Novel Bispecific Degrader BHV-1310 Achieves Rapid, Robust and Selective IgG Reduction in Preclinical Models Including Nonhuman Primates

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Anna Bunin, Ph.D. is an employee of and holds stock/stock options in Biohaven Pharmaceuticals.

Biohaven's Novel Degrader Platform: Design Characteristics

FAST AND DEEP

Removes disease-causing proteins within hours

EASY-TO-USE

- Easy-to-use autoinjector for self-administration
- Allows for concomitant use of biologics

PATIENT CENTRIC

LIFE ALTERING

SELECTIVE

Designed to target specific pathogenic species for maximal efficacy and minimal side effects

TUNABLE

- Level of degradation carefully modulated by dose level and frequency
- Employs body's natural mechanism for removal of senescent proteins

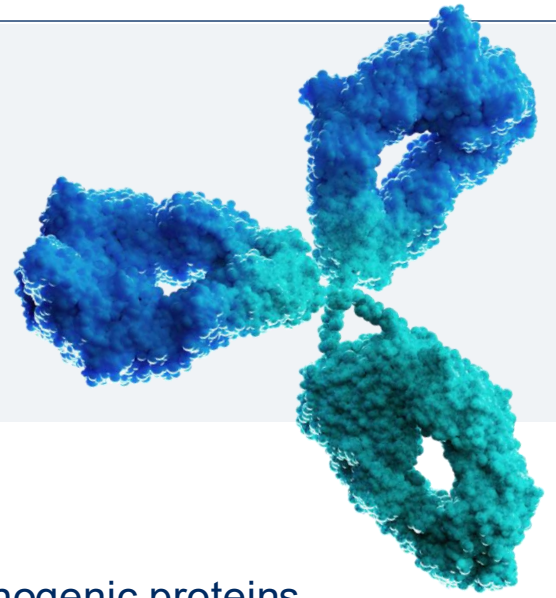
Targeted Extracellular Protein Degradation is a Next-Generation Approach for Treating Antibody Mediated Diseases

ANTIBODY MEDIATED NEUROLOGICAL DISEASES SUCH AS MYASTHENIA GRAVIS

Pathogenic autoantibodies (IgG) target specific components of the nervous system leading to disease onset and progression

EXTRACELLULAR PROTEIN DEGRADATION CAN LOWER PATHOGENIC ANTIBODIES

Potentially offers significant advantages over existing therapeutic approaches



MOLECULAR DEGRADER OF EXTRACELLULAR PROTEIN (MoDE™)

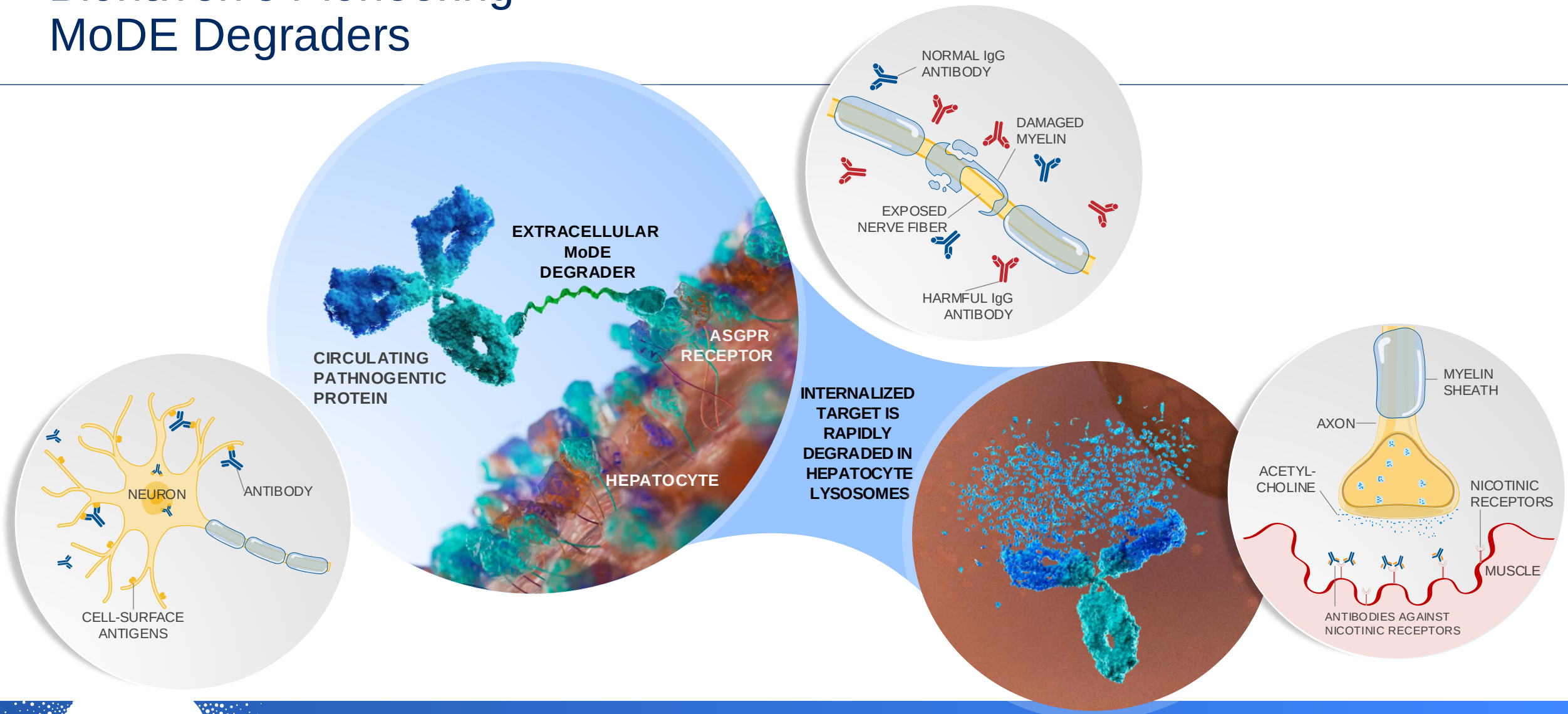
- Powerful new approach to treat antibody mediated diseases
- Harnesses the body's protein recycling machinery to degrade pathogenic proteins
- Several potential benefits compared to other IgG lowering therapies (FcRn inhibitors)

