biohaven®

DAYS MATTER™

Biohaven R&D Day

May 28, 2025

BHVN
LISTED
NYSE

Forward-Looking Statements

This presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statements about Biohaven Ltd. (the “Company”) and our planned and ongoing trials for our troriluzole, taldefgrobep alfa, BHV-7000, BHV-2100, BHV-8000, BHV-1300, BHV-1400, BHV-1510, and BHV-1600 development programs, the timing of and the availability of data from our clinical trials, the timing and our decisions to proceed with our planned regulatory filings, the timing of and our ability to obtain regulatory approvals for our product candidates, the clinical potential utility of our product candidates, alone and as compared to other existing potential treatment options, and the potential advancement of our early phase programs including BHV-1310, BHV-1530, and BHV-1500. The use of certain words, including “continue”, “plan”, “will”, “believe”, “may”, “expect”, “anticipate” and similar expressions, is intended to identify forward-looking statements. Investors are cautioned that any forward-looking statements, including statements regarding the future development, timing and potential marketing approval and commercialization of our development candidates, including the potential FDA approval and commercialization of troriluzole for SCA, are not guarantees of future performance or results and involve substantial risks and uncertainties. Actual results, developments and events may differ materially from those in the forward-looking statements as a result of various factors including: the expected timing, commencement and outcomes of Biohaven's planned and ongoing clinical trials; the timing of planned interactions and filings with the Food and Drug Administration, including those regarding the potential FDA approval of troriluzole for SCA; the timing and outcome of expected regulatory filings; complying with applicable U.S. regulatory requirements; the potential commercialization of Biohaven's product candidates; the potential for Biohaven’s product candidates to be first-in-class, best-in-class, best-in-clinic or best-in-category therapies; and the effectiveness and safety of Biohaven's product candidates, including open label clinical data in ongoing studies. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. Additional important factors to be considered in connection with forward-looking statements are described in the Company’s filings with the Securities and Exchange Commission, including within the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations”. This presentation also contains market data and other information based on industry publications, reports by market research firms or published independent sources. Some market data and information are also based on the Company’s good faith estimates, which are derived from management’s knowledge of its industry and such independent sources referred to above.

WELCOME

Vlad Coric, MD

Chairman and Chief Executive Officer

biohaven®

BHVN
LISTED
NYSE

DIVERSIFIED PORTFOLIO

TOP AREAS OF INNOVATION

RARE DISEASE

ONCOLOGY

RENAL

CARDIOVASCULAR

OBESITY

NEUROSCIENCE

IMMUNOLOGY & INFLAMMATION

CLINICALLY VALIDATED MoDE™ AND TRAP™ DEGRADERS

ADVANCING CANCER TREATMENTS

Integrated **DISCOVERY ENGINE**

PIONEERING THERAPIES FOR RARE DISEASES

Working Towards Commercialization of **NOVEL THERAPEUTICS**

INNOVATING
EXECUTING
CREATING VALUE

biohaven®

biohaven®

Pioneering Degrader Platform
With 3 Assets in the Clinic

Initiating Pivotal Trials
Graves' — 2H 2025
IgAN — 1H 2026
Myasthenia gravis — 1H 2026
β1AR — 2H 2026

Proprietary ADC Platform and
Collaboration with Merus Bispecifics

2 ADCs in the Clinic
First-in-Clinic FGFR3 ADC
TROP2 Combo with Anti-PD-1

Weight Loss
Phase 2 Obesity — 2H 2025

SMA Path Forward
FDA Interaction — 1H 2025

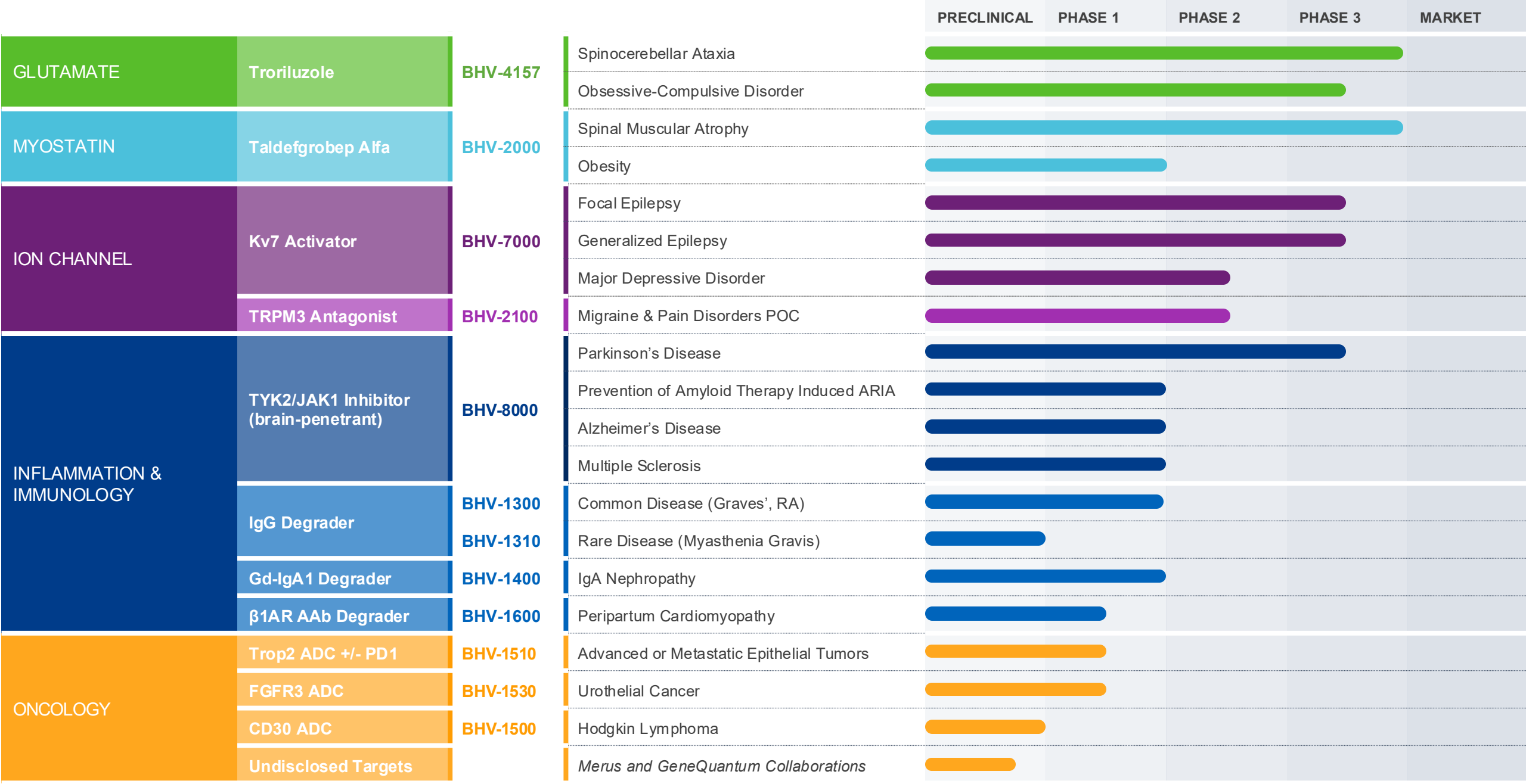
Kv7 Program Expecting Pivotal
Topline Results
Depression — 2H 2025
Epilepsy — 1H 2026

TRPM3 Completed Phase 1
**Proof of Concept Across Pain
Disorders 2025–2026**

Neuroinflammation
**Initiated Early Parkinson's —
1H 2025**

SCA NDA Under Priority Review
PDUFA — 2H 2025

INNOVATING
EXECUTING
CREATING NEAR-TERM VALUE



ARIA, Amyloid-related imaging abnormalities; **AAb**, Autoantibody.

Melissa Beiner, MD

Senior Medical Director

biohaven®

John Tilton

Chief Commercial Officer, Rare Disease

biohaven®

Patricia E. Greenstein, MB.BCh

Neurology Residency Training Program, Assistant Professor

HARVARD MEDICAL SCHOOL

Jennifer

Living with SCA3

Participant in the Troriluzole Clinical Study

Glutamate

biohaven®

Melissa Beiner, MD

Senior Medical Director

biohaven®

Glutamate Platform — Troriluzole Clinical Impact

Troriluzole US NDA Currently Under Priority Review for SCA

2H 2025

biohaven®

Significant Unmet Need in SCA With No Available Treatment

- Rare, relentlessly progressive, inherited neurodegenerative disease
- ~15,000 patients in US

US Priority Review of NDA With FDA Is Underway

- Completed mid-cycle review and inspections of HQ and clinical trial sites
- Preparing for Advisory Committee and late-cycle meetings
- PDUFA date 2H 2025

Efficacy and Safety Demonstrated Over 8 Years

- Study 206-RWE met prespecified primary endpoint (f-SARA at Year 3) in all SCA genotypes
- Additional confirmatory evidence from Study 206-RWE, Study 206 and Study 201

Biohaven Will Be Ready to Serve Patients Upon Anticipated Approval

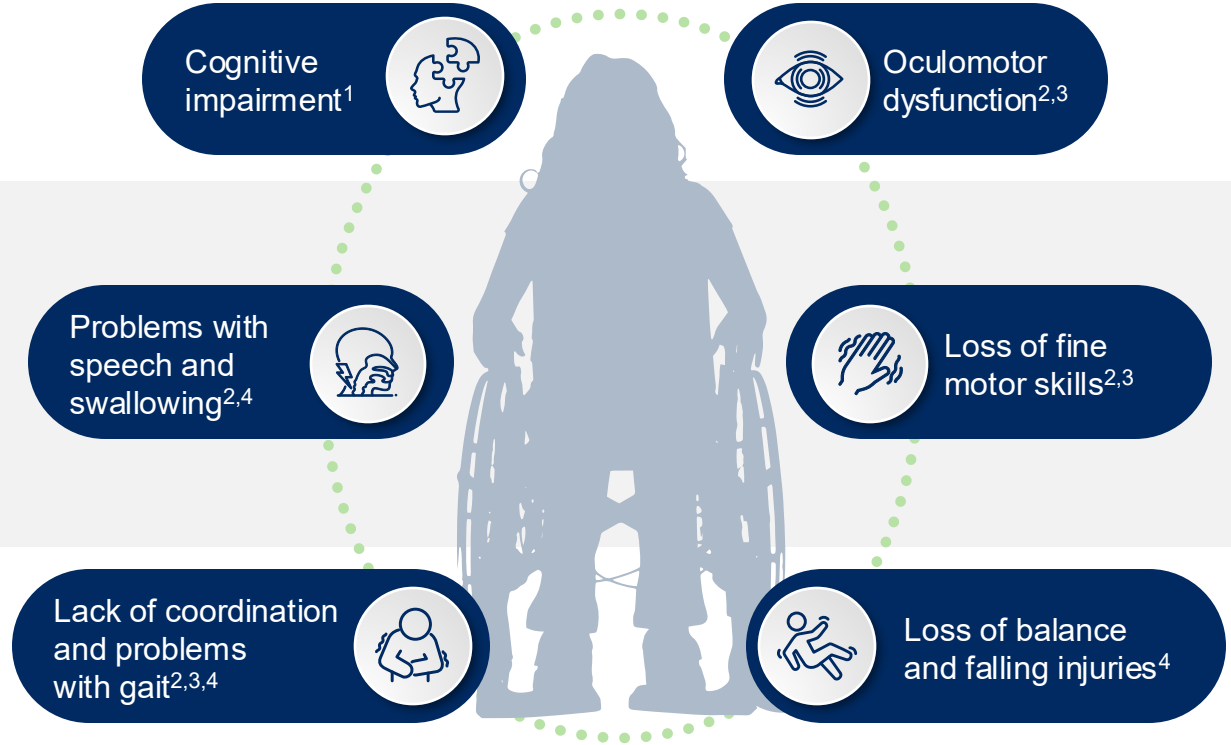
- EAP currently expanding across multiple sites in the US due to patient demand
- Preparing for US commercial launch in 2H 2025 in event of approval

SCAs Are Characterized by Relentlessly Progressive Cerebellar Degeneration and Premature Death

TRORILUZOLE

CLINICAL HALLMARKS OF SCA

Autosomal Dominant
SCA genotypes differ in:
- **Range of symptoms[5]**
- **Disease severity and progression[5]**



Increasing disability over time with wheelchair dependence, inability to carry out activities of daily living and progressive speech impairment

1. Moriarty A, et. al. Orphanet *J Rare Dis*. 2016;11(1):82. 2. National Ataxia Foundation. Accessed May 12, 2025. https://www.ataxia.org/what-is-ataxia/#whatIsAtaxia. 3. Klockgether T, et al. *Nat Rev Dis Primers*. 2019;5(1):24. 4. NIH. Accessed May 12, 2025. https://www.ninds.nih.gov/health-information/disorders/spinocerebellar-ataxias-including-machado-joseph-disease. 5. Brooker SM, et al. *Ann Clin Transl Neurol*. 2021;8(7):1543-1556.

