing countries.

HAEi helping Japanese patients organize an inaugural patient/physician meeting

At the end of 2012 we were fortunate to welcome JAEA (Japan AngioEdema Association) as a national member organization to HAEi. JAEA coordinates its work with CREATE (Center for Research, Education, and Treatment of Angioedema).

The clinical features of HAE in Japan as well as those in other Asian countries are still unknown. However, JAEA and CREATE have reviewed all the reports on Japanese patients (132 reports from 1969 until 2010), revealing that the mean delay in diagnosis was 19 years, which would indicate the need for HAE to be recognized in Japan.

HAEi is planning the first ever HAE physician/patient meetings in Japan. We have been working with the mother of a patient who is highly motivated along with a Japanese doctor who is interested in helping angioedema patients. ViroPharma, CSL Behring and possibly one more company have shown interest in providing financial support for patient/physician meetings that will take place this spring in Osaka and Tokyo.



HAEi working in Turkey to assist planning a patient/physician workshop

In 2012 more than 40 patients from the Istanbul area participated in an initial patient meeting in Istanbul, and a book as well as a poster on HAE was distributed to 30,000 doctors and hospitals all over Turkey. As a result of this initial effort, a group of Turkish HAE physicians headed by Dr. Okan Gülbahar has set a major goal for 2013: They want to host a patient/physician workshop in Turkey in September.

HAEi's efforts in Turkey have led to some exciting results. Two books (one for physicians and one for patients), and several medical journal articles have been written and disseminated. In addition, patients have been provided with "information cards" that describe HAE symptoms and therapeutic options.

The Ministry of Health has been convinced that it is necessary to increase awareness about HAE – and a fruitful dialogue has been established with one of the major health insurance foundations of Turkey to secure future therapies for Turkish HAE patients.

HAEi will of course be involved in the September workshop and will do our very best to help the Turkish efforts further in the right direction.

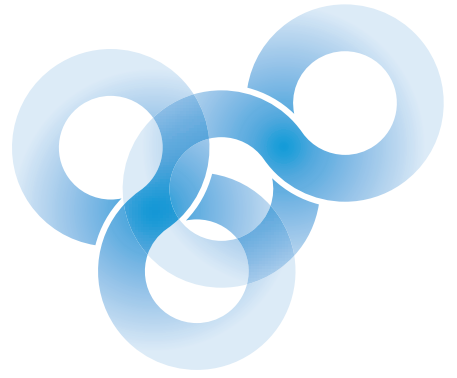
Website to be launched in Russian by February 2013

The translators are done and now we are busy uploading the Russian version of the HAEi website. We expect everything to be up and running later this month.

hae day :-) 2013 in the making

On 16 May 2013 we will once again celebrate global **hae day :-)** and HAEi will once again serve as the international hub for HAE activities sponsored by our member organizations.

The goal of **hae day :-)** is to (1) raise awareness of HAE among the general public as well as the medical community, (2) create an environment for earlier and more accurate diagnosis, and (3) spread knowledge that HAE patients can use to advocate for better care that will lead a healthier life.



During the last few weeks we have been working on the 2013 version of the **hae day :-)** website – please have a look at www.haeday.org. At the website you can follow the planning of national and international events for **hae day :-)** and – most importantly – you can upload your own events on the website. Also, you can upload your smile in our “smiles across the globe” campaign – please help us to literally cover the world with smiles.

We made a lot of noise with our 2012 **hae day :-)** campaign – and, in 2013, we are aiming at being even more visible and securing additional awareness of the global need for early and accurate HAE diagnosis and access to suitable therapies.