FIRST-IN-CLASS IgG LOWERING

- **Rapid onset of IgG lowering**
- **Depth of IgG lowering**
- **Lower risk of infection**
- **SC self-administration**
- **Co-administration with Fc-containing biologics**

SC, subcutaneous; **FcRn,** neonatal Fc receptor; **IgG**, immunoglobulin.

Biohaven's Pioneering MoDE Degraders



KEY POINT

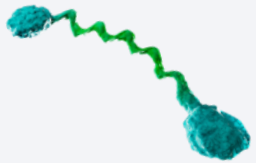
Poised to transform the treatment of neurological disorders across therapeutic areas:
Myasthenia Gravis | CIDP | Autoimmune encephalitis | NMOSD | MOGAD

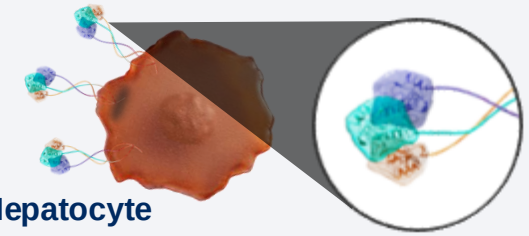
A Novel Mechanism: Hepatic ASGPR Receptor Harnessed for Efficient and Safe Removal of Circulating Pathogenic Targets

Legend

Degradation Target

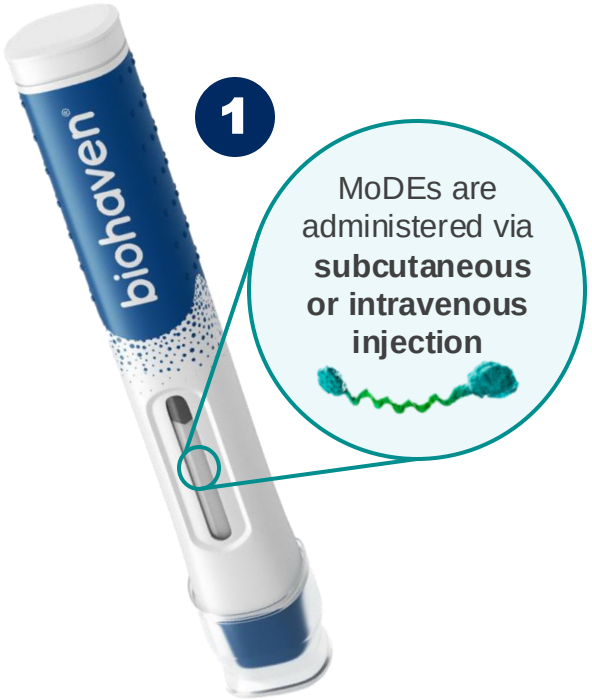
Bifunctional MoDE Degrader





Hepatocyte

Asialoglycoprotein Receptor* on hepatocyte

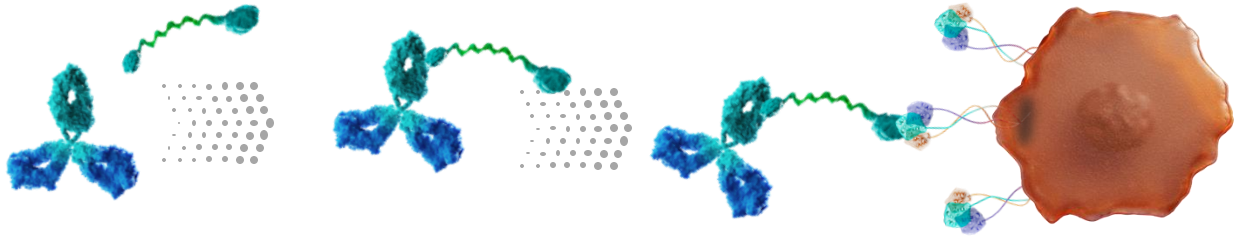


1

MoDEs are administered via **subcutaneous or intravenous injection**

2

MoDE™ degrader binds circulating target and efficiently delivers it to ASGPRs on hepatocytes