KEY POINT

Troriluzole will be the first treatment for people living with SCA (if approved)

Troriluzole Restores Glutamate Homeostasis and Delays Disease Progression Across SCA Genotypes

TRORILUZOLE

Strong Mechanistic Rationale

Preclinical and clinical evidence for role of glutamate in SCA

Clinically Meaningful Effect on f-SARA

Clear evidence for troriluzole benefit in SCA

Impact on Disease Progression

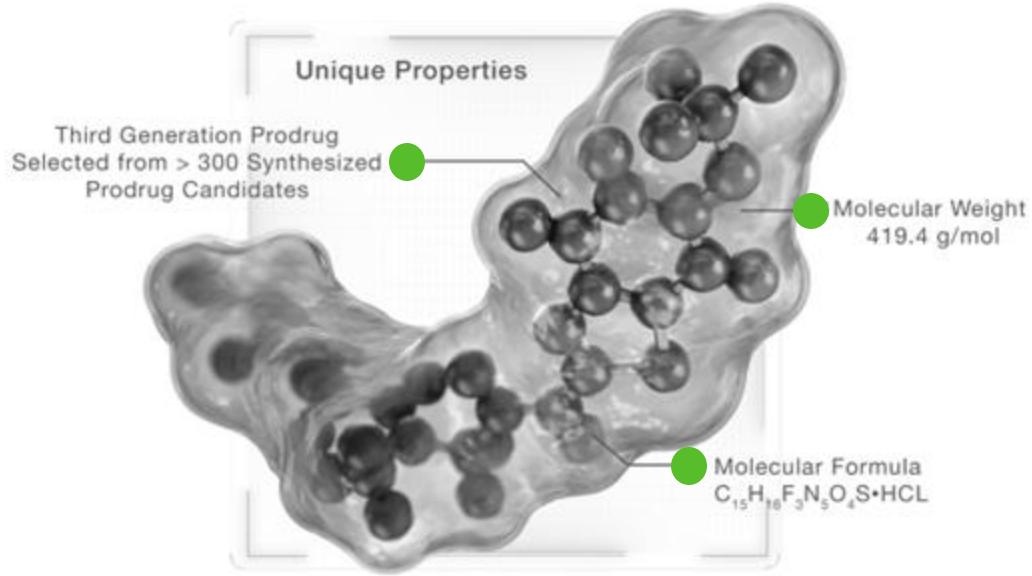
Observed across the 8-year SCA development program

Reduction in Falls

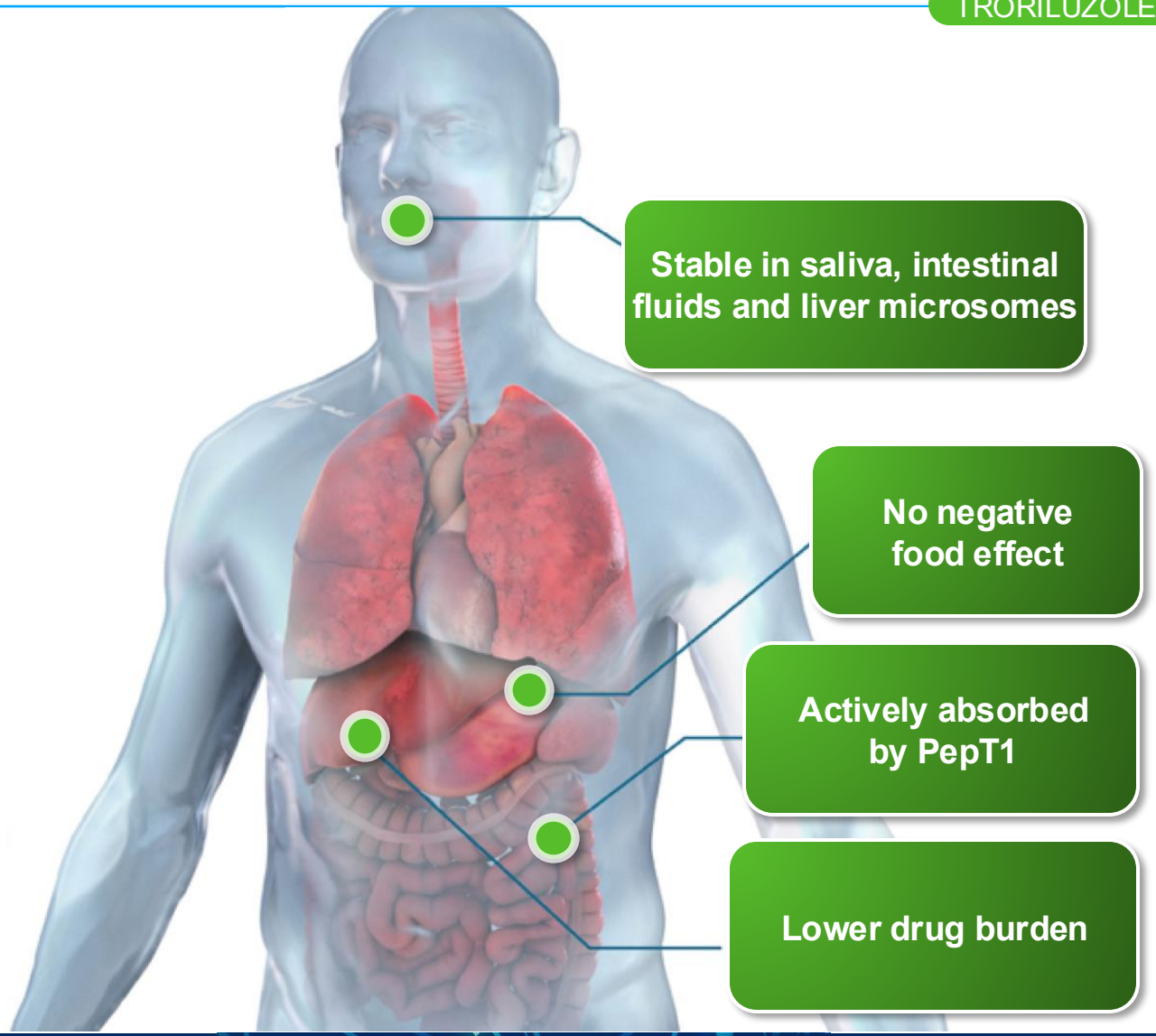
Falling is cardinal feature of SCAs leading to injury and reduced QoL

Troriluzole Was Rationally Designed to Optimize Therapy

TRORILUZOLE



- ✓ Improved absorption
- ✓ Enhanced bioavailability
- ✓ Reduced drug burden
- ✓ Reduced first pass metabolism
- ✓ Favorable safety profile
- ✓ Once-daily dosing



PepT1, peptide ttransporter 1.

SCA is Slowly Progressive Disease with Multiple Genotypes: Requires Multi-Year Followup to Assess Efficacy Across Genotypes

TRORILUZOLE

STUDY 201

Phase 2b/3
8 Wk Primary Endpoint
(2016) + OLE

High variability in appendicular items of SARA and 8-week duration too short to demonstrate efficacy

‘201 data leads to new validated f-SARA scale to focus on functional changes over time; also provides long-term OLE and challenge/dechallenge data

STUDY 206

Phase 3
1 Yr Primary Endpoint
(2019) + OLE

SCA3 is sentinel genotype that shows efficacy on f-SARA, CGI and reduction in falls

1-year RCT insufficient duration to show efficacy in all genotypes

Longer, multi-year RWE study is necessary to assess treatment effect in all genotypes

STUDY 206-RWE

3 Yr Primary Endpoint
(2024)

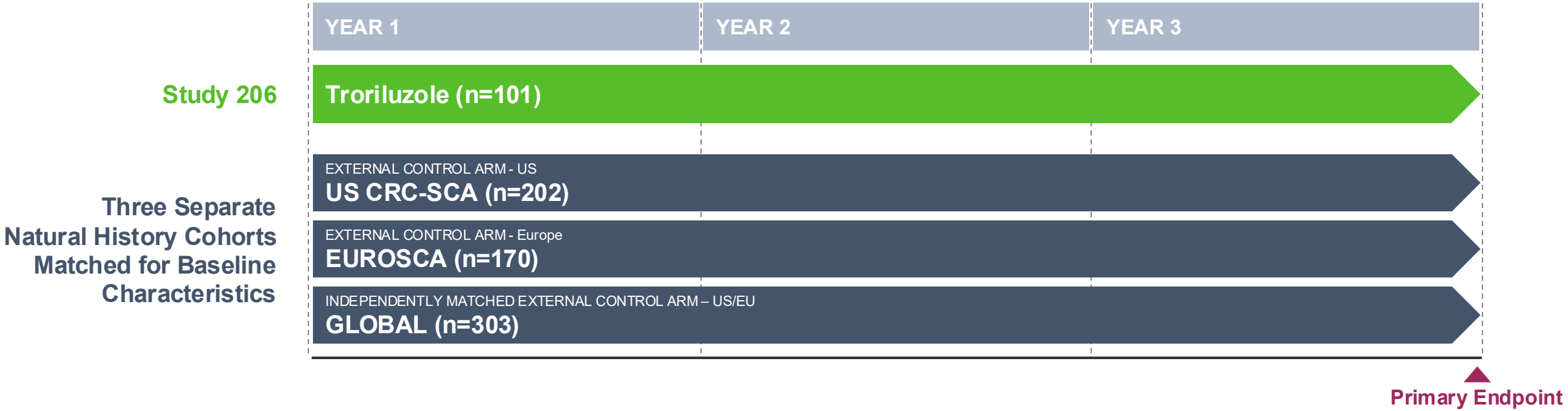
50–70% delay in disease progression out to year 3 across all genotypes

Regulatory precedent exists for the use of RWE in rare disease

RWE Study Was Designed With FDA Input & Following RWE Guidance

TRORILUZOLE

3-year real-world evidence protocol with external control using propensity score matching



PRIMARY ENDPOINT

f-SARA Change from baseline at 3 years in troriluzole-treated subjects vs untreated subjects from US Natural History control (CRC-SCA)

SECONDARY ENDPOINTS

f-SARA Change from Baseline:

- at 2-and 1-years vs US Natural History external control (CRC-SCA)
- at 3-, 2-, and 1-years vs EU Natural History external control (EUROSCA)
- at 3-, 2-, and 1-years vs Global, US and EU Natural History external control (CRC-SCA and EUROSCA)

US and EU Natural History Study Comparators Provide Reliable and Comprehensive Real-World Data (RWD) in SCA

The Clinical Research Consortium for the Study of Cerebellar Ataxia (CRC-SCA)

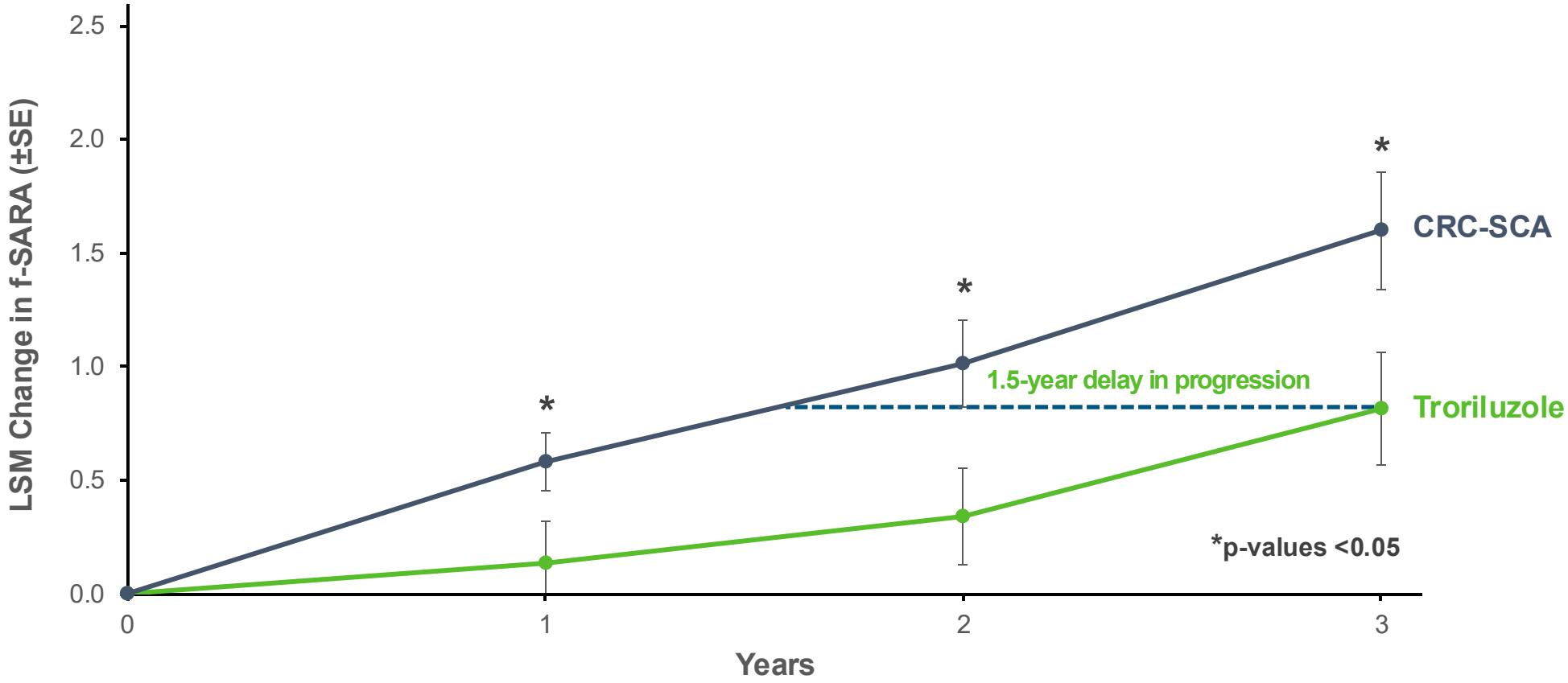
- US multicenter NH study
- Primary objective of assessing disease progression in individuals with SCA 1, 2, 3, 6, 7, 8 and 10
- Used validated neurological rating scales and timed performance measures
- Study design of BHV4157-206 modeled after CRC-SCA study design
- Conducted by KOLs at Ataxia Centers of Excellence

European Integrated Project on Spinocerebellar Ataxias (EUROSCA)

- European multicenter NH study
- Conducted to help understand and integrate the clinical natural history and biology of autosomal dominant spinocerebellar ataxias (SCAs) SCA1, SCA2, SCA3 and SCA6
- Used to set a foundation for the discovery and testing of rational therapeutics for SCA
- World's largest SCA patient DNA registry (EUROSCA-R) generated by geneticists and clinicians
- Conducted by European experts in SCA

Troriluzole vs Matched US Natural History External Control Shows 50% Slowing of Disease Progression at Year 3

TRORILUZOLE

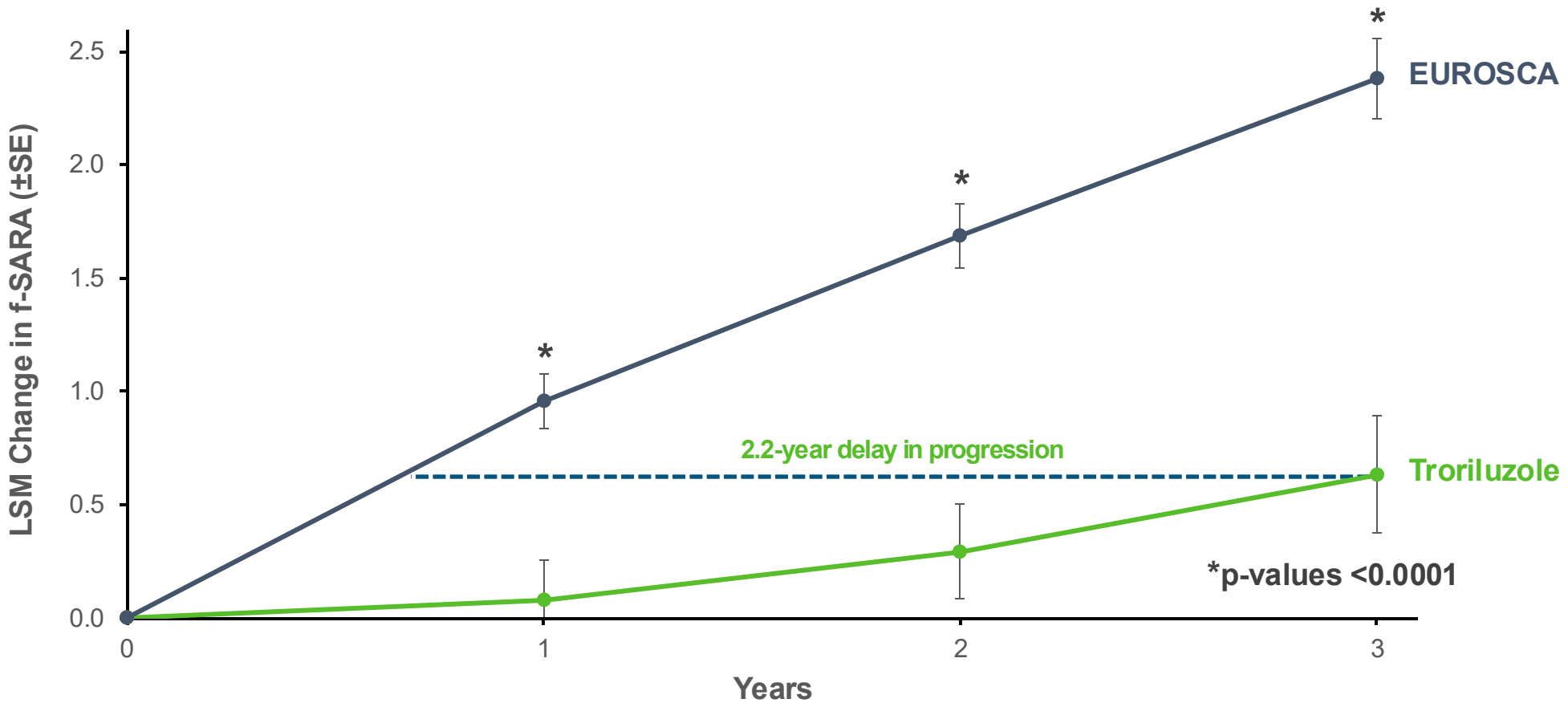


Troriluzole (n)	101	90	75	61
CRC-SCA (n)	202	177	65	43

CRC-SCA, Clinical Research Consortium for SCA; **f-SARA**, Functional Scale for the Assessment and Rating of Ataxia; **LSM**, least squares mean.

