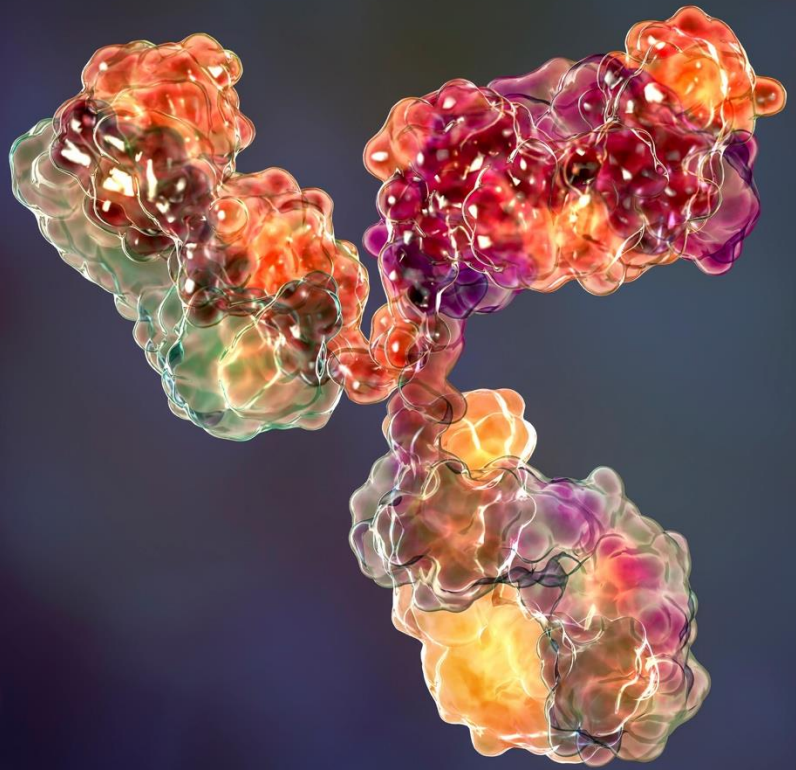
HNSA-5487 demonstrates very rapid and highly robust IgG reduction and clear redosing potential in Phase 1 FIH trial



HANSA BIOPHARMA

7 October 2024

Søren Tulstrup, CEO
Hitto Kaufmann, CR&DO

IgG cleaving technologies have the potential to transform autoantibody treatment landscape

80 + types of autoimmune diseases, which are chronic, unpredictable, and have debilitating, recurring symptoms. **IgG is a significant factor in many autoimmune diseases.**

Current approaches to care have **significant side effects, are time consuming, and may not be effective for all patients**. For many conditions there are no FDA approved treatments.

Clinical guidelines call for **fast, effective reduction of IgG** in both the acute and recurring stages of the disease.

Published data from pre-clinical models and NHP has **yet to be replicated in clinical trials.**

HNSA-5487 is a next generation IgG cleaving molecule engineered for high potency, specificity and safety. The NICE-01 study and 12-month follow up analysis aimed to demonstrate HNSA-5487's ability to very rapidly and robustly reduce IgG and establish redosing potential.

"List of Autoimmune Diseases". Autoimmune Registry Inc. https://www.autoimmuneregistry.org/autoimmune-diseases. Accessed June 4, 2024
Pisetsky, D.S. Pathogenesis of autoimmune disease. Nat Rev Nephrol 19, 509–524 (2023). https://doi.org/10.1038/s41581-023-00720-1
Theofilopoulos A N, Dixon F J. Adv Immunol. 1985;37:269–390.
Feldmann M, Brennan F M, Maini R N. Cell. 1996;85:307–310.
Kotzin B L. Cell. 1996;85:303–306.
Hellmich B, Sanchez-Alamo B, Schirmer JH, et al EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update Annals of the Rheumatic Diseases 2024;83:30-47.
Cherin P, Marie I, Michallet M, et al. Management of adverse events in the treatment of patients with immunoglobulin therapy: A review of evidence. Autoimmun Rev. 2016 Jan;15(1):71-81. doi: 10.1016/j.autrev.2015.09.002. Epub 2015.