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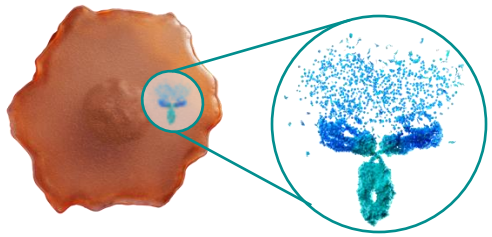
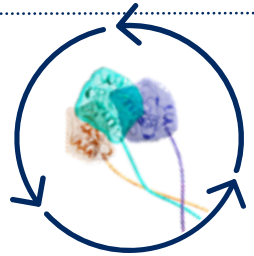


- Internalized target is rapidly degraded in hepatic lysosomes
- Degree of target degradation is precisely controlled

4

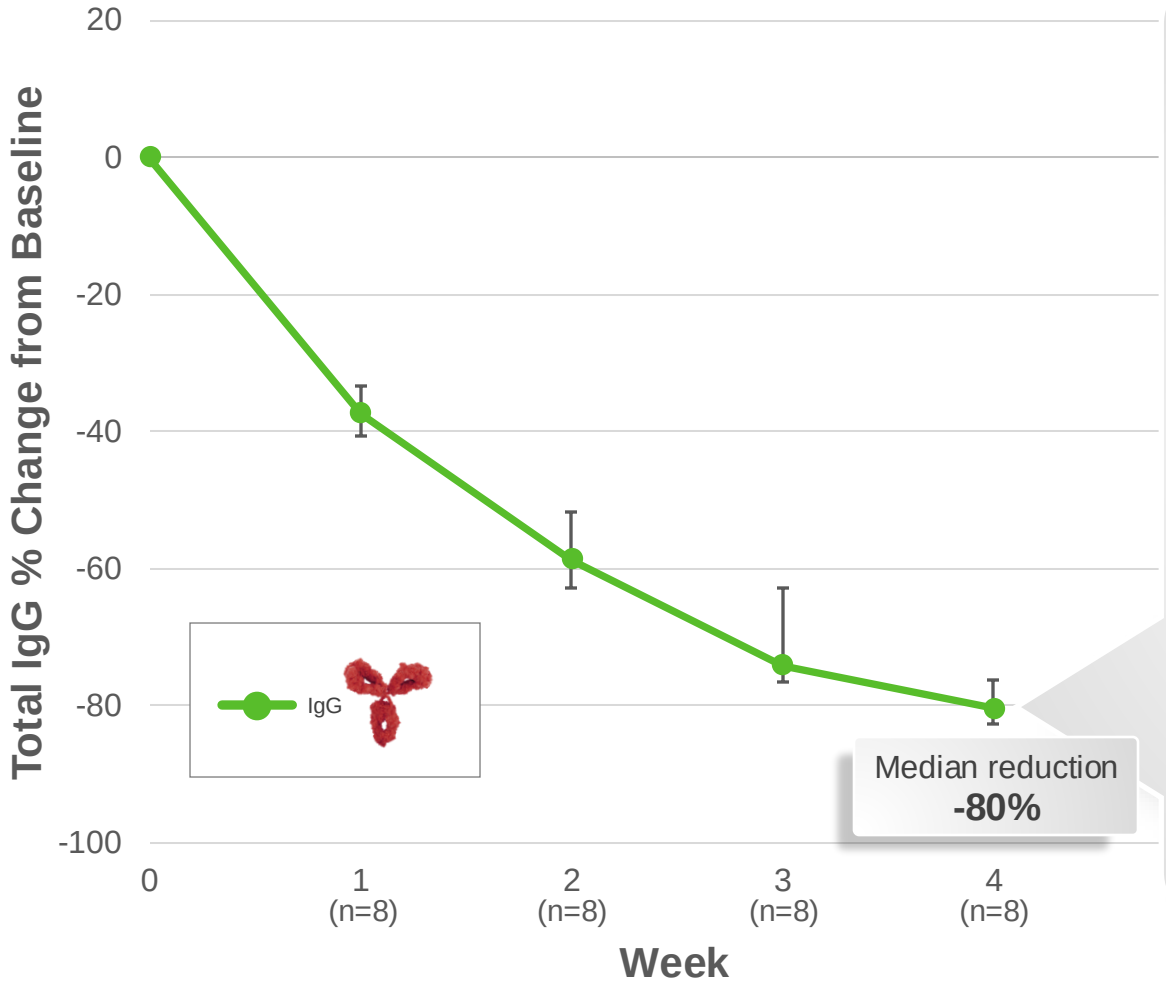


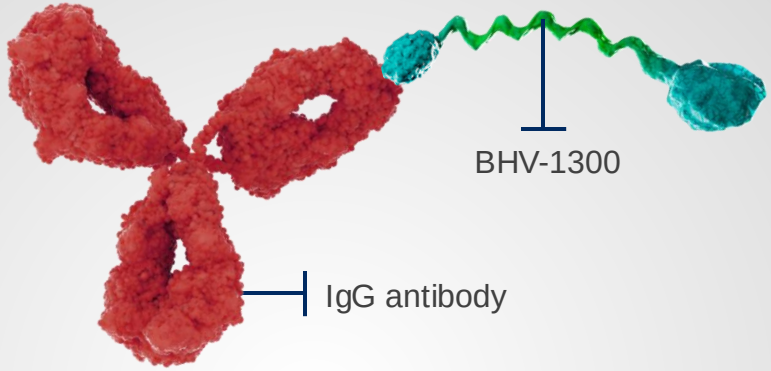
- ASGPRs are rapidly recycled
- Optimized safety and efficacy is achieved through balancing of relative affinities for ASGPR and target protein

*Stylistic representation

ASGPR, asialoglycoprotein receptor; **MoDE™**, molecular degraders of extracellular proteins