Troriluzole vs Independent Matched EU Natural History External Control Shows 70% Slowing of Disease Progression at Year 3

TRORILUZOLE



Troriluzole (n)	85	78	65	54
EUROSCA (n)	170	157	146	112

EUROSCA, European registry of SCA; **f-SARA**, Functional Scale for the Assessment and Rating of Ataxia; **LSM**, least squares mean.

Troriluzole Met 9 Prespecified Consecutive Hierarchical Endpoints Demonstrating Robust and Durable Treatment Benefit Over 3 Years

TRORILUZOLE

	f-SARA at Year	p-value
 **US External Control (CRC-SCA)**	3	<0.05
	2	<0.05
	1	<0.05
 **Europe External Control (EUROSCA)**	3	<0.0001
	2	<0.0001
	1	<0.0001
 **Global External Control (CRC+EURO)**	3	<0.0001
	2	<0.0001
	1	<0.003

CRC-SCA, Clinical Research Consortium for SCA; **EUROSCA**, European registry of SCA; **f-SARA**, Functional Scale for the Assessment and Rating of Ataxia; **Global**, CRC-SCA & EUROSCA.

Untreated SCA Patients Have Higher Likelihood of Significant Worsening

TRORILUZOLE

	Odds Ratio of f-SARA ≥2-Point Worsening in Untreated	p-value
US External Control vs Troriluzole*	**2.4**	0.0359
EU External Control vs Troriluzole	**6.1**	<0.0001
Global External Control vs Troriluzole	**4.1**	<0.0001

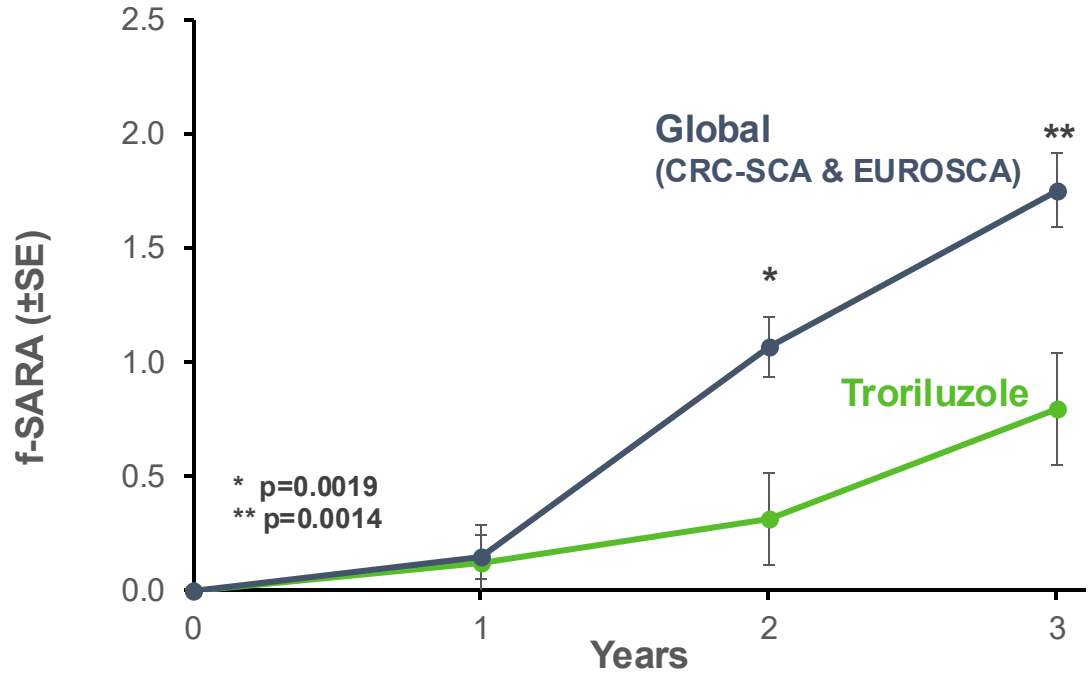
*Prespecified

KEY POINT

f-SARA ≥2-point change at 3 years represents a clearly defined worsening of SCA disease

Anchoring Analysis Confirms Need for 3 Year Study to Overcome Heterogeneity in SCA Progression Patterns

TRORILUZOLE



Troriluzole (n)	101	90	75	61
Global (n)	273	273	162	129

- External control was anchored to Study 206 placebo progression rate over 1-year using PSM
- Anchored analysis shows efficacy at Years 2 and 3 consistent with primary results from Study 206-RWE
- Addresses any potential bias introduced by differences in progression rates between RWE and Study 206 patients
- Supports reliability and interpretability of using external control arm in assessing troriluzole

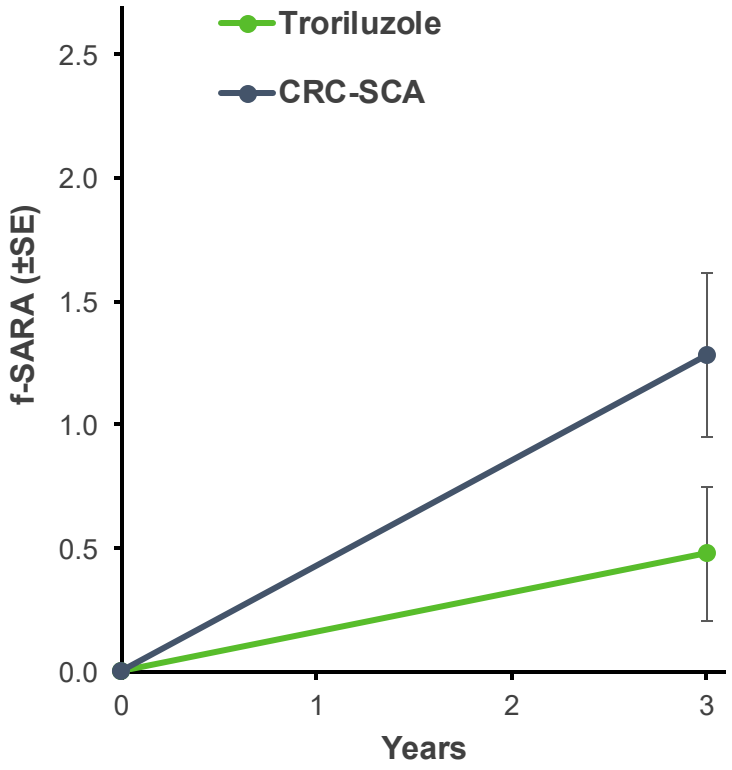
CRC-SCA, Clinical Research Consortium for SCA; **EUROSCA**, European registry of SCA; **f-SARA**, Functional Scale for the Assessment and Rating of Ataxia; **PSM**, Propensity Score Matching.

KEY POINT

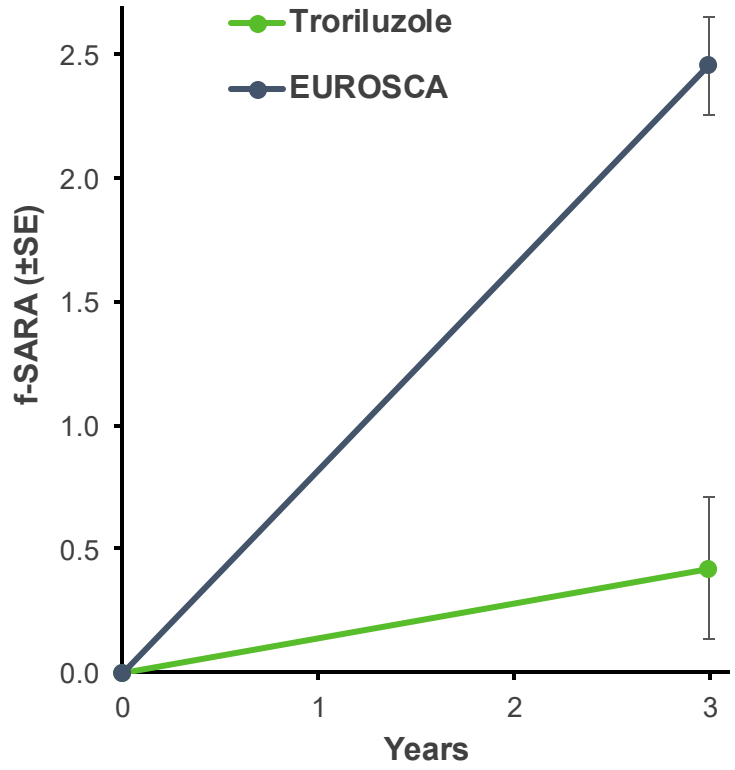
Anchoring analysis shows RWE findings are independent and highly consistent with 1-year RCT (Study 206) and closely reflects potential results of a 3 Year RCT study

New Data From Subjects Completing 3 Years of Treatment Was Consistent With Primary Results in Each External Control Arm

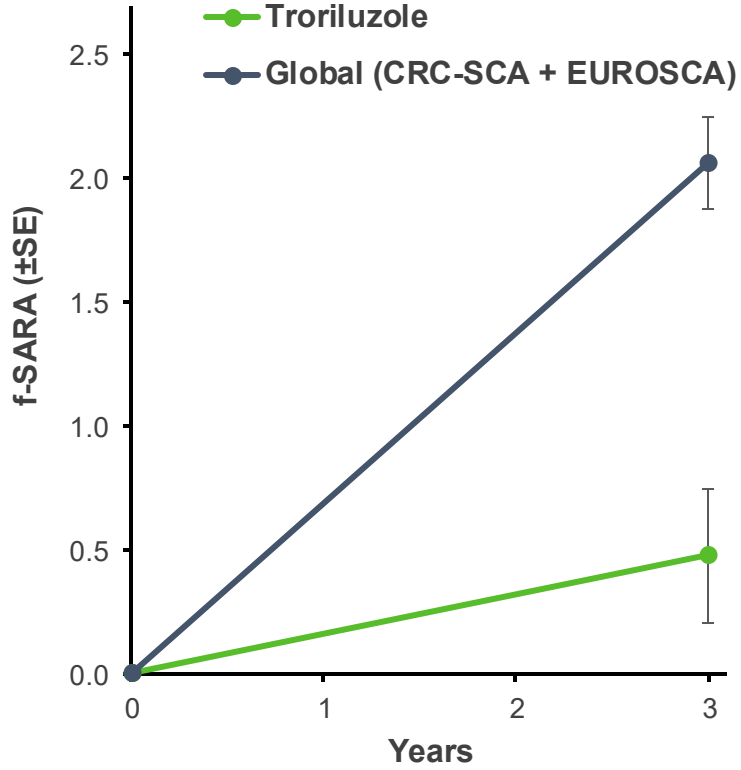
TRORILUZOLE



Troriluzole (n)	21	21
CRC-SCA (n)	202	43



Troriluzole (n)	19	19
EUROSCA (n)	170	112



Troriluzole (n)	21	21
Global (n)	303	129

CRC-SCA, Clinical Research Consortium for SCA; **EUROSCA**, European registry of SCA; **f-SARA**, Functional Scale for the Assessment and Rating of Ataxia.