HNSA-5487 is a next generation molecule that can very rapidly and robustly reduce IgG with clear redosing potential

HNSA-5487

- ❑ Next generation IgG cleaving enzyme based on an animal pathogen
- ❑ Inactivates IgG by cleaving the heavy chains of IgG, effectively eliminating the Fc-dependent effector functions
- ❑ Engineered for high potency, specificity and safety
- ❑ Immunogenicity profile that supports redosing potential
- ❑ Safe and well tolerated

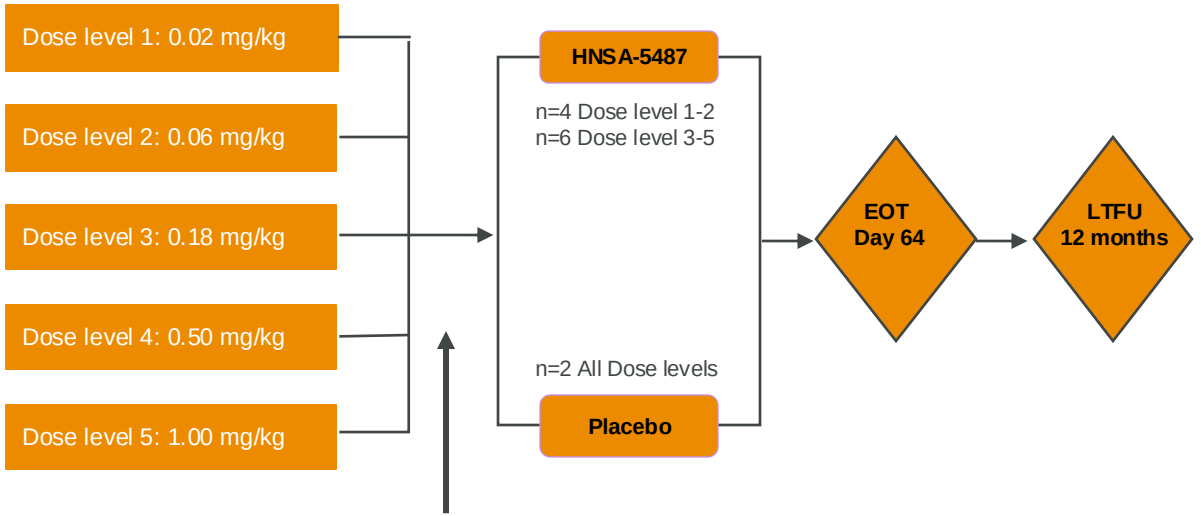
Rapid & robust IgG reduction	• Reduces IgG levels by more than 95 percent within a few hours • IgG levels returning to normal range six months after initial dosing • As efficacious as imlifidase in reducing total IgG levels
Redosing potential	• Lower ADA pre-treatment levels and significantly reduced ADA response as compared to imlifidase • Efficient IgG reduction in serum samples at six- and 12-months post initial dose
Address unmet need	• Focus where autoantibodies drive the disease • Need for management of symptoms at onset of disease and during recurrent immune system attacks • Diseases with little to no advanced treatment options

NICE-01 is the first in human trial of HNSA-5487

Key Takeaways

- PK and PD were in line with expectations
- No serious AEs, favorable safety and tolerability profile
- Additional analysis conducted to understand immunogenicity and potential for redosing

Double blind, randomized, placebo-controlled trial in 36 healthy volunteers received a single ascending doses of HNSA-5487 administered as a single intravenous (IV) infusion. Assessed safety, tolerability, PK and PD, and immunogenicity