BHV-1300: SC Clinical Dosing Deeply Reduces Total IgG by up to 84% With a Median of 80% Reduction With 1000mg Weekly Dosed for Four Weeks

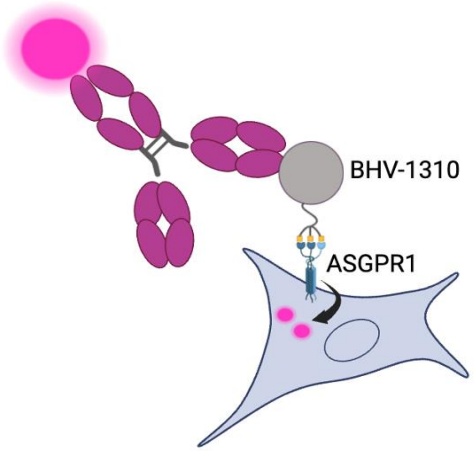




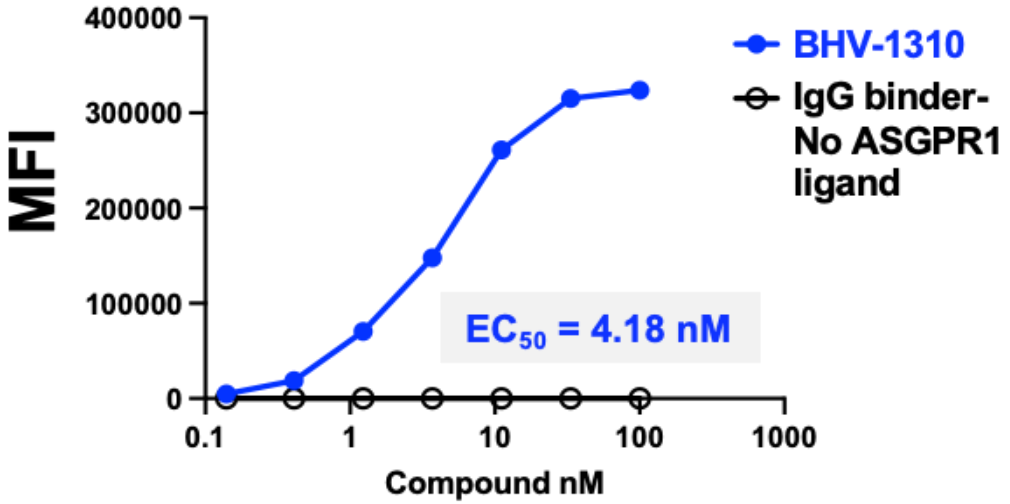
Subcutaneous BHV-1300 achieved reductions in total IgG up to 84% with a median reduction of 80% by day 25

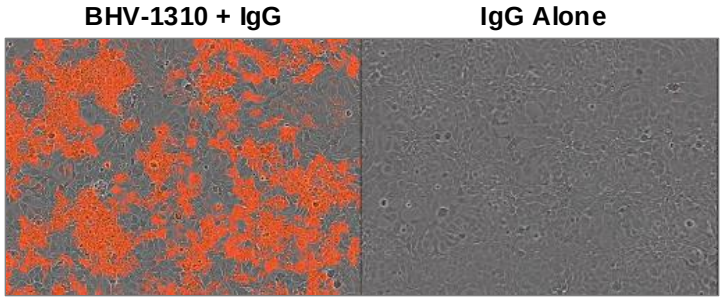
Baseline is the Average of Day -1 and Day 1 Pre-dose
Solid dot represents the median of the maximal total IgG % change from baseline at each week and bars represent the 25th and 75th percentiles