SCA Is Lead Indication for Future Development of Troriluzole

TRORILUZOLE

Potential benefit across an array of **cerebellar disorders**

Spinocerebellar Ataxia (SCA)

- Friedreich's Ataxia
- Sporadic Ataxia
- Other Ataxias
- Essential Tremor

Troriluzole Demonstrates Compelling Treatment Effect and Meaningful Delay in SCA Disease Progression

TRORILUZOLE

Clear Impact on Disease Progression

- 50–70% slowing of disease progression, representing 1.5–2.2 years delay in disease progression over 3-year RWE Study
- Multiple sensitivity analyses confirm reliability and interpretability of study results

Consistent Treatment Effect Over Three Studies

- Efficacy data from Studies 201, 206 and RWE
- 53% risk reduction in falls

Strong Safety/Tolerability Profile of Troriluzole

- Well-characterized safety profile of troriluzole assures a positive benefit-risk profile for SCA
- Studied in over 2,000 subjects across 8 years

KEY POINT

NDA under Priority Review with anticipated approval and commercialization in 4Q 2025

John Tilton

Chief Commercial Officer,
Rare Disease

biohaven®

Commercializing Troriluzole

BREAKING NEWS:

VYGLXIA®

name conditionally accepted by the FDA

pending product approval

biohaven®

Existing SCA Market Dynamics Creates Opportunities for VYGLXIA® and Biohaven

VYGLXIA®

SCA MARKET DYNAMIC	VYGLXIA OPPORTUNITY
No approved therapies for SCA and no therapies in pivotal development	Establish VYGLXIA as the Standard of Care in SCA
SCA disease severity and ongoing progression	• VYGLXIA value proposition • Urgency to treat with need for chronic utilization
Autosomal dominant, inherited disease	Genetic testing programs to identify SCA patients and confirm diagnosis and map pattern of inheritance
Strong KOL and patient advocacy	• Motivated customers to drive early adoption of VYGLXIA • Support reimbursement
Centralized care in Centers of Excellence	Nimble, focused commercial footprint to launch VYGLXIA

15,000
Est. US Prevalence[1]

~6,000
Diagnosed and linked to HCP[2]

1. Ruano L, et al. *Neuroepidemiology*. 2014;42(3):174-83. 2. Data on File based on claims data purchased from IQVIA.

KEY POINT

VYGLXIA® would be the first and only approved treatment for SCA

Strategic Imperatives to Drive Successful Launch in SCA

VYGLXIA®

SCA Launch Priorities

01 Identify patients, drive early diagnosis

02 Establish VYGLXIA® as SOC in SCA

03 Create access and reimbursement

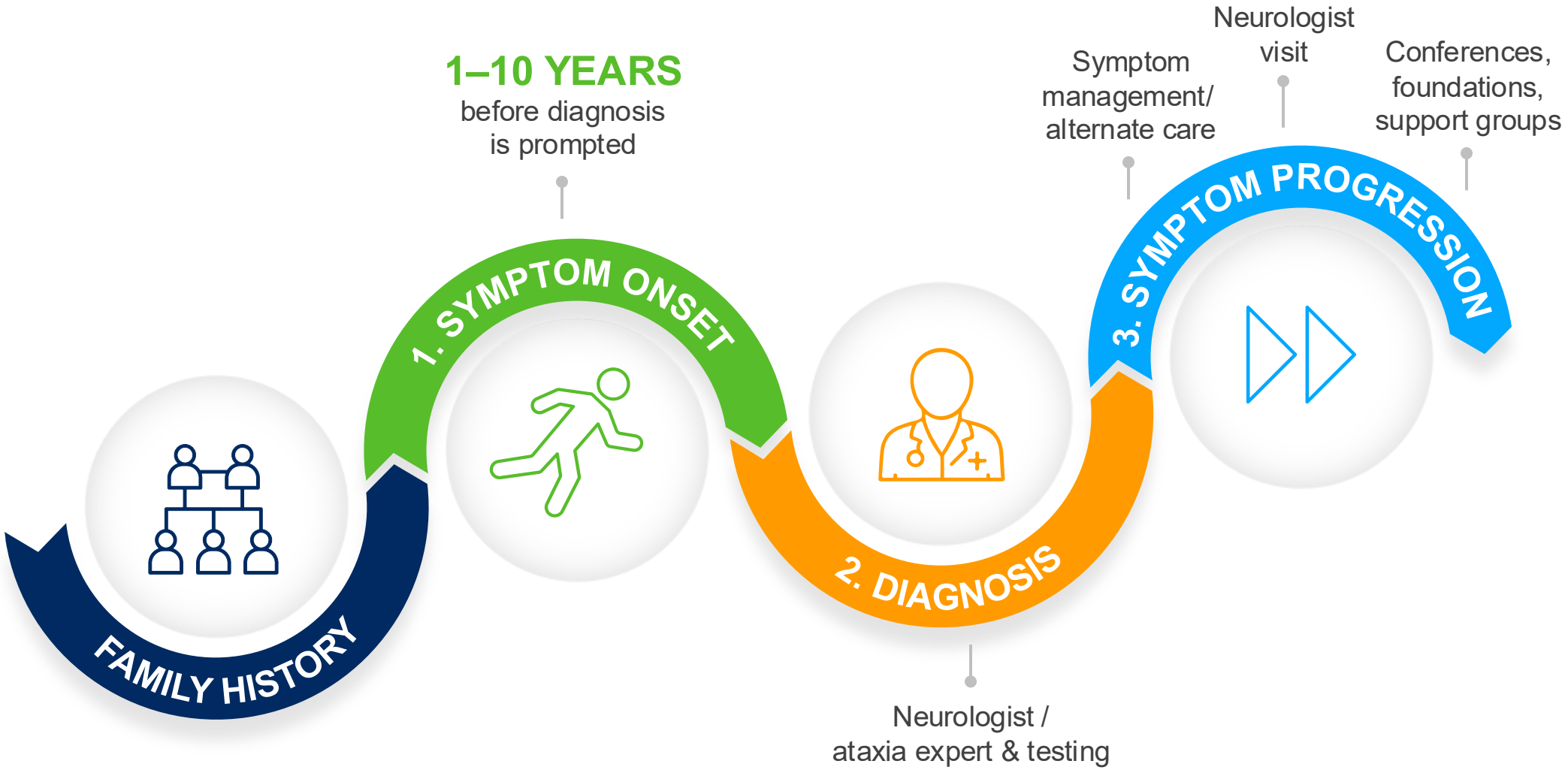
04 Ensure ongoing treatment

KEY POINT

SCA launch relies on identifying patients and driving diagnosis

Driving Patient Identification and Diagnosis Are Critical to Launch Success and Long-Term Growth

VYGLXIA®



Source: SCA Patient Journey Market Research. Conducted at NAF 2017 by Burke Institute. Updated: April 5, 2017

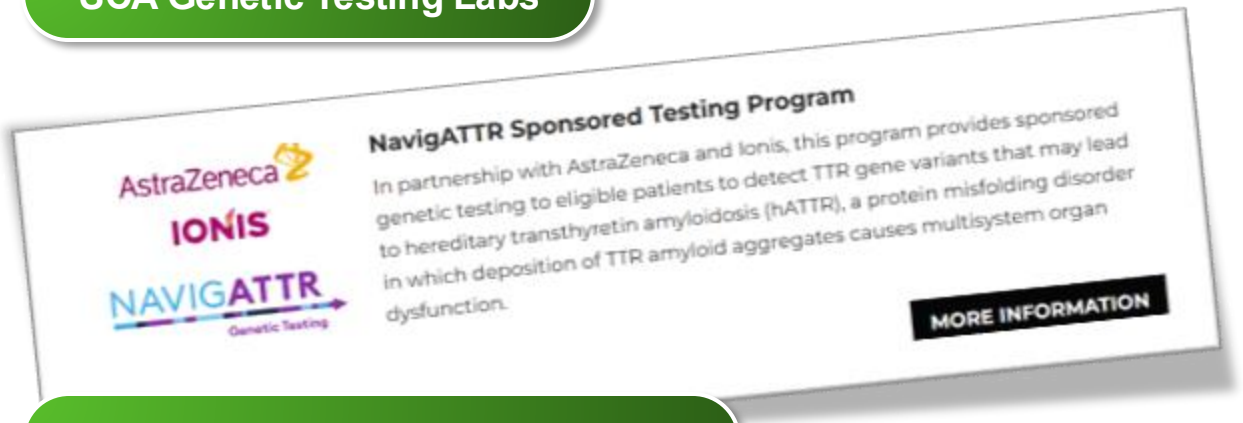
Focused Tactics to Drive Patient Identification and Early Diagnosis

VYGLXIA®

Patient ID and Diagnostic Initiatives:

- Deploy medical affairs team in advance of approval
- Leverage AI, claims, electronic health records, to generate leads
- Disease education campaign and website
- Familial tracing for people diagnosed with SCA
- Partner with experts to create content for non-expert clinicians on how to recognize SCA
- Ensure awareness of initiatives to patient advocacy groups and ataxia experts
- Genetic Testing Sponsorship Programs and collaborations with companies that test for SCA

SCA Genetic Testing Labs



Example of Genetic Testing Program

SCA Centralized Treatment Allows for Targeted and Efficient Commercialization Plan

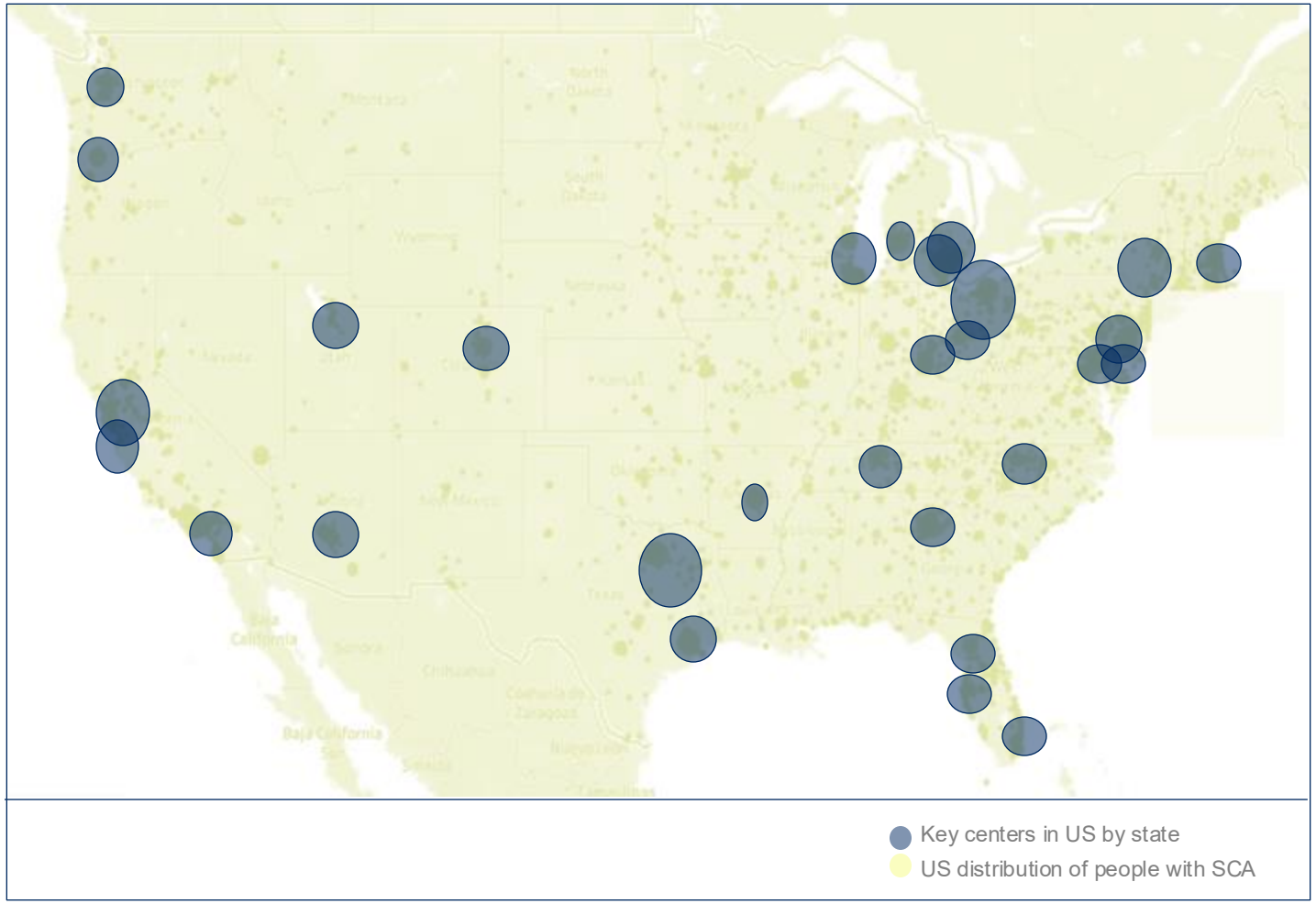
VYGLXIA®

SCA treatment at key centers

121 KOLs, 22 NAF Ataxia Centers of Excellence and 73 additional Movement Disorder and Ataxia Centers have been identified and manage many patients[1,2]

Experienced, efficient commercial team

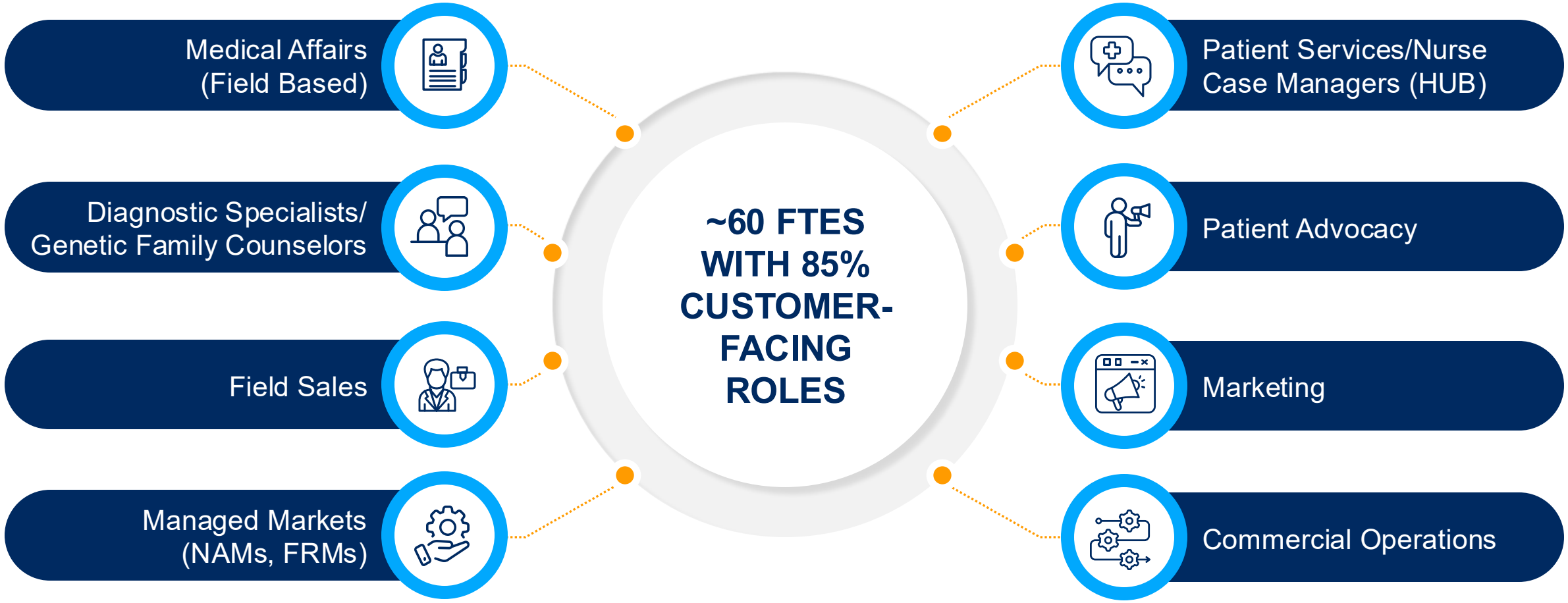
- Proven track record in successful rare disease launches
- Planning to deploy dedicated SCA FTEs to drive a focused and rapid US launch



1. National Ataxia Foundation. Accessed May 12, 2025. https://www.ataxia.org/neurologists-and-specialty-clinics/. 2. Data on File based on claims data purchased from IQVIA.