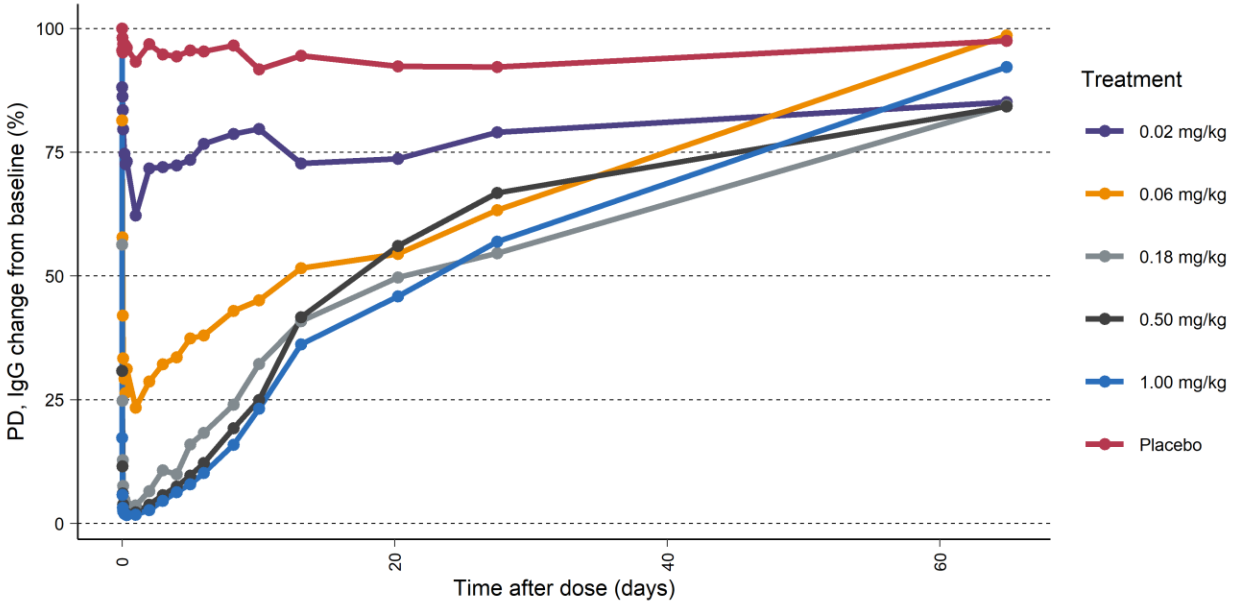


Acronyms: EOT = End of Trial; LTFU = Long term Follow-up

HNSA-5487 demonstrated rapid, robust reduction of IgG by 95% after a single dose

HNSA-5487 is as efficacious as imlifidase in reducing IgG levels

- In the analysis, IgG levels were reduced by more than 95 percent
- Six months after initial dosing, IgG levels returned to normal range



	0.02 mg/kg n=4	0.06 mg/kg n=4	0.18 mg/kg n=6	0.50 mg/kg n=6	1.00 mg/kg n=6	Imlifidase** 0.25 mg/kg n=23
Responders*	0%	25%	83%	100%	100%	88%

*A subject with IgG level <5% of baseline 24 hours post dosing
** Data from 18-HMedIdes-15 and 21-HMedIdeS-29