MoDE™ IgG Degrader Results in Rapid and Efficient IgG Lowering via Uptake and Degradation in ASGPR expressing cells



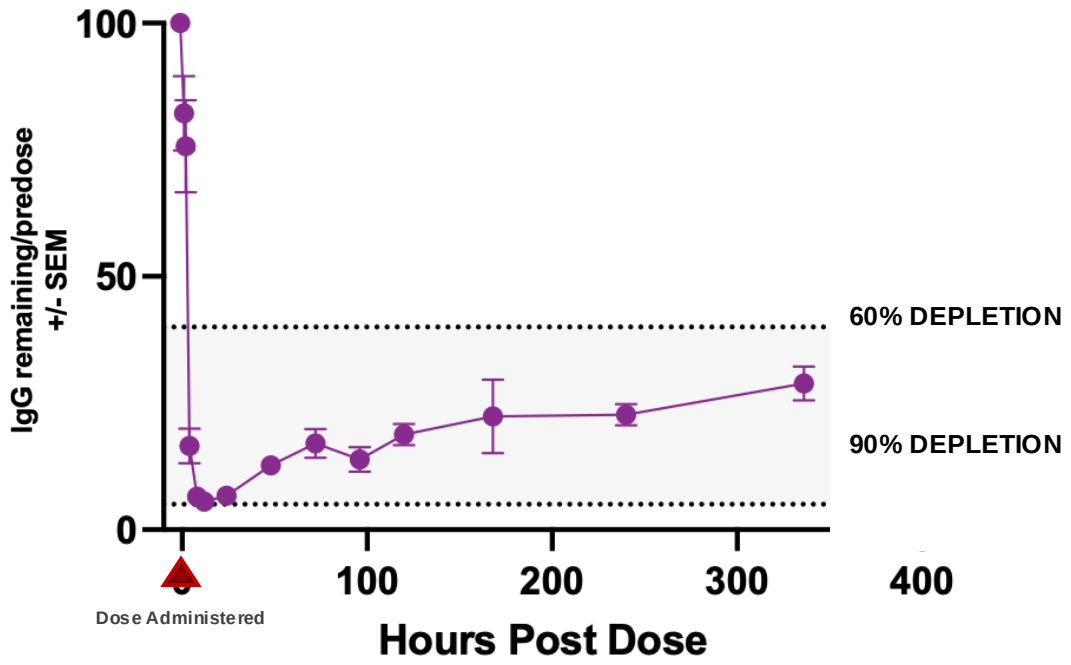
Internalization and Degradation in Cells





Single Dose Administration of BHV-1310 Results in 90% IgG Reduction in Preclinical Species

BHV-1310 Preclinical Pharmacodynamics
(Single Dose)



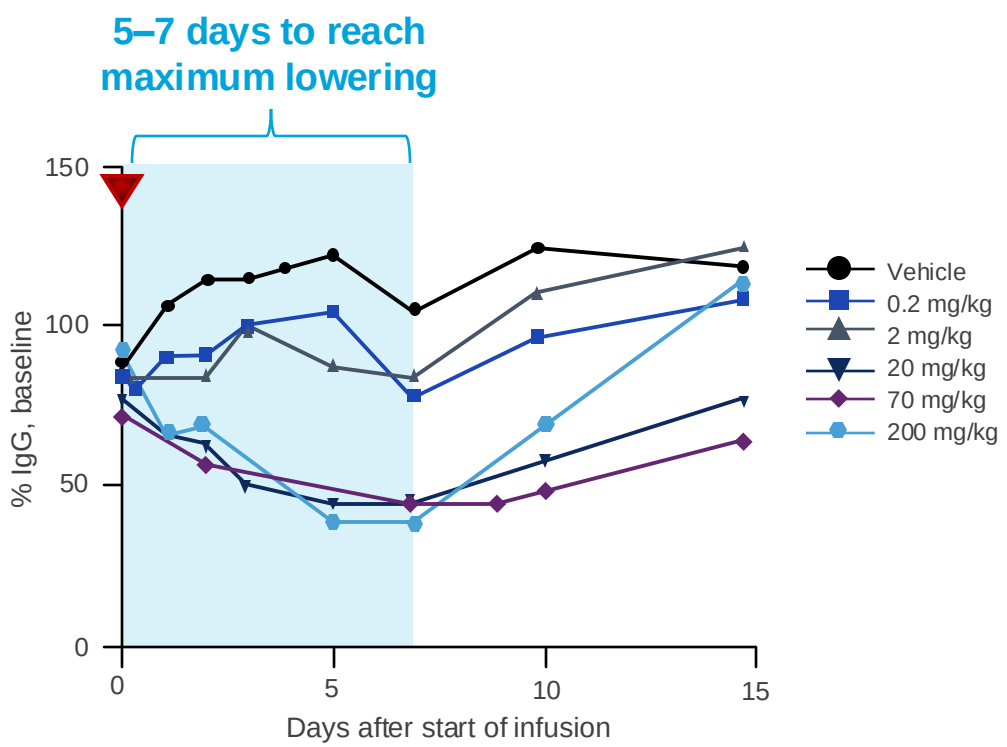
ACUTE indications — e.g., myasthenia gravis

