

Zürich Switzerland 6th of April 2018 – EVAX AG today announced the publication of Proof of Concept results from a study in horses with a vaccine for treating insect-bite hypersensitivity (IBH) in the renowned Journal of Allergy and Clinical Immunology. The data is published online 4th of April 2018 in an article entitled “Treating insect-bite hypersensitivity in horses with active vaccination against IL-5”¹.

Furthermore, the paper on equine IBH is being published “back to back” with a manuscript entitled “Vaccination against IL-31 for the treatment of atopic dermatitis in dogs”². The vaccine described in this other work utilizes the same platform technology as that used by EVAX.

Antonia Gabriel (Fettelschoss), PhD, CEO of EVAX AG comments, “The positive result achieved with our therapeutic vaccine in IBH affected client-owned horses is a significant development milestone and suggests our product candidate has the potential to make a significant contribution to the treatment of this highly debilitating disease. The tandem publications also establish the ability of our therapeutic virus-like particle vaccine platform to induce clinically effective levels of neutralizing, target-specific antibodies and demonstrate its potential as a new class of veterinary biological medicine.”

The Journal of Allergy and Clinical Immunology publishes high-impact, cutting-edge clinical and translational research papers for allergists, immunologists, dermatologists, gastroenterologists, and other physicians and researchers interested in allergic diseases and clinical immunology. The JACI is the most-cited journal in the field of allergy and clinical immunology. (<http://www.jacionline.org/>)

About the IBH vaccine DERMA VAX

The vaccine candidate represents a unique and novel approach to treat IBH in horses. The vaccine utilizes a new enhanced vaccine platform combining latest biotechnological and immunological insights. Thus the vaccine platform is optimized for a high responder rate leading to induction of strong immunity³. This cutting-edge technology enables the latest advances in biologic medicines to be translated for use in companion animals at affordable prices - an option that will likely change the way we will medically treat our horses.

DERMA-VAX is a vaccine against allergic dermatitis and chronic irritations of the skin for horses that suffer from allergies such as IBH, also known as summer eczema or sweet itch, and other chronic skin problems. *DERMA-VAX* instructs the horse patients’ immune system to produce clinically effective levels of neutralizing target specific anti-cytokine antibodies, which resulted in dramatically improved disease symptoms in immunized horses. This has previously only been achieved by passive immunization with high amounts of monoclonal antibodies. *DERMA-VAX* is the first-in-class breakthrough therapy for IBH in horses demonstrating proof of concept for this class of medicine and thus enabling the development of similar vaccines targeting other diseases in the future.

About equine Insect-Bite Hypersensitivity (IBH)

Insect-bite hypersensitivity (IBH) of horses, also known as sweet itch, summer eczema, Kasen or Queensland itch manifests in a chronic relapsing seasonal allergic dermatitis caused by the biting of insects of the genus *Culicoides spp*⁴⁻⁸.

Culicoides midges are found in various areas of the world⁹⁻¹¹. The incidence of IBH strongly correlates with the geographical distribution of *Culicoides* showing highest incidence in some parts of Australia (60%)¹²⁻¹⁴. Overall, approximately 10% of all horses worldwide are affected by IBH¹⁵⁻¹⁸ and all breeds can succumb to the allergic disease in principal. IBH affected horses suffer during warmer months of the year from hairless, weeping and sometimes even ulcerative lesions caused by inflammation and severe itching. Lesions are characterized by hyperkeratosis, lichenification of the skin, bleeding, swelling, scales and crust formation. Histological hallmarks of IBH lesions are thickening of stratum corneum, epidermis and dermis, with abundant fibrosis in the latter¹². Commonly, bacteria, mites, and fungi as secondary infections can cause further local irritation, enhancing lesion formation.