Planning Dedicated Commercialization Team to Drive a Focused, Rapid US Launch

VYGLXIA®



KEY POINT

Focused US launch begins with high-volume HCPs and people with SCA that have already demonstrated interest in troriluzole through clinical trials and/or early access programs

Commercial Leadership Team in Place With Proven Rare Disease Experience

VYGLXIA®

SOLIRIS® (eculizumab) Injection for Intravenous Use 300 mg/30 mL vial

Myozyme® (alglucosidase alfa)

ZYKADIA® ceritinib 150 mg tablets

Fabrazyme® agalsidase beta

Signifor® (pasireotide) Injection

ULTOMIRIS® (ravulizumab-cwvz) injection for intravenous use 300 mg/3 mL vial

Lumizyme® (alglucosidase alfa)

Galafold® (migalastat) 123 mg capsule

Cystadrops® (cysteamine ophthalmic solution) 0.37%

AFINITOR® (everolimus) tablets 2.5mg | 5mg | 7.5mg | 10mg

Strensiq® (asfotase alfa) for injection | 40 mg/mL

Xenpozyme® (olipudase alfa-rpcp) For Injection, 20 mg

Nexviazyme® (avalglucosidase alfa-ngpt)

Pombiliti® + Opfolda®
(cipaglucosidase alfa-atga) (miglustat) 65 mg capsules

UPLIZNA® inebilizumab-cdon

SUTENT® capsules sunitinib malate

DepoCyt

ADAGEN® (pegademase bovine)

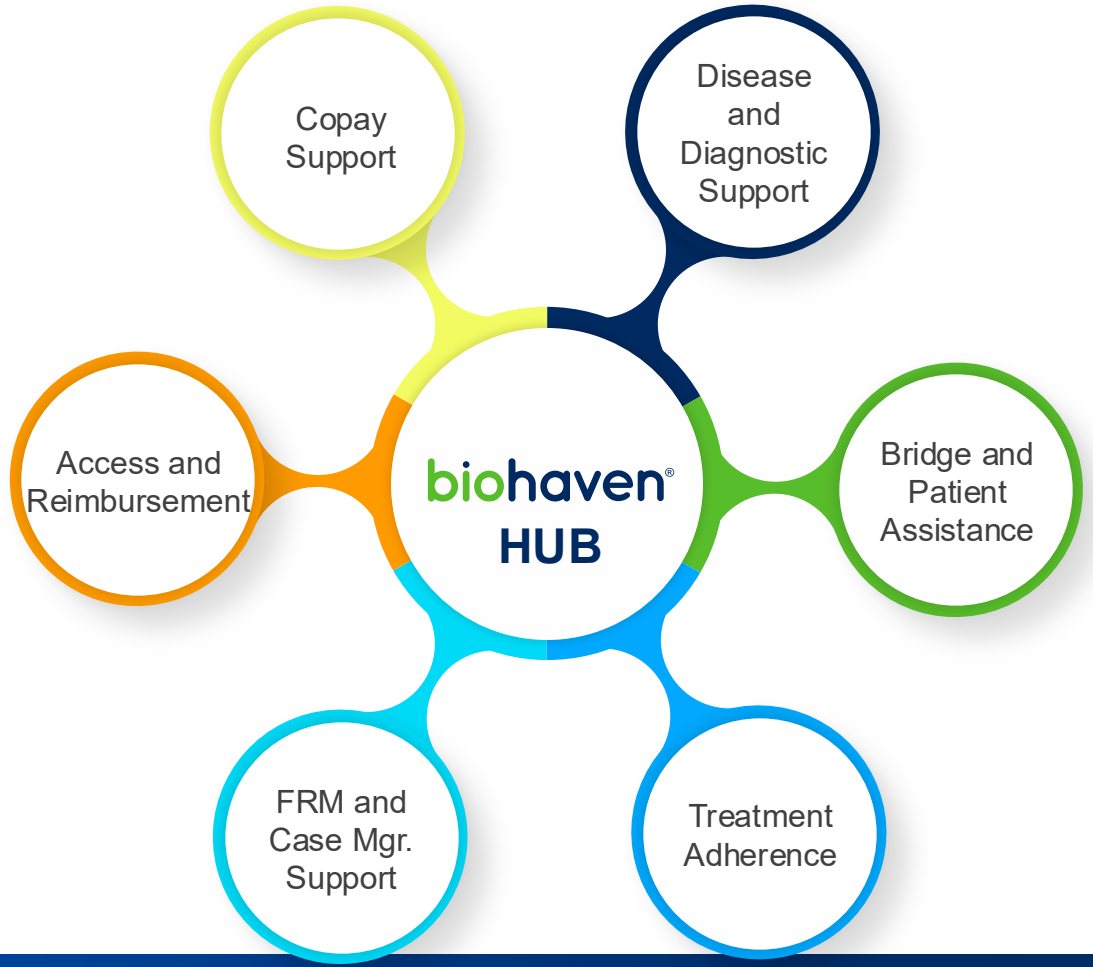
Sandostatin® LAR octreotide IM INJECTION

Building Comprehensive Patient Access and HCP Support

VYGLXIA®

Biohaven HUB will be a central point of contact for patients, caregivers and HCPs

- Insurance and reimbursement support
- Copay, early access and patient assistance programs
- Integrated specialty pharmacy
- Highly coordinated field reimbursement and case management teams
- Disease education and diagnostic assistance
- Treatment adherence program



KEY POINT

At Biohaven, we will strive to ensure all SCA patients will have access to VYGLXIA®

Creating Access by Building Biohaven Patient Services HUB and Engaging With Payers

VYGLXIA®

Selecting Specialty Pharmacy and Patient Services Partner

- Negotiations underway for partner in commercialization of Specialty Pharmacy and HUB Patient Services

Payer Engagement Readiness

- Prepared to communicate value proposition pre-approval
- Focused national account team is planned

Maintaining Strong, Long-Standing Collaborations With Ataxia Organizations to Serve SCA Patients

VYGLXIA®

- **COLLABORATIONS** with leading SCA researchers
- **PARTNERSHIPS** with advocacy organizations
- **SCIENTIFIC MEMBERSHIP** in research groups
- **KEY CONTRIBUTION** to the ongoing development of a quality natural history study in SCA

ARCA GLOBAL

MGH 1811

EBERHARD KARLS UNIVERSITÄT TÜBINGEN

CPTA CRITICAL PATH TO THERAPEUTICS FOR THE ATAXIAS

CRC-SCA Clinical Research Consortium for the Study of Cerebellar Ataxia

ATAXIA Ataxia UK

HOUSTON Methodist CONTINUING CARE HOSPITAL

ATAXIA GLOBAL INITIATIVE

SCA Global

MDA Muscular Dystrophy Association

NAF National Ataxia Foundation

Biohaven Pharmaceuticals Inaugural Partner of National Ataxia Foundation's Drug Development Collaborative

Continuing KOL Engagement Ensures Current Market Understanding of SCA Prior to Anticipated Approval

VYGLXIA®

Ongoing KOL Engagement

- Ongoing one-on-one meetings and research working groups (e.g., Ataxia Global Initiative)
- Recent congress engagement, presentations and sponsorships: American Academy of Neurology (AAN), Muscular Dystrophy Association (MDA) and World Orphan Drug Congress (WODC)

Extending Our Integration of the SCA Community Perspective Into Biohaven Programs With Recent and Upcoming Engagement

VYGLXIA®

Recent and Upcoming Collaboration

- Patient Advisory Board: Held at March 2025 NAF Annual Ataxia Conference (AAC)
- Ataxia UK and Biohaven Meetings
- Ataxia Patient Conference Sponsorships
- NORD Content Engagement
- Podcast Collaboration with *Ataxia Did You Know?*

VYGLXIA® in SCA Represents a Significant Commercial Opportunity

Readily identifiable patients will drive initial uptake

- High-volume ataxia experts and people with SCA interested or involved in clinical research programs/registries
- People already diagnosed with SCA and their families

Biohaven's HUB will facilitate access to VYGLXIA®

- HUB will be a central point of contact for the SCA community
- Strive to ensure all SCA patients will have access to VYGLXIA®

Patient ID and early diagnosis fuel long-term growth

- Focused initiatives that drive patient ID and early diagnosis strategy are critical
- Targeted commercialization plan includes experienced rare disease leaders

KEY POINT

If approved, the Biohaven team will be prepared to serve people living with SCA

Patricia E. Greenstein, MB.BCh

Neurology Residency Training Program,
Assistant Professor

HARVARD MEDICAL SCHOOL

Jennifer

Living with SCA3

Participant in the Troriluzole Clinical Study

Panel

MODERATOR

Tessa Romero

Equity Analyst

J.P.Morgan

PANELISTS

Patricia E. Greenstein, MB.BCh

Program Director: Neurology Residency Training Program, Assistant Professor
Harvard Medical School

Melissa Beiner, MD

Senior Medical Director
Biohaven

John Tilton

Chief Commercial Officer, Rare Disease
Biohaven

BHVN
LISTED
NYSE

Raman Sankar, MD, PhD, FAAN, FAES

Emeritus Professor of Neurology and Pediatrics, Emeritus
Chief of Pediatric Neurology
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA

Irfan Qureshi, MD

Chief Medical Officer
BIOHAVEN

John H. Krystal, MD

Robert L. McNeil, Jr. Professor of Translational Research;
Chair, Department of Psychiatry
YALE UNIVERSITY SCHOOL OF MEDICINE
Chief of Psychiatry
YALE-NEW HAVEN HOSPITAL

Professor Thomas Voets

Medical Director
Laboratory of Ion Channel Research
VIB Center for Brain and Disease Research
KU LEUVEN

Volkan Granit, MD, MSc

Senior Medical Director, Head of Neuromuscular Disease
BIOHAVEN

Ion Channel

biohaven®

Raman Sankar, MD, PhD, FAAN, FAES

Emeritus Professor of Neurology and Pediatrics,
Emeritus Chief of Pediatric Neurology

UCLA David Geffen School of Medicine

The Potential for BHV-7000 to Alter the Landscape of Epilepsy Therapeutics

biohaven®

Unmet Needs in Persons With Epilepsy Include Efficacy and Quality of Life

Kv7

Medication side effects lower quality of life in epilepsy

- A European study clearly demonstrated improvement in quality of life when the treatment regimen was adjusted for adverse side effects of ASMs[1]
- Preliminary data on BHV-7000 demonstrate very low risk of adverse effects and exceptional tolerability

Comorbidities negatively impact quality of life in epilepsy

- Depression appears to be the most prevalent comorbidity of epilepsy with the greatest impact on subjective health status[2]
- Potential for Kv7.2/3 openers to be effective in treating depressive disorders adds to the special value these compounds can bring to people with epilepsy

1. Gilliam F, et al. *Epilepsy & Behavior*, 2002. 2. Uijl SG, et al., *Eur J Neurol*, 2009.

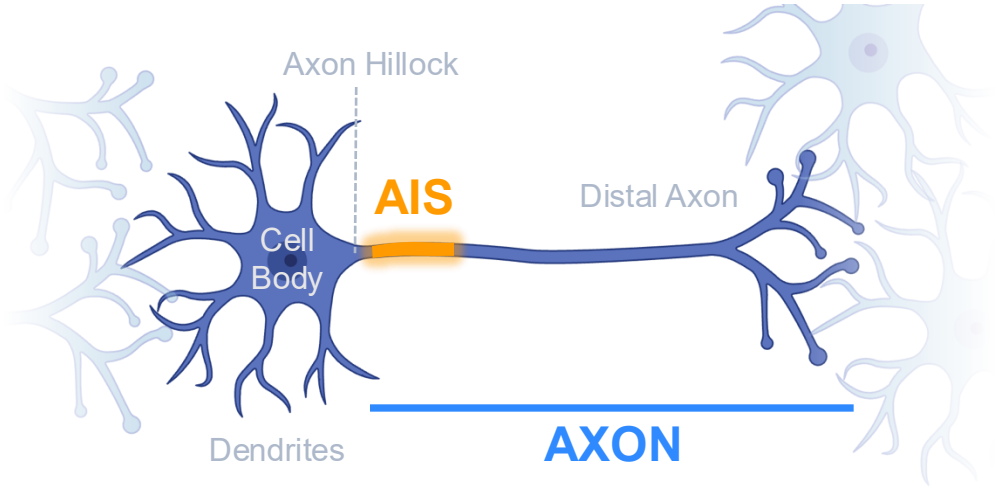
KEY POINT

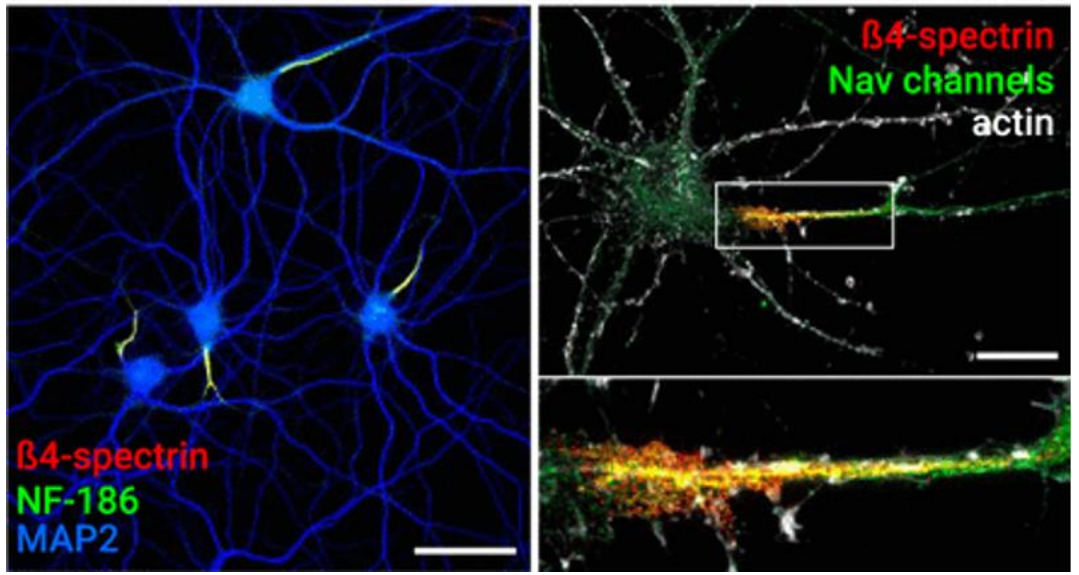
BHV-7000 has the potential to treat epilepsy while significantly improving quality of life

The Target: Kv7

biohaven®

Kv7 Channels Are Positioned at a Crucial Location for Controlling Initiation and Propagation of Action Potentials