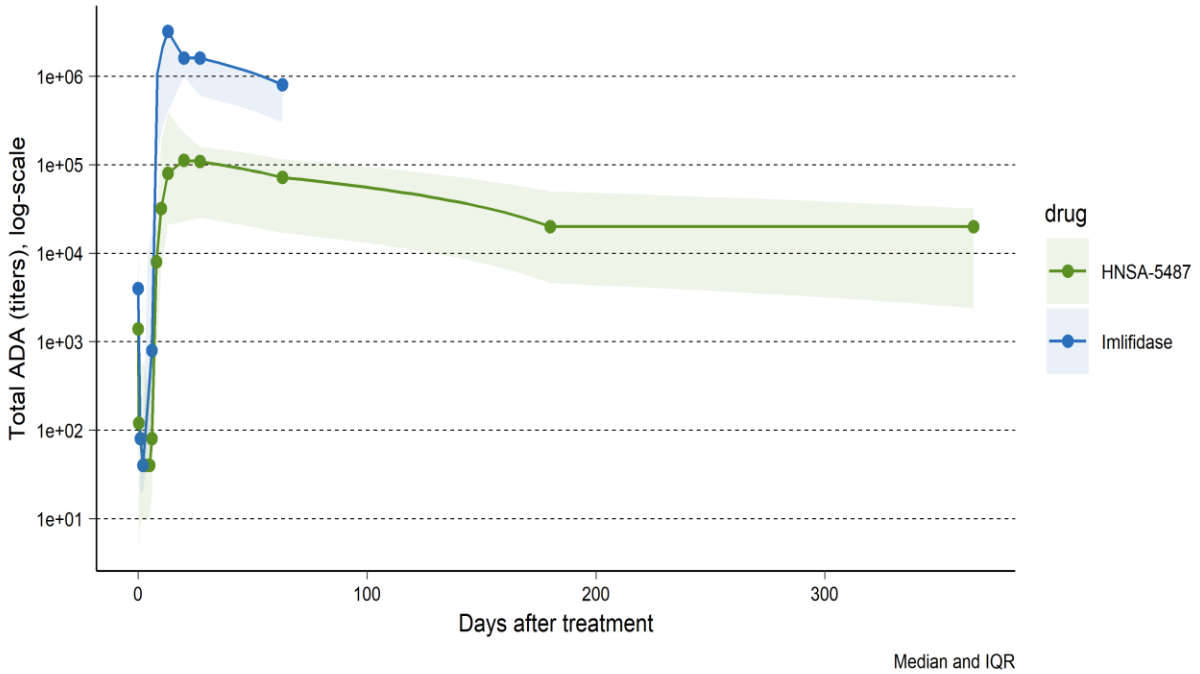
HNSA-5487 achieved lower peak ADA responses and faster return to cleavable levels confirming clear redosing potential

HNSA-5487 can be redosed effectively at six- and 12-months

- Lower pre-treatment levels and peak responses*
- Faster return to cleavable levels*
- Immunogenicity not dose dependent

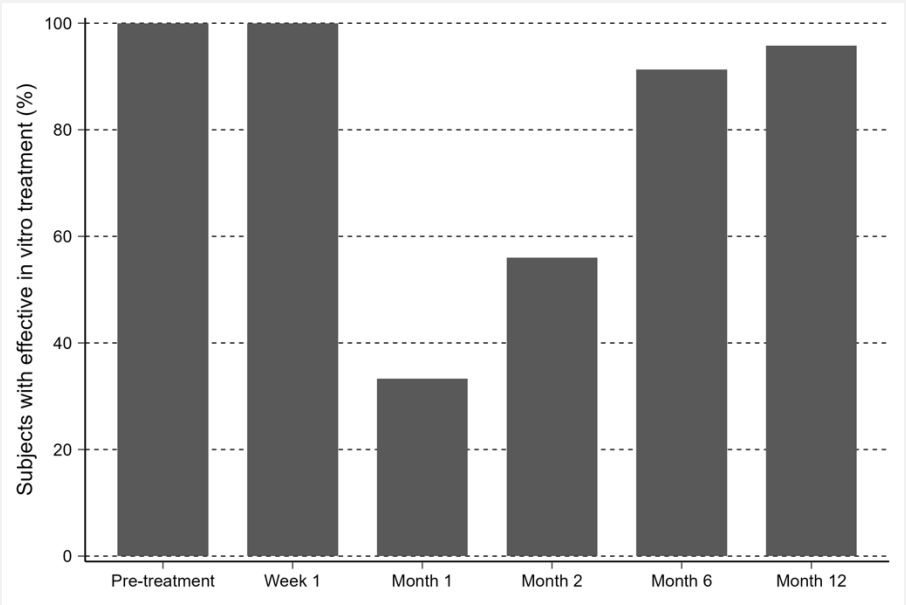
**As compared to imlifidase*

Data plotted using two separate Phase 1 trials in healthy human subjects
No head-to-head trial has been conducted between HNSA-5487 and imlifidase



HNSA-5487 data from NICE-01, healthy subjects (n=26)
Imlifidase data from 18-HMedIdeS-15, healthy subjects (n=11)

ADA reduction confirms HNSA-5487 redosing potential with optimized IgG reduction



HNSA-5487

Development of in vitro efficacy assay provided a method to assess potential redosing efficacy of HNSA-5487