KEY POINT

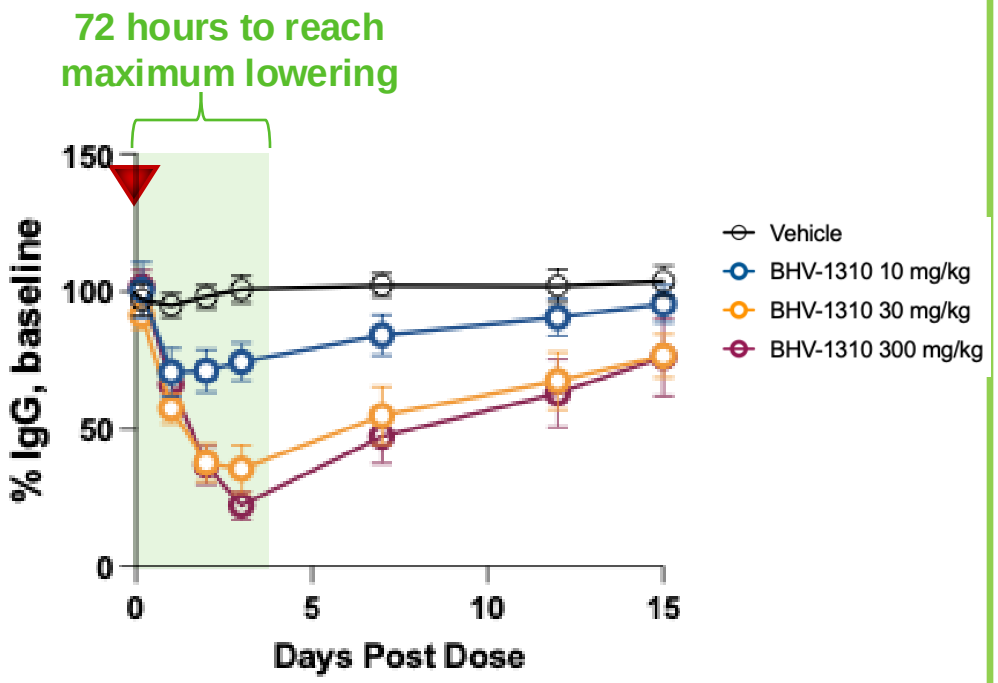
Optimization of degrader technology (BHV-1310) allows for deeper reductions in IgG after single dose

BHV-1310 Demonstrates Potential for Superior Clinical Efficacy Compared to FcRn Inhibitors