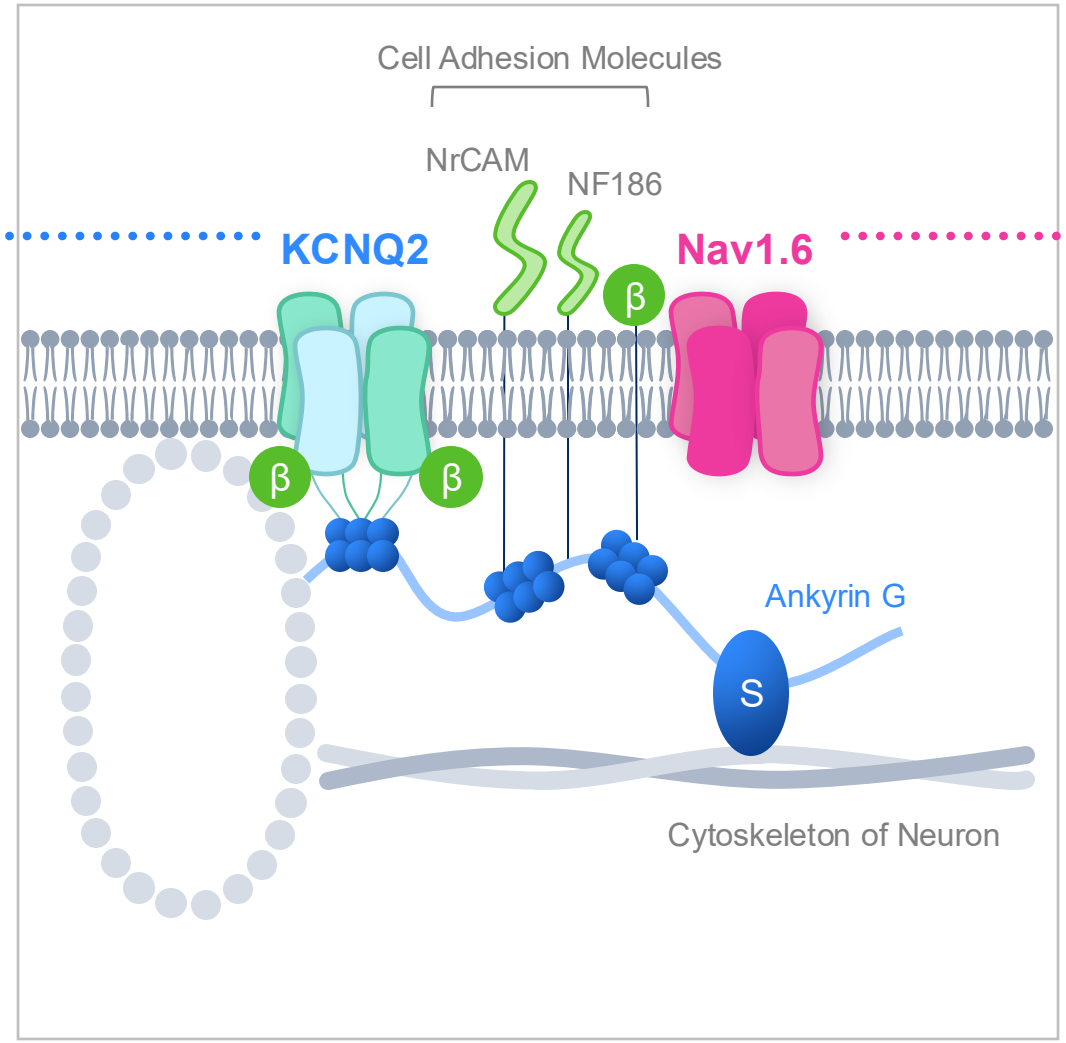
- Axon initial segment (AIS) generates and shapes the action potential before it is propagated along the axon
- Neuronal excitability thus depends crucially on the AIS composition and position, and these adapt to developmental and physiological conditions

Leterrier C, *J Neurosci*, 2018.

Kv7 Channel Activity Is a Key Contributor to Membrane Stabilization Thereby Preventing Seizure Activity

Kv7.2/3 (KCNQ2) Channels

Contribute to a hyperpolarizing (or stabilizing) current, preventing seizure activity. A loss of function mutation can be epileptogenic.



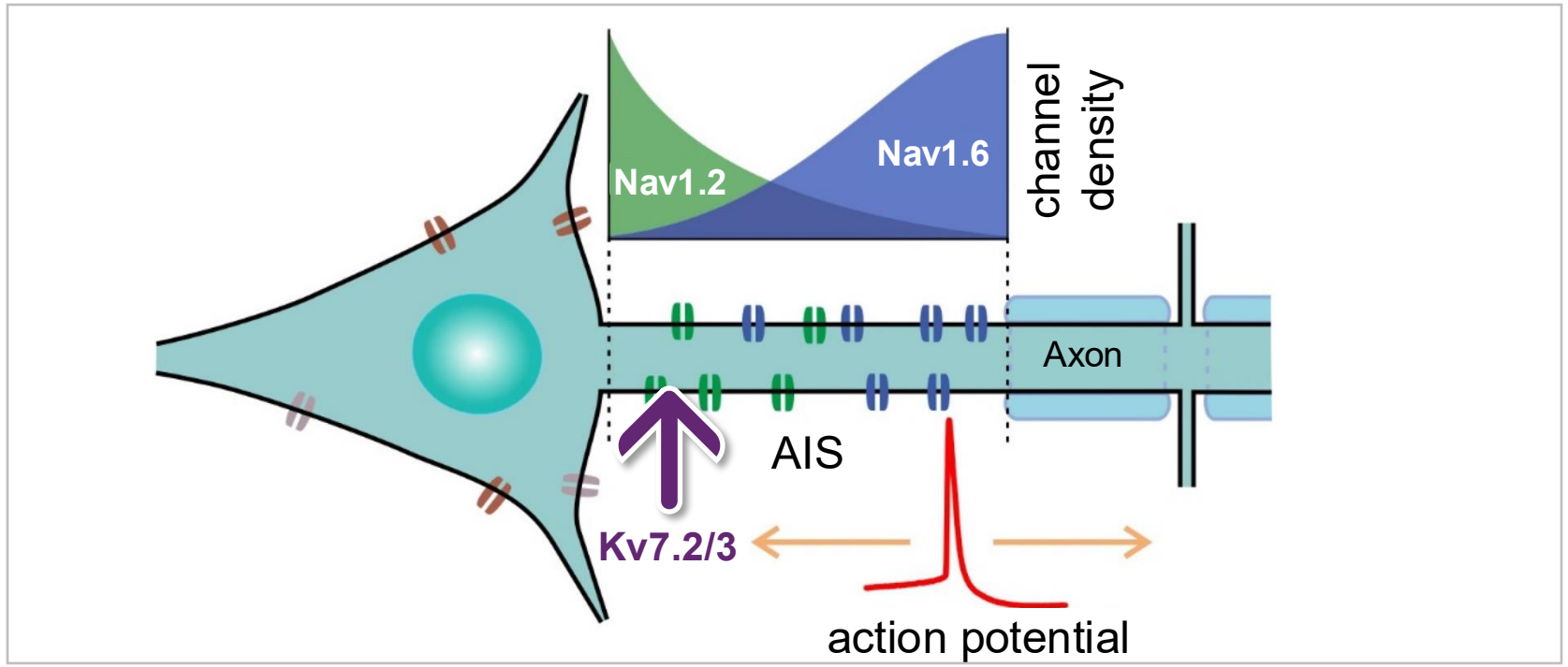
Nav1.6 or Nav1.2 Channels

Promote depolarizing currents, and mutations involving gain of function produce epileptic conditions

Figure from Salzer JL, PNAS, 2019

Kv7.2/3 Channels at the AIS Function as Emergency Brakes & Prevent Transmission of "Runaway" Excitation

Kv7



Nav1.2 are high threshold firing

Nav1.6 have a lower threshold for firing

This arrangement moves the action potential down the axon

REVIEWS
PHYSIOLOGY 26: 365–376, 2011; doi:10.1152/physiol.00009.2011

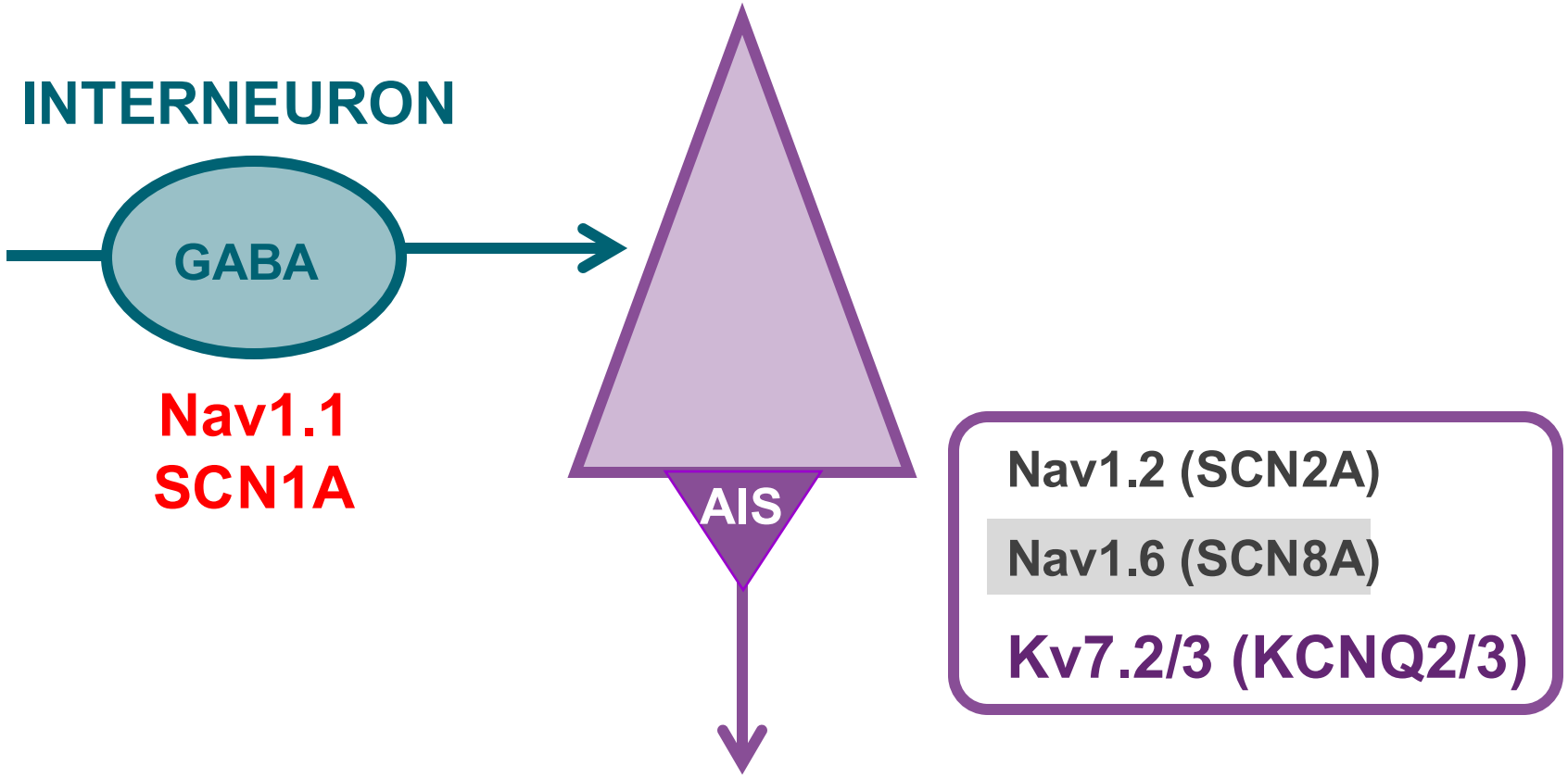
Driving With No Brakes: Molecular Pathophysiology of Kv7 Potassium Channels

Maria Virginia Soldovieri,[1] Francesco Miceli,[2,3] and Maurizio Taglialatela[1,2]

Romanaova DY, et al. *Biophysica* 2022, 2(3), 184-193.

Many Available ASMs Target Na Channels Non-selectively and Have the Potential to Compromise Inhibition

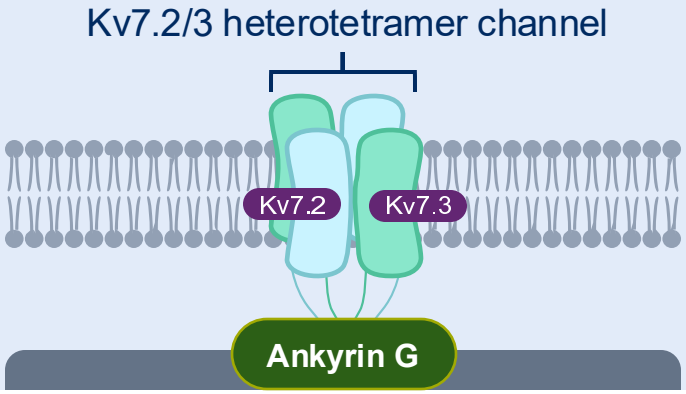
Kv7

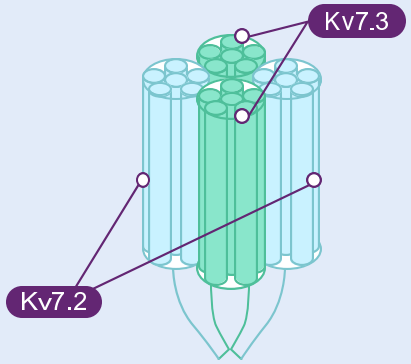


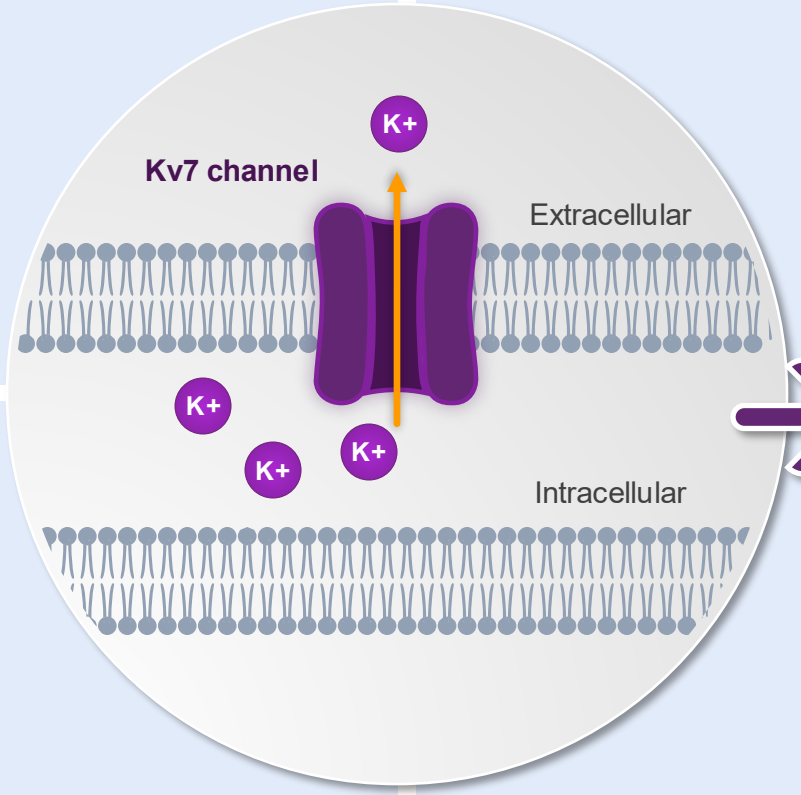
KEY POINT

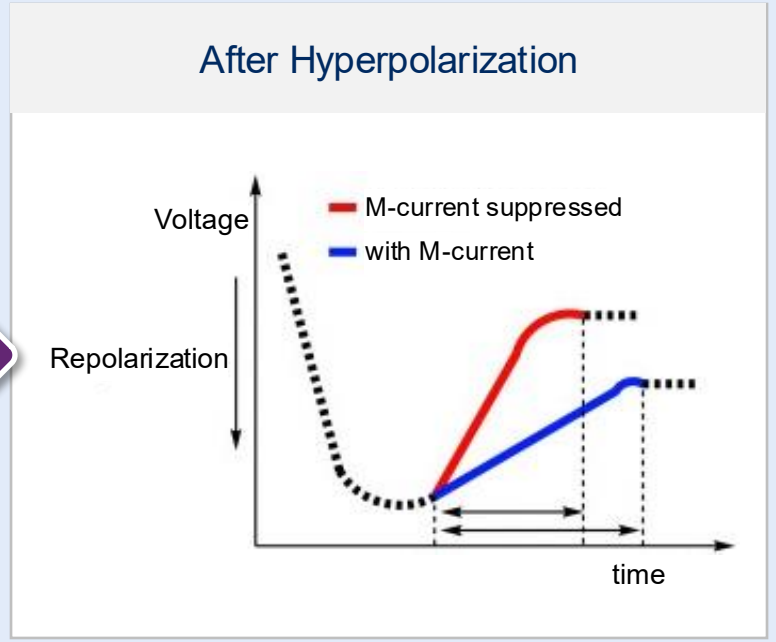
Augmenting Kv7, rather than blocking Nav1 channels, preserves inhibitory interneuron activity

Kv7 Channels Generate the M-Current









Borgini M, et al. *RSC Med Chem*, 2021, 12, 483–537.