Data confirmed potential for short term redosing to extend IgG low window

Data confirmed robust reduction in IgG levels in nearly 100 percent of samples collected in the trial at six- and 12-months after the initial dose

IMLIFIDASE

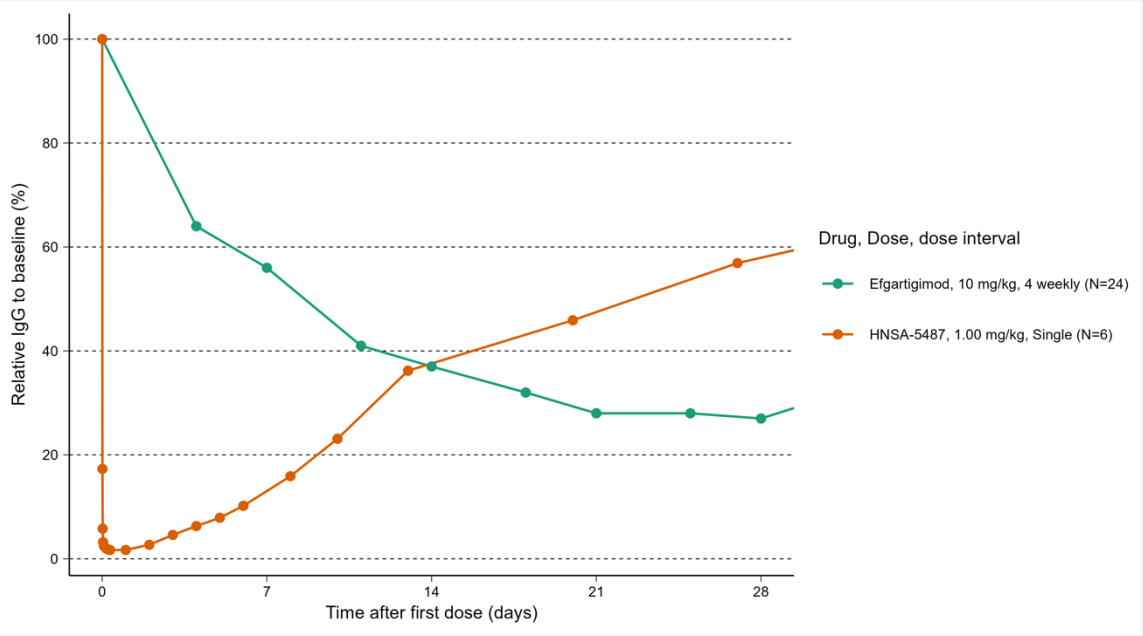
In healthy human subjects administered imlifidase, **ADA levels were not cleavable in any subjects after 2 months** and likely not in more than a few after 6 months

Only 40% of kidney transplant recipients* who received imlifidase had cleavable ADA levels after 6 months

**T-cell depletion, steroids, tacrolimus and mycophenolate mofetil*

HNSA-5487 is uniquely positioned to treat acute and chronic conditions due to its rapid IgG reduction

HNSA-5487 provides unmatched speed in reducing IgG



IgG cleaving enzymes cleave antibodies across all domains

IgG lowering modalities	Intravascular IgG	Extravascular IgG	Cell bound IgG
Imlifidase	✓	✓	✓
HNSA-5487	✓	✓	✓
FcRn inhibitor	✓	-	✗
PLEX	✓	✗	✗

Idefirix Summary of Product Characteristics. https://www.ema.europa.eu/en/documents/product-information/idefirix-epar-product-information_en.pdf. Accessed June 2024.
Gil I. Wolfe, E. Sally Ward, Hans de Haard, Peter Ulrichts, Tahseen Mozaffar, Mamatha Pasnoor, Gestur Vidarsson,. gG regulation through FcRn blocking: A novel mechanism for the treatment of myasthenia gravis, Journal of the Neurological Sciences,Volume 430, 2021,118074, ISSN 0022-510X,https://doi.org/10.1016/j.jns.2021.118074.(https://www.sciencedirect.com/science/article/pii/S0022510X2100770X).