Efgartigimod NHP Pharmacodynamics



BHV-1310 NHP Pharmacodynamics

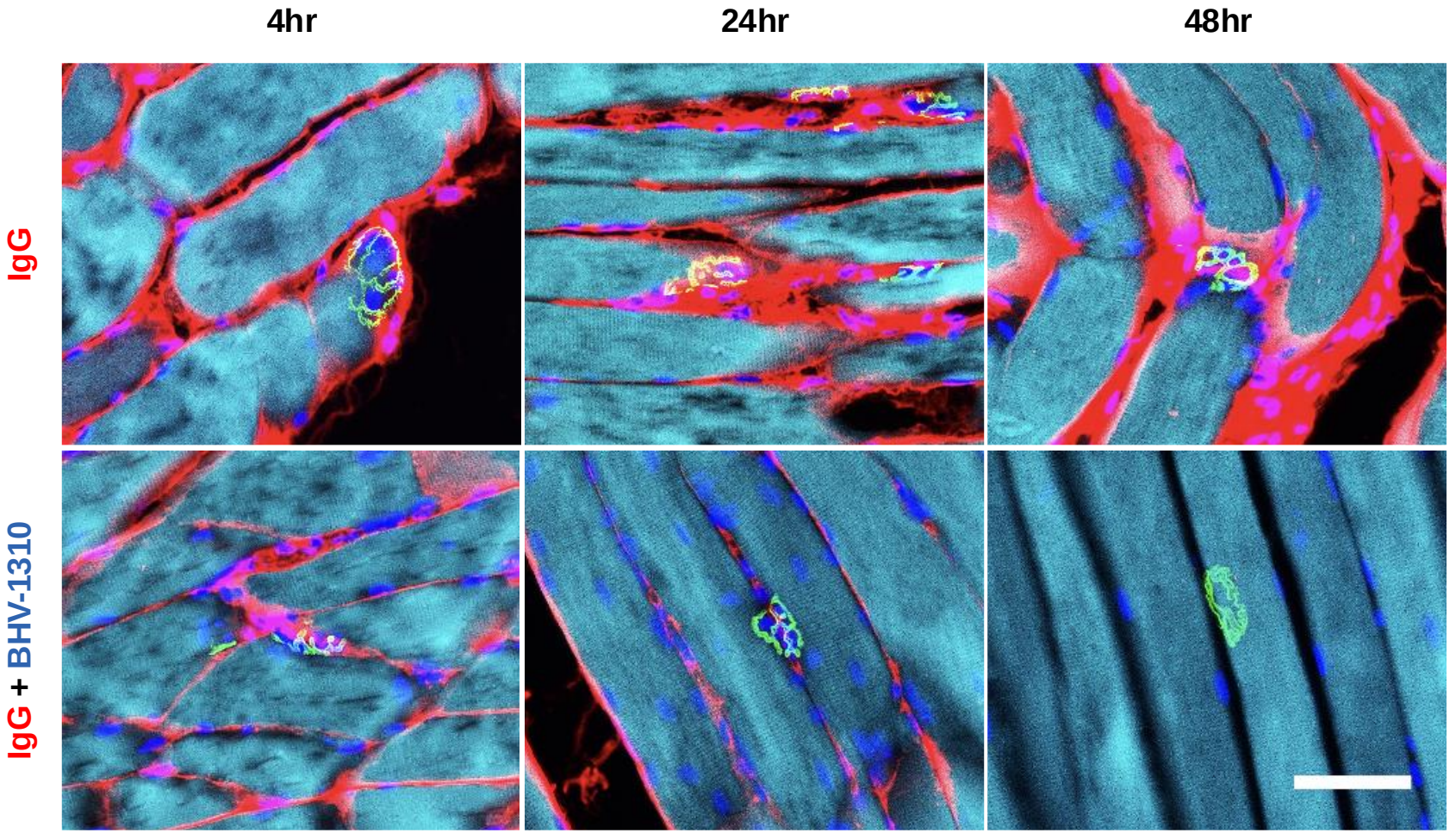


Ulrichts P et al, J Clin Invest. 2018 Oct 1;128(10):4372-4386. doi: 10.1172/JCI97911. Epub 2018 Jul 24. PMID: 30040076; PMCID: PMC6159959.