KEY POINT

The M-current is essential to control neuronal excitability, opposing depolarization and protecting against seizures

Epilepsia, 53(3):412–424, 2012
doi: 10.1111/j.1528-1167.2011.03365.x

CRITICAL REVIEW AND INVITED COMMENTARY

The mechanism of action of retigabine (ezogabine), a first-in-class K^+ channel opener for the treatment of epilepsy

*Martin J. Gunthorpe, †Charles H. Large, and ‡Raman Sankar

*New Frontiers Science Park, GlaxoSmithKline plc, Harlow, Essex, United Kingdom; †Medicines Research Center, GlaxoSmithKline S.p.A., Verona, Italy; and ‡Departments of Pediatrics and Neurology, David Geffen School of Medicine at UCLA, Los Angeles, California, U.S.A.

Epilepsia, 53(3):425–436, 2012
doi: 10.1111/j.1528-1167.2011.03364.x

CRITICAL REVIEW AND INVITED COMMENTARY

The spectrum of anticonvulsant efficacy of retigabine (ezogabine) in animal models: Implications for clinical use

*Charles H. Large, *David M. Sokal, †Astrid Nehlig, ‡Martin J. Gunthorpe, §Raman Sankar, ¶Christopher S. Crean, #Kevan E. VanLandingham, and **H. Steve White

Epilepsia, 51(Suppl. 3):39–42, 2010
doi: 10.1111/j.1528-1167.2010.02607.x

ANTIEPILEPTIC DRUGS (AEDs) IN THE DEVELOPING BRAIN

Evaluation of development-specific targets for antiepileptogenic therapy using rapid kindling

*†Raman Sankar, ‡Stéphane Auvin, §Young Se Kwon, *Eduardo Pineda, *Don Shin, and *Andrey Mazarati

Epilepsia, 49(10):1777–1786, 2008
doi: 10.1111/j.1528-1167.2008.01674.x

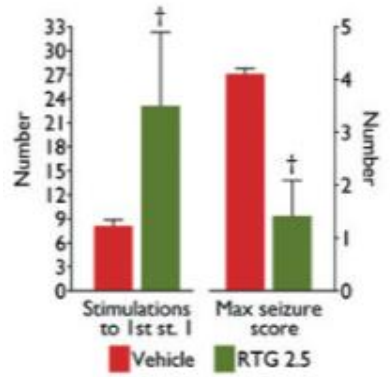
FULL-LENGTH ORIGINAL RESEARCH

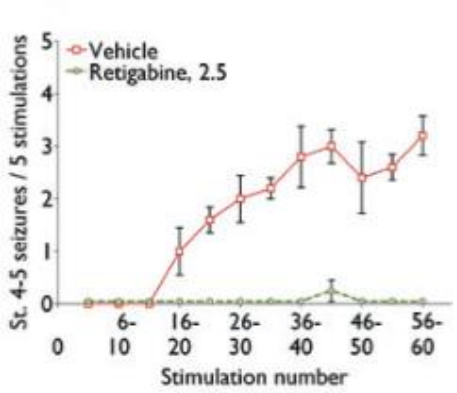
Antiepileptogenic and antiictogenic effects of retigabine under conditions of rapid kindling: An ontogenic study

*Andrey Mazarati, †Jim Wu, *Don Shin, *‡Young Se Kwon, and *§Raman Sankar

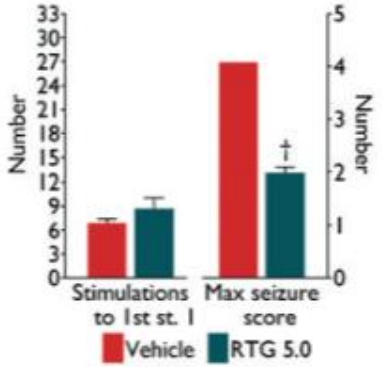
Kv7 Activation Prevents Development of Seizures From Kindling

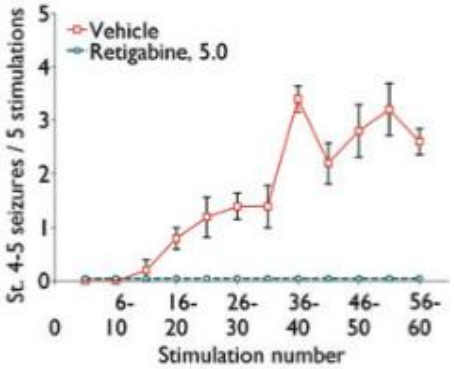
Postnatal Day 14



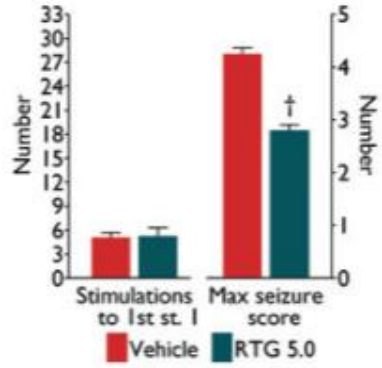


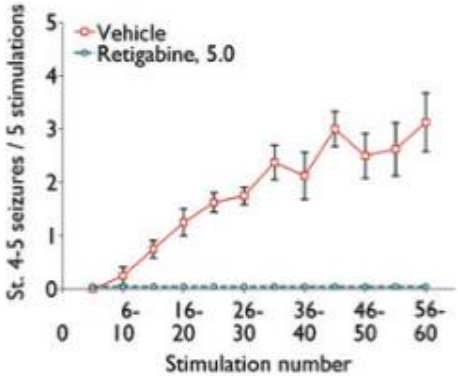
Postnatal Day 21





Postnatal Day 35





Bar graphs show number of kindling stimulations required to reach first stage I seizure, as well as maximal score of behavioral seizures observed during rapid kindling. Line graphs show the progression of full kindled seizures, expressed as the number of stage 4-5 convulsions recorded in response of five consecutive kindling trials. Data are presented as Mean ‡ SEM. Dagger, $p < 0.05$ versus Vehicle (Student t-test).

Mazarati, et al. *Epilepsia*, 2008.

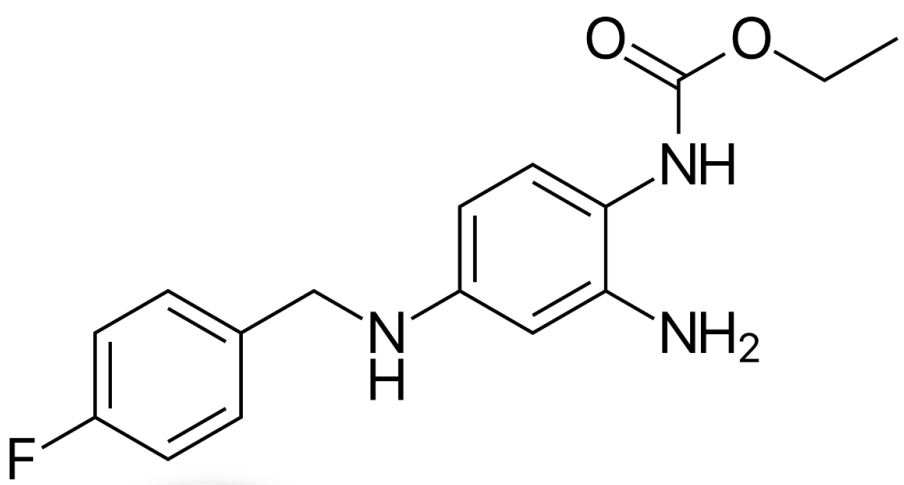
The Molecule: BHV-7000

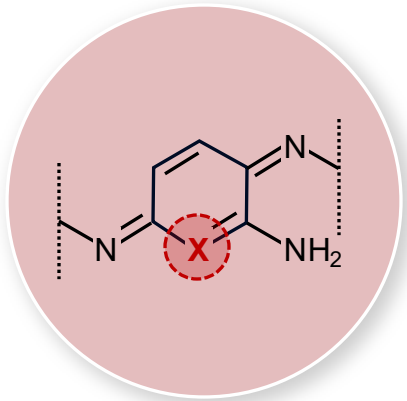
biohaven®

BHV-7000 Was Developed to Be Safe Without the Chemical Structure-Related Liabilities of Retigabine

Kv7

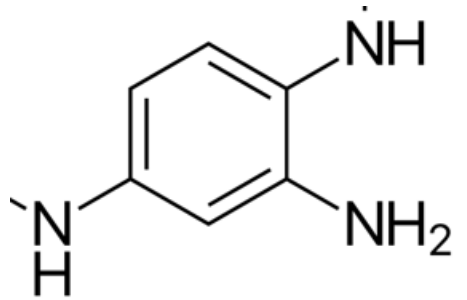
Retigabine (Ezogabine)





Reactive (toxic) Intermediate

BHV-7000 Lacks the Reactive Moiety



Resistant to **quinone diimine** intermediate in the toxification pathway

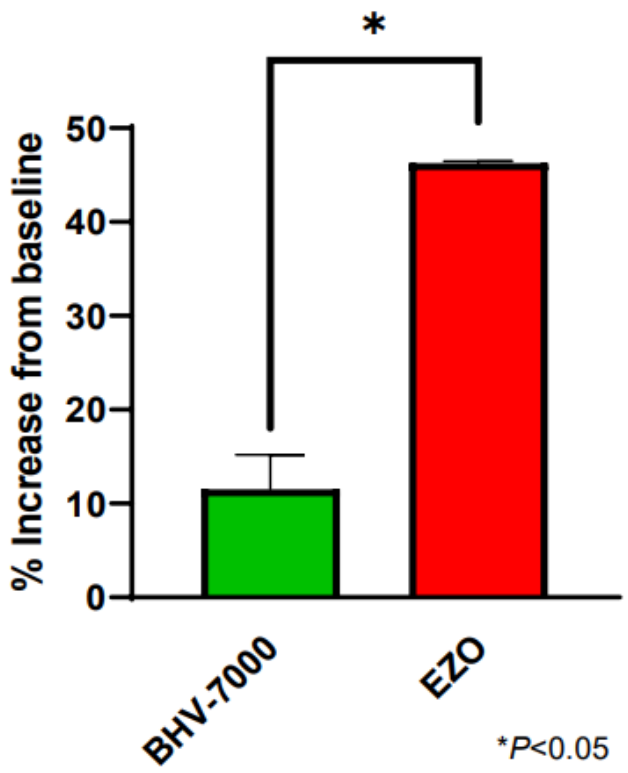
Under development for FOS, IGE and MDD

FOS, focal onset seizures; **IGE**, idiopathic generalized epilepsy; **MDD**, major depressive disorder.

Lack of Somnolence With BHV-7000 Is Related to Very Low $GABA_A$ Agonist Activity

Kv7

Change from Baseline in $GABA_A$ Response

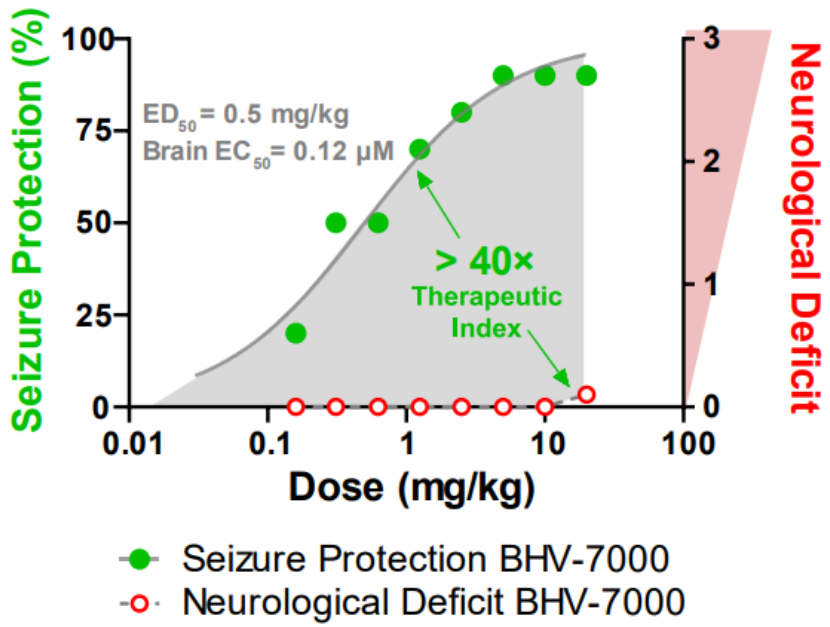


BHV-7000 Has Wide Therapeutic Index With Minimal Neurological Deficit

Kv7

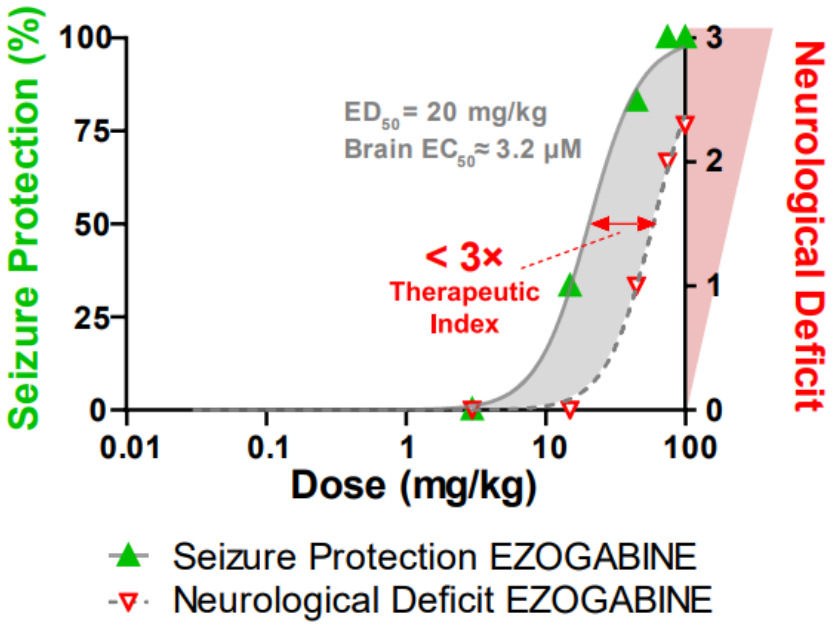
BHV-7000

Measured by maximal electroshock testing



BHV-7000 protects against MES-induced seizures, with an ED_{50} of 0.5 mg/kg while having no impact on neurobehavior and wide therapeutic index > 40x

Ezogabine



Assessed by change in activity, ataxia and body posture

Ezogabine has an ED_{50} of 20 mg/kg and impacts neurobehavior at similar doses required for efficacy, producing a therapeutic index < 3x

Picchione K, et al. AES 2023. Poster 2.24.