An opportunity to address high unmet medical need in autoantibody driven conditions

Neuromyelitis Optica (NMO)

The body's immune system mistakenly attacks healthy cells and proteins in the body, most often those in the spinal cord and eyes

Symptoms

Eye pain and vision loss, weakness or paralysis of arms and legs, and severe vomiting and nausea.

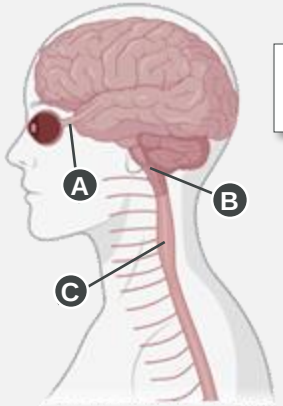
Prevalence

Approximately seven in every 100,000 people in the US. About 22,000 people in the US are living with the condition.

Treatment

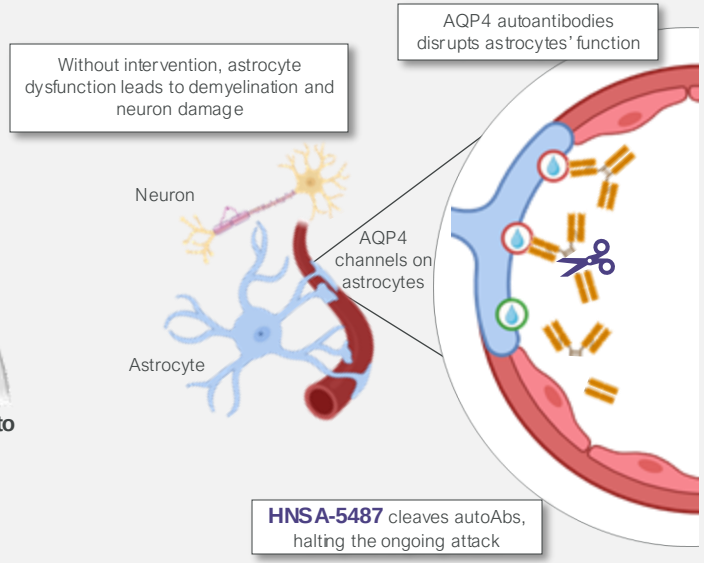
No cure for NMO. Relapses and attacks are treated with corticosteroid drugs and plasma exchange. **There are no approved drugs managing acute attacks, only for prevention of relapses.**

In NMO, more than 80% of patients have IgG antibodies against the water-channel aquaporin 4 (AQP4)*



Autoantibodies can lead to permanent damage to

A. Optic nerve
B. Brainstem
C. Spinal cord



*AQP4 is involved in cerebrospinal fluid transport in brain, water transport in the kidney collecting duct, aqueous humor transport in the eye, and airway hydration in the lung.

Created with BioRender.com

Briggs FB, Shaia J. Prevalence of neuromyelitis optica spectrum disorder in the United States. Multiple Sclerosis Journal. 2024;30(3):316-324. doi:10.1177/13524585231224683

Neuromyletis optica (NMO). Available at https://www.ninds.nih.gov/health-information/disorders/neuromyelitis-optica. Accessed on 17 September 2024.

An opportunity to address high unmet medical need in autoantibody driven conditions

Myasthenia Gravis (MG)

A rare, chronic autoimmune neuromuscular disorder that is characterized by fluctuating weakness of the voluntary muscle groups.

Symptoms

Weakness in eye muscles including double or blurred vision and drooping eyelid. Can develop widespread weakness in face, arms, or legs.