IBH is classified as IgE-dependent type-I allergy¹⁹ with a strong involvement of type-IV allergy hypersensitivity reactions^{7,20}. Besides IgE-mediated crosslinking of the high-affinity IgE receptor (FcεRI) on mast cells and basophils with subsequent histamine release, type I allergies also consist of a late phase reaction with

eosinophilia and recruitment of eosinophils into the allergic site. Intradermal injection of *Culicoides* extract into IBH affected horses leads to recruitment of Th₂ cells and eosinophils to the site of injection²¹. Moreover, besides the role of IgE and type I allergy in IBH, an involvement of cell-mediated type IV allergic reaction, also called delayed-type hypersensitivity (DTH), has been discussed in recent years²².

Although IBH was first described already in 1840 and is currently the best characterized allergic disease in horses, treatment options are still poor and currently no satisfactory treatment of IBH is available^{12,22}.

References

- 1 Antonia Fettelschoss-Gabriel, V. F., Franziska Thoms, Christoph Giese, Michelle Daniel, Florian Olomski, Jivko Kamarachev, Katharina Birkmann, Maya Bühler, Martin Kummer, Andris Zeltins, Eliane Marti, Thomas M. Kündig, Martin F. Bachmann. Treating insect bite hypersensitivity in horses by active vaccination against Interleukin-5. *The Journal of Allergy and Clinical Immunology* (2018).
- 2 Martin Bachmann; Martin Fabian Bachmann, P. A. Z. G. K. I. B. N. F. A. R. K. T. C. F. Vaccination against IL-31 for the treatment of atopic dermatitis in dogs. *The Journal of Allergy and Clinical Immunology* (2018).
- 3 Andris Zeltins, J. W., Franziska Zabel, Aadil El Turabi, Ina Balke, Stefanie Haas, Melanie Maudrich, Federico Storni, & Paul Engeroff, G. T. J., Abhay Kotecha, David I Stuart, John Foerster and Martin F. Bachmann. Incorporation of tetanus-epitope into virus-like particles achieves vaccine responses even in older recipients in models of psoriasis, Alzheimer's and cat allergy. *Vaccines* (2017) **2** (2017).
- 4 Baker, K. P. & Quinn, P. J. A report on clinical aspects and histopathology of sweet itch. *Equine Vet J* **10**, 243-248 (1978).
- 5 Braverman, Y. *et al.* Epidemiological and immunological studies of sweet itch in horses in Israel. *Vet Rec* **112**, 521-524 (1983).
- 6 Anderson, G. S., Belton, P., Jahren, E., Lange, H. & Kleider, N. Immunotherapy trial for horses in British Columbia with *Culicoides* (Diptera: Ceratopogonidae) hypersensitivity. *J Med Entomol* **33**, 458-466 (1996).
- 7 Kurotaki, T., Narayama, K., Oyamada, T., Yoshikawa, H. & Yoshikawa, T. Immunopathological study on equine insect hypersensitivity ("kasen") in Japan. *J Comp Pathol* **110**, 145-152 (1994).
- 8 Anderson, G. S., Belton, P. & Kleider, N. *Culicoides* *obsoletus* (Diptera: Ceratopogonidae) as a causal agent of *Culicoides* hypersensitivity (sweet itch) in British Columbia. *J Med Entomol* **28**, 685-693 (1991).
- 9 Quinn, P. J., Baker, K. P. & Morrow, A. N. Sweet itch: responses of clinically normal and affected horses to intradermal challenge with extracts of biting insects. *Equine Vet J* **15**, 266-272 (1983).
- 10 Fadok, V. A. & Greiner, E. C. Equine insect hypersensitivity: skin test and biopsy results correlated with clinical data. *Equine Vet J* **22**, 236-240 (1990).
- 11 Greiner, E. C., Fadok, V. A. & Rabin, E. B. Equine *Culicoides* hypersensitivity in Florida: biting midges aspirated from horses. *Med Vet Entomol* **4**, 375-381 (1990).
- 12 Schaffartzik, A. *et al.* Equine insect bite hypersensitivity: what do we know? *Vet Immunol Immunopathol* **147**, 113-126, doi:10.1016/j.vetimm.2012.03.017 S0165-2427(12)00090-6 [pii] (2012).
- 13 van Grevenhof, E. M., Ducro, B., Heuven, H. C. & Bijma, P. Identification of environmental factors affecting the prevalence of insect bite hypersensitivity in Shetland ponies and Friesian horses in The Netherlands. *Equine Vet J* **39**, 69-73 (2007).
- 14 Steinman, A., Peer, G. & Klement, E. Epidemiological study of *Culicoides* hypersensitivity in horses in Israel. *Vet Rec* **152**, 748-751 (2003).
- 15 Halldorsdottir, S. & Larsen, H. J. An epidemiological study of summer eczema in Icelandic horses in Norway. *Equine Vet J* **23**, 296-299 (1991).
- 16 Bjornsdottir, S., Sigvaldadottir, J., Brostrom, H., Langvad, B. & Sigurdsson, A. Summer eczema in exported Icelandic horses: influence of environmental and genetic factors. *Acta Vet Scand* **48**, 3, doi:1751-0147-48-3 [pii] 10.1186/1751-0147-48-3 (2006).
- 17 Brostrom, H., Larsson, A. & Troedsson, M. Allergic dermatitis (sweet itch) of Icelandic horses in Sweden: an epidemiological study. *Equine Vet J* **19**, 229-236 (1987).
- 18 Marti, E., Gerber, H. & Lazary, S. On the genetic basis of equine allergic diseases: II. Insect bite dermal hypersensitivity. *Equine Vet J* **24**, 113-117 (1992).
- 19 Hellberg, W., Mellor, P. S., Torsteinsdottir, S. & Marti, E. Insect bite hypersensitivity in the horse: comparison of IgE-binding proteins in salivary gland extracts from *Simulium vittatum* and *Culicoides nubeculosus*. *Vet Immunol Immunopathol* **132**, 62-67, doi:10.1016/j.vetimm.2009.09.016 S0165-2427(09)00319-5 [pii] (2009).