Many thanks to our **hae day :-)** sponsors

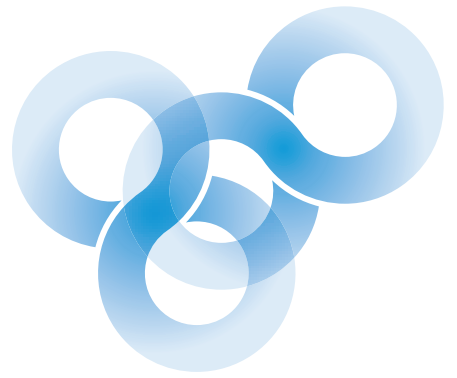
HAEi wish to thank these **hae day :-)** 2013 sponsors:

Diamond: **CSL Behring**
 ViroPharma Incorporated
Gold: **Shire HGT**
Silver: **Dyax Corp.**
Basic: **Santarus Inc.**

There is still space for additional **hae day :-)** 2013 sponsors. If you are interested in becoming a **hae day :-)** sponsor, please contact HAEi Executive Director Henrik Balle Boysen at h.boysen@haei.org.

6,500 likes on Facebook

During December 2012 the **hae day :-)** page on Facebook reached amazing 6,500 likes. Have a look at www.facebook.com/haeday – and please “like” if you are not among the many people who have done so already.



HAEi's global advocacy work

Because of HAEi's position as the global umbrella organization for HAE patients and their caregivers, we are frequently invited to make presentations or participate in discussions about our work at international meetings. Below is a brief overview of recently attended and future meetings:

In December 2012 HAEi was invited to speak about HAEi and the patient perspective at the **Federation of African Immunological Societies (FAIS)** in Durban, South Africa.

In January 2013 HAEi took part in the **Arab Health Conference** in Dubai, the major health conference in the Middle East. Here we worked with Mr. Rashad Matraji, who is the local patient representative in Dubai, as well as the pharmaceutical industry in order to further raise awareness of HAE and initiate educational sessions for physicians from the Arab region.

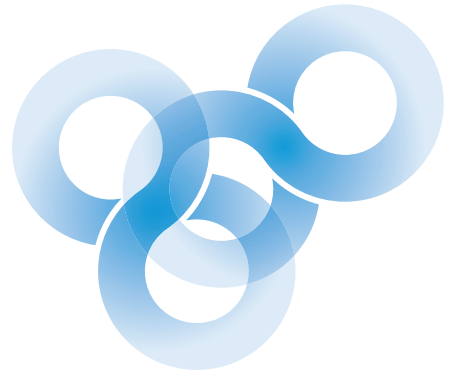
In February HAEi will be present at the **American Academy of Asthma, Allergy and Immunology (AAAAI)** 2013 annual meeting in San Antonio, USA, a significant HAE focus event in Northern America.

In April HAEi has been asked to speak at a meeting organized by Sanquin. The topic of our talk will be, **"The role of patients and patient organizations in the management of HAE"**. Other speakers will include Prof. Marcus Maurer, Prof. Marcel Levi and Prof. Anette Bygum.

News from the industry

Health Canada has approved a New Drug Submission for **Cinryze™** (C1 inhibitor [human]) from **ViroPharma Incorporated**. The approval was granted for routine prevention of attacks in adult and adolescents with HAE. Until now, there have been no approved plasma derived C1 inhibitor therapies for routine prevention of HAE attacks in Canada. ViroPharma anticipate Cinryze™ to be commercially available in Canada in the second quarter of 2013.

Shire plc has entered into a long-term, broad based, multi-indication research collaboration in rare diseases with Fondazione Telethon, a major Italian biomedical charitable foundation, for research carried out at the Telethon Institute of Genetics and Medicine (TIGEM). This alliance will facilitate research on 13 undisclosed rare



disease indications and has the potential to add multiple, novel therapeutic candidates into Shire's early stage pipeline.

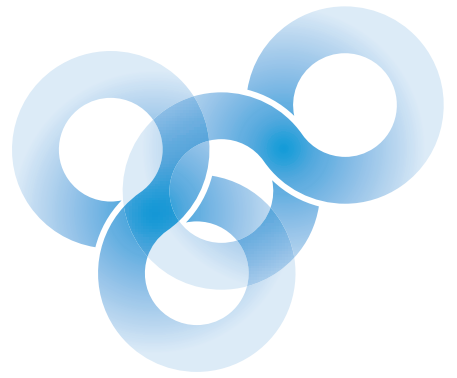
The partnership underscores Shire's long-term commitment to bring innovative therapies to patients with rare diseases worldwide. The collaboration brings together Shire's established capabilities in developing and distributing effective, life-altering therapies for patients with rare diseases and TIGEM's world renowned research expertise in gene therapy and other novel therapeutics. Under the terms of the agreement, Shire will provide M17 EUR funding over five years for several research projects that collectively address a number of different lysosomal storage disorders and neurodegenerative diseases. The majority of the research will be conducted in TIGEM's facility in Naples, Italy under the direction of Andrea Ballabio.