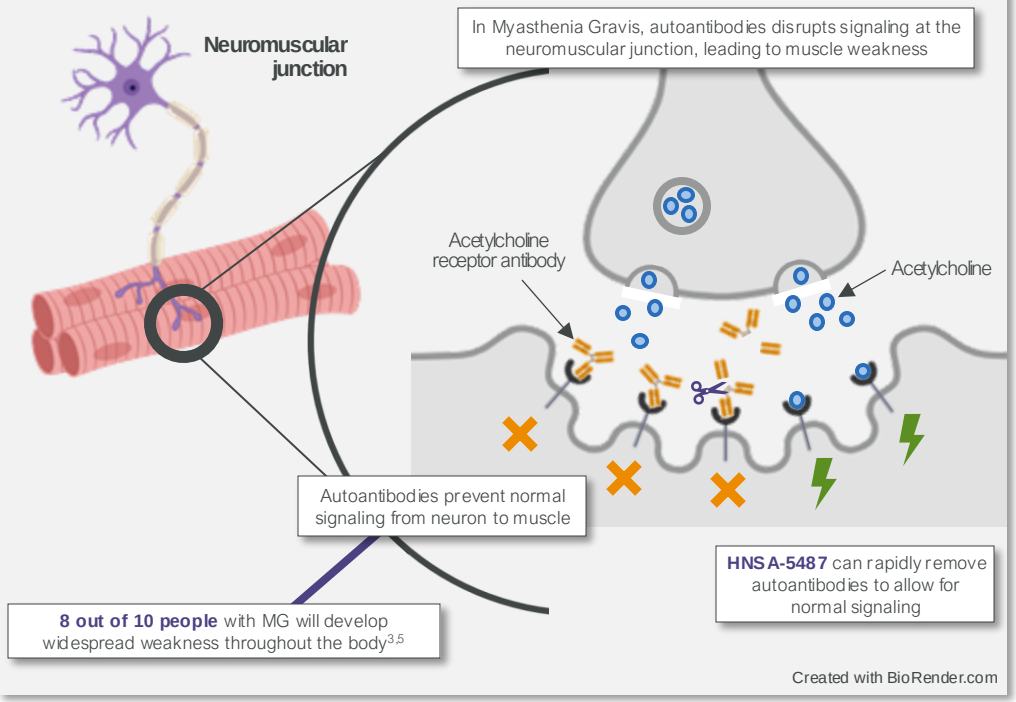
Prevalence

Globally, approximately 150 to 200 out of every million people have MG. In the US 37 out of every 100,000 people have MG.[3]

Treatment

Current immunomodulatory treatments do not achieve sufficient improvement or resolution of symptoms and more targeted therapies are needed.[4] **No approved treatments for severe exacerbations and myasthenic crisis.**

Most people with MG have IgG antibodies against the acetylcholine receptor



Dresser L, Wlodarski R, Rezania K, et al. Myasthenia gravis: epidemiology, pathophysiology and clinical manifestations. *J Clin Med* 2021; 10: 2235.

Schneider-Gold, Christiane, and Nils Erik Gilhus. "Advances and challenges in the treatment of myasthenia gravis." Therapeutic advances in neurological disorders vol. 14 17562864211065406. 21 Dec. 2021, doi:10.1177/17562864211065406

Punga A, Maddison P, Heckmann J, et al. Epidemiology, diagnostics, and biomarkers of autoimmune neuromuscular junction disorders. Lancet Neurol 2022; 21: 176–188.

An opportunity to address high unmet medical need in autoantibody driven conditions

Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD)

Inflammatory disorder of the central nervous system characterized by attacks of immune-mediated demyelination predominantly targeting the optic nerves, brain, and spinal cord.[6]

Symptoms

Changes in vision, weakness and numbness of the limbs, and paralysis caused by disruption of nerve signals.[7]

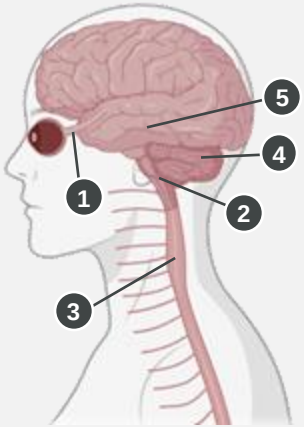
Prevalence

Affects 1.3 – 2.5 in every 100k people worldwide and approx. 30 percent of all cases are in children.[8]

Treatment

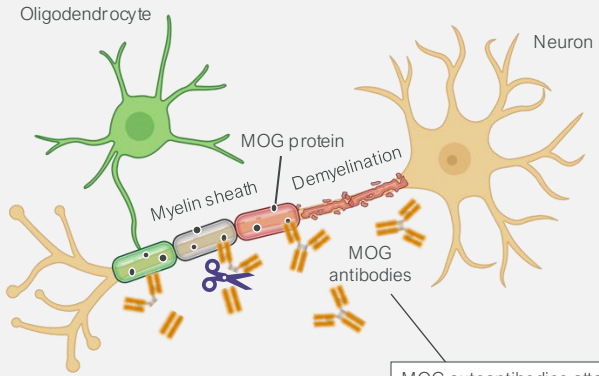
Treatment for sudden onset and long terms symptom management may include steroids, plasma exchange, intravenous immunoglobin, or immunosuppressants.
There are no approved treatments for MOG.