- 20 Kurotaki, T. *et al.* Langerhans cells within the follicular epithelium and the intradermal sweat duct in equine insect hypersensitivity "Kasen". *J Vet Med Sci* **64**, 539-541 (2002).
- 21 McKelvie, J., Foster, A. P., Cunningham, F. M. & Hamblin, A. S. Characterisation of lymphocyte subpopulations in the skin and circulation of horses with sweet itch (*Culicoides* hypersensitivity). *Equine Vet J* **31**, 466-472 (1999).
- 22 Cunningham, F. M. & Dunkel, B. Equine recurrent airway obstruction and insect bite hypersensitivity: understanding the diseases and uncovering possible new therapeutic approaches. *Vet J* **177**, 334-344, doi:10.1016/j.tvjl.2007.10.005 (2008).

For further information, please contact:

EVAX AG Hörnlistrasse 3 CH-9542 Münchwilen

Antonia Gabriel, PhD

CEO

antonia@evax.ch

evax.ch

About EVAX AG

EVAX AG is a privately held Swiss biotechnology company that was formed as a spin-off from the University of Zurich in 2014. EVAX develops therapeutic vaccines for the treatment of chronic diseases in horses, such as equine allergies and respiratory diseases.

Forward looking statement. This communication does not constitute an offer or invitation to subscribe for or purchase any securities of EVAX AG. This publication may contain certain forward-looking statements and assessments or intentions concerning the company and its business. Such statements involve certain risks, uncertainties and other factors, which could cause the actual results, financial condition, performance or achievements of the company to be materially different from those expressed or implied by such statements. Readers should therefore not place reliance on these statements, particularly not in connection with any contract or investment decision. The company disclaims any obligation to update these forward-looking statements, assessments or intentions.

EVAX AG • Hörnlistrasse 3 • CH-9542 Münchwilen • hello@evax.ch • evax.ch