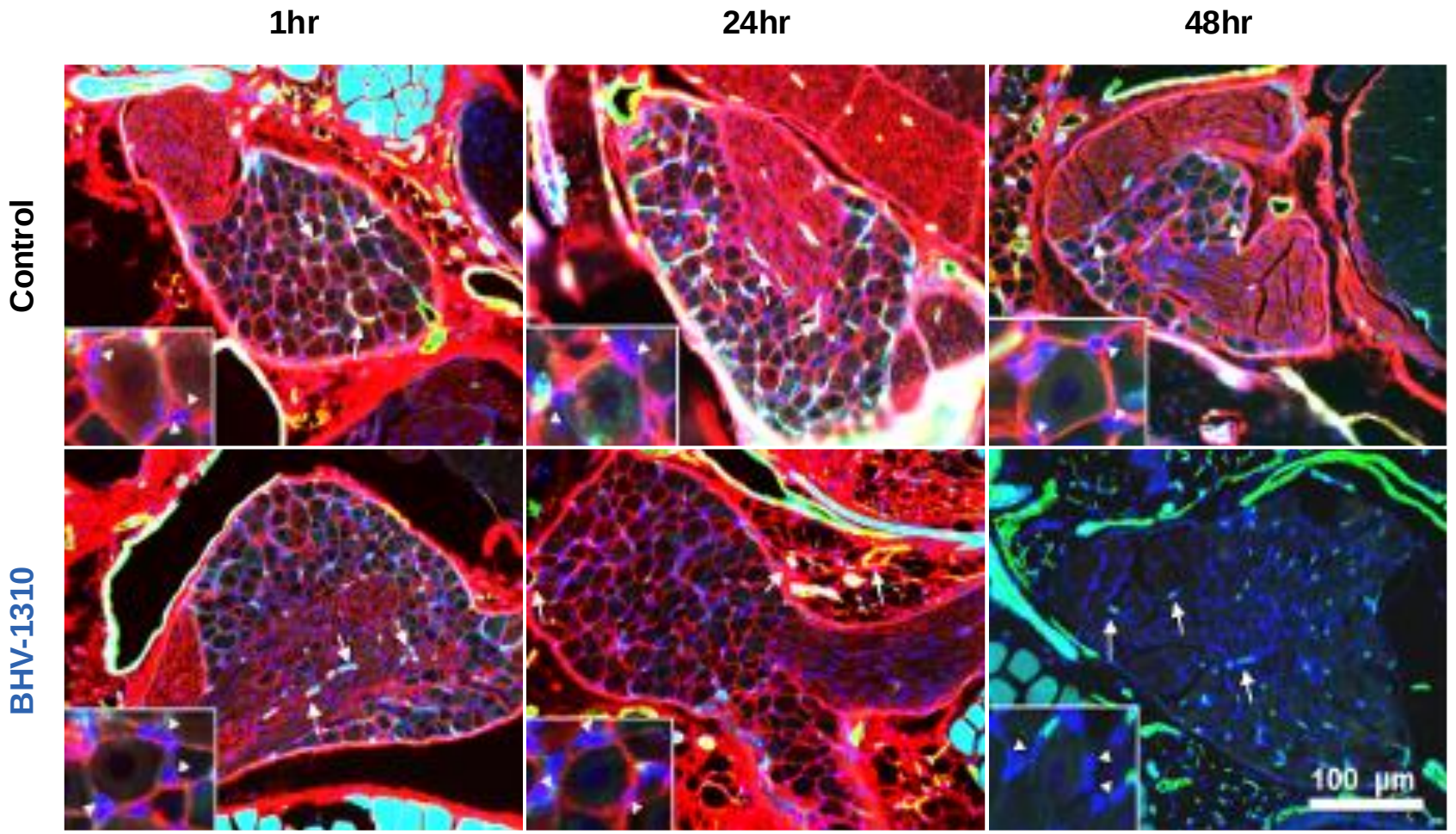
KEY POINT

BHV-1310 achieves more rapid and deeper IgG lowering than FcRn inhibitors

BHV-1310 Administration in a Mouse Model Results in Clearing of IgG From Interstitial Space at Neuromuscular Junction



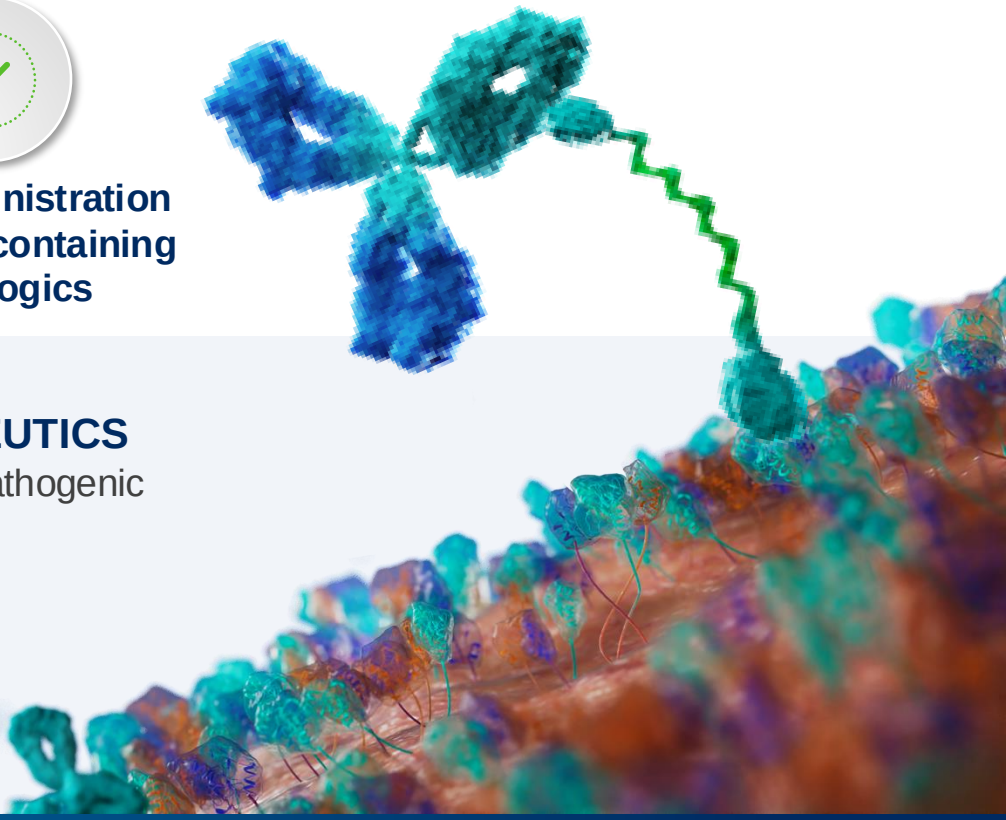
BHV-1310 Administration in a Mouse Model Results in Clearing of IgG From Interstitial Space around Dorsal Root Ganglion



Targeted Extracellular Protein Degradation is a Next-Generation Approach for Treating Antibody Mediated Diseases

MoDE™ degraders offer many potential advantages:

- **Rapid onset of IgG lowering**
- **Depth of IgG lowering**
- **Lower risk of infection**
- **SC self-administration**
- **Co-administration with Fc-containing biologics**



MoDE™: AN INNOVATIVE PLATFORM FOR A PIPELINE OF THERAPEUTICS

Potential to develop numerous clinical drug candidates for targeted degradation of pathogenic antibodies and other extracellular proteins to treat a broad range of diseases

NOVEL MODULAR IgG LOWERING PLATFORM

Exemplify a first-in-human approach for efficient removal of pathogenic IgG species in multiple antibody mediated disorders

FcRn, neonatal Fc receptor; **IgG**, immunoglobulin.