MOGAD is associated with the presence of antibodies directed against MOG which disrupts the transmission of nerve signals



Autoantibodies can lead to permanent damage to

1. Optic nerve
2. Brainstem
3. Spinal cord
4. Cerebellum
5. Cerebral White Matter

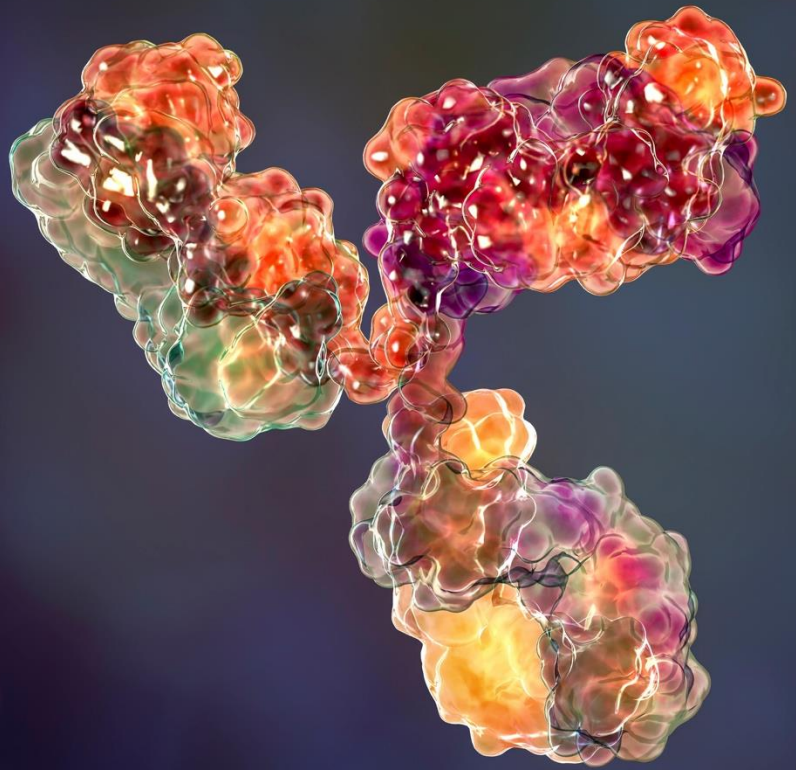


HNSA-5487 cleaves auto antibodies and may potentially stop disease progression and prevent permanent damage

Created with BioRender.com

Flanagan E, et al. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): Clinical features and diagnosis. Available at https://www.uptodate.com/contents/myelin-oligodendrocyte-glycoprotein-antibody-associated-disease-mogad-clinical-features-and-diagnosis#references. Accessed on September, 2024.
MOGAD Disorder and Multiple Sclerosis: Understanding Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD). National MS Society. March 2023. https://www.nationalmssociety.org/understanding-ms/what-is-ms/related-conditions/mogad. Accesses 17 September 2024.
Hor, Jyh Yung, and Kazuo Fujihara. "Epidemiology of myelin oligodendrocyte glycoprotein antibody-associated disease: a review of prevalence and incidence worldwide." Frontiers in neurology vol. 14 1260358. 15 Sep. 2023, doi:10.3389/fneur.2023.1260358.

HNSA-5487 demonstrates very rapid and highly robust IgG reduction and clear redosing potential in Phase 1 FIH trial



HANSA BIOPHARMA

7 October 2024

Søren Tulstrup, CEO
Hitto Kaufmann, CR&DO