The pivotal Phase III clinical study of **Santarus Inc.** and **Pharming Group NV** to evaluate the safety and efficacy of the investigational drug **Ruconest[®]** (recombinant human C1 esterase inhibitor) 50 U/kg for the treatment of acute HAE attacks has met the primary endpoint of time to beginning of symptom relief.

A statistically significant difference in the time to beginning of symptom relief was observed in the intent-to-treat population (n=75) between Ruconest[®] and placebo (p=0.031, log-rank test); the median time to beginning of symptom relief was 90 minutes for Ruconest[®] patients (n=44) and 152 minutes for placebo patients (n=31). Santarus licensed exclusive rights to commercialize Ruconest[®] in North America for the treatment of acute HAE attacks as well as other potential future indications from Pharming. Under the terms of the license agreement, a M10 USD milestone is now payable to Pharming as a result of the successful achievement of the primary endpoint of the Phase III clinical study.

ViroPharma Incorporated has announced important data from an open-label, multicenter study to assess the safety, tolerability, and treatment effect of escalating doses of C1 INH-nf in patients with HAE who were not adequately controlled with 1000 U every 3 or 4 days. The study, presented at the 2012 annual meeting of the American College of Allergy, Asthma and Immunology (ACAAI), provide evidence for the safety profile of **Cinryze[®]** (C1 esterase inhibitor [human]) at doses up to 2500 units in patients with HAE.

BioCryst Pharmaceuticals, Inc. is implementing a focused strategy to advance its HAE and antiviral programs. The restructuring is intended to significantly reduce the company's cost structure and scale the organization appropriately for its current portfolio. The company plans to direct its cash and other resources primarily to enable the achievement of important near-term milestones for the BCX4161 HAE, BCX4430 broad spectrum antiviral and BCX5191 hepatitis C (HCV) programs.



ViroPharma Incorporated has launched an unbranded campaign focusing on moments lost to HAE attacks to raise awareness among physicians of the emotional and psychological burden of HAE on patients' lives. The campaign can be found at www.momentsmissed.com.

At the American College of Allergy, Asthma and Immunology (ACAAI) 2012 Annual Scientific Meeting **Dyax Corp.** presented updated **Kalbitor®** (ecallantide) data in pediatric patients with HAE and HAE patients with abdominal attacks. The presentations pooled results from patients enrolled in four different clinical trials of ecallantide for the treatment of acute HAE attacks: DX-88/19, an open-label continuation study; EDEMA2®, an open-label, Phase 2 dose-ranging, repeat-dosing study; and EDEMA3® and EDEMA4®, two Phase 3 double-blind, placebo-controlled studies. Kalbitor® is indicated for the treatment of acute attacks of HAE in patients 16 years of age and older.

ViroPharma Incorporated has initiated its Phase 2b double blind, multicenter, dose ranging study to evaluate the safety and efficacy of subcutaneous administration of Cinryze® (C1 esterase inhibitor [human]) in combination with Halozyme's Enhance™ technology, a proprietary drug delivery platform using Halozyme's recombinant human hyaluronidase enzyme (rHuPH20), in adolescents and adults for prevention of HAE attacks. Cinryze is currently approved for intravenous administration.

From **CSL Behring**: According to Allergy & Asthma Proceedings – the official journal of Regional, State & Local Allergy, Asthma and Immunology Societies (RSLAAIS) and the American Association of Certified Allergists (AACAA) – a high level of health-related quality of life is achievable for patients managing HAE when effective treatment such as C1-inhibitor (INH) concentrate is available. More than half of the HAE patients participating in the assessment reported feeling somewhat or much better with the availability of C1-INH concentrate, and more than 80 percent of participants indicated a more optimistic outlook on the future.

Further information on these news can be found at www.haei.org.