Phase 1 Multiple Dose Studies With BHV-7000 Demonstrate a Very Favorable Safety and Tolerability Profile

Kv7

BHV-7000

FAVORABLE SAFETY AND TOLERABILITY

- No serious AEs, severe AEs, or dose-limiting toxicities
- Most common AEs: headache (11.3%) and back pain (11.3%)
- **No AEs reported with BHV-7000 75 mg extended release, highest dose in ongoing Phase 2/3 studies**
- Low rates of central nervous system-related AEs with **no somnolence reported**
- Majority of AEs were mild and resolved spontaneously

Awsare B, et al. AES 2024. Poster 486

BHV-7000 Has Potential to Alleviate Depression in Epilepsy

Kv7

Depression is one of the important co-morbidities of epilepsy adversely affecting the quality of life for patients

Kv7 activation is promising mechanism of action for the treatment of depression

Combined with low to non-existent CNS adverse effects, **BHV-7000 is one of the most promising ASM candidates**

Irfan Qureshi, MD

Chief Medical Officer

biohaven®

BHV-7000

Pivotal MDD topline results expected 2H 2025

1st focal epilepsy study topline results expected 1H 2026

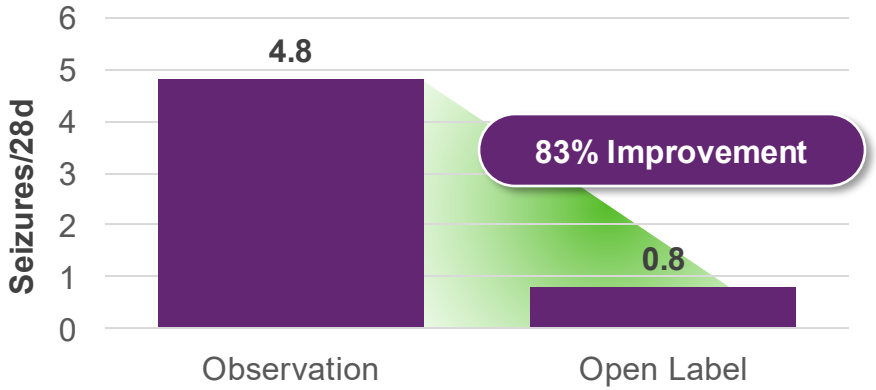
biohaven®

BHV-7000: Patient Case Report From OLE

Kv7

Sample Patient Case Report

- **Subject**: 71-year-old male
- **Type of seizure**: focal impaired awareness
- **Seizure description**: tingling and twitching of cheek spreading to neck and arm followed by arm rigidity and impaired awareness
- **Failed treatments**: levetiracetam, valproate
- **Seizure frequency**: 83% improvement from observation



Preliminary data, study ongoing.

*"Subject has experienced a total of 5 seizures during 176 days in the OLE period. However, he has been **seizure-free for the past 3 months**. Additionally, **no side effects** have been reported during this time. The patient has also demonstrated **meaningful improvement in his quality of life**, reported by both him and his family. They have expressed satisfaction with the treatment and are very positive about their overall experience."*

-- BHV-7000 Focal Epilepsy Clinical Trial Investigator

KEY POINT

BHV-7000 has substantial seizure reduction in selected OLE patient

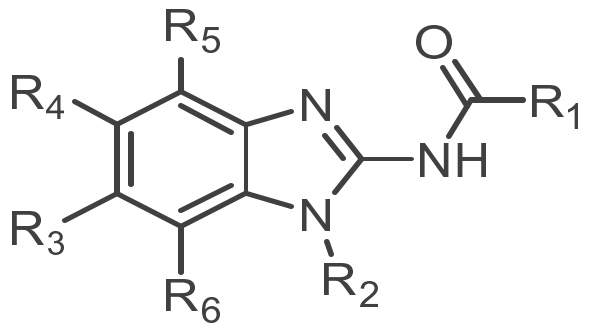
BHV-7000 Med-Chem Designed to Fully Leverage Kv7 Target Potential

Kv7

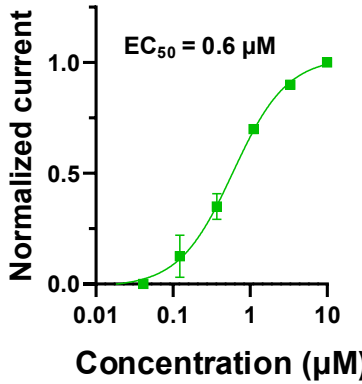
Key areas of differentiation to discover and develop best-in-class Kv7 activator

Pharmacophore-based design principles	Screening and Tier I ADME	Advanced bridging *in vitro* and *in vivo* assays	Clinical
Novel scaffolds	Functional primary screen	Potent context pharmacology	Wide therapeutic index
Photostability	Off-target screening (GABA)	Anti-seizure activity and tolerability	CNS active without delta enhancement

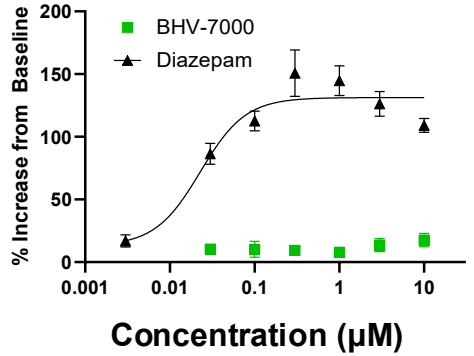
Bicyclic Imidazole



Concentration Dependent Activation



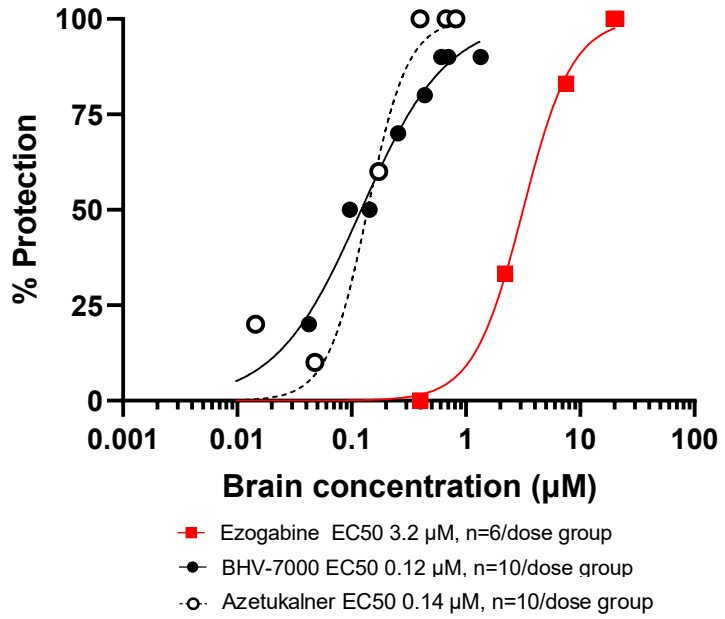
$GABA_A$ PAM activity at α1β3γ2 receptor



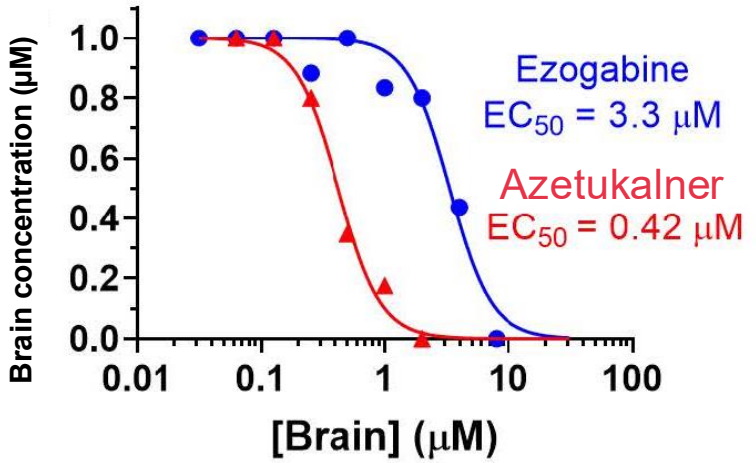
BHV-7000 Equipotent With Azetukalner in Preclinical MES Assay

Kv7

Efficacy of BHV-7000, Azetukalner and Ezogabine in the Rat AC-MES Assay



Efficacy of Azetukalner and Ezogabine in the Mouse AC-MES Assay[1]



1. Dean, AES 2020. Poster #654.

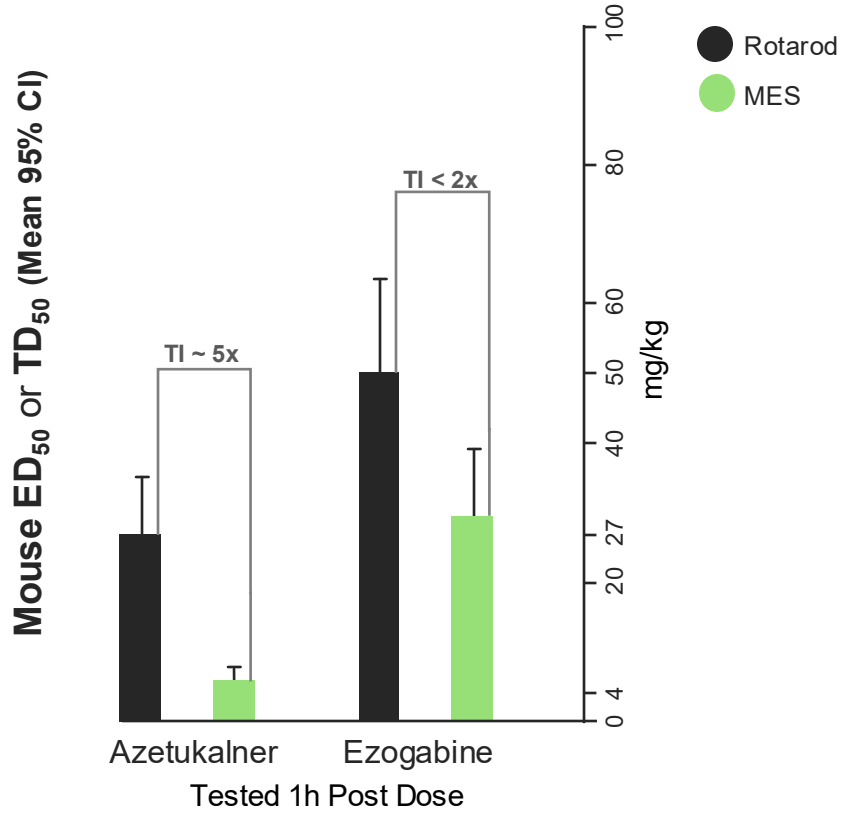
KEY POINT

BHV-7000 potency consistently ~ 120 nM in complex neuronal system assays

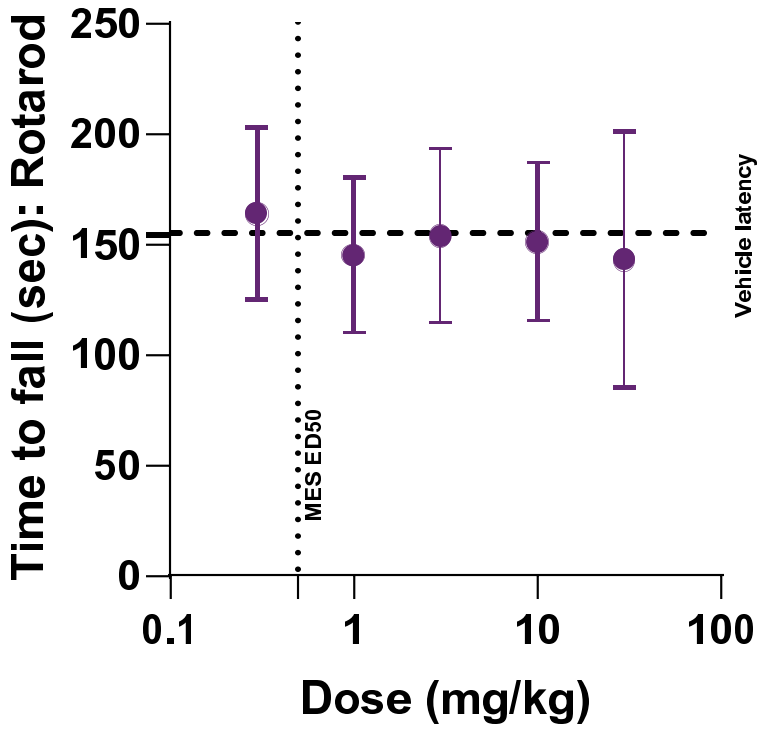
BHV-7000 Differentiated Preclinically From Ezogabine and Azetukalner With Superior Tolerability

Kv7

Efficacy/Tolerability Index



BHV-7000 Efficacy/Tolerability Index



KEY POINT

No effect of BHV-7000 on rotarod fall latency at 60x the ED_{50} — TI not calculable

Single Doses of BHV-7000 IR Achieve Multiples Above MES EC_{50} and Are Well-Tolerated in Healthy Volunteers

Kv7

BHV-7000

Dose (mg)	Cmax (ng/mL)	MES EC_{50} (ng/mL)	Cmax: MES EC_{50}	Nervous System AEs, n (%)[1]		
				Somnolence	Dizziness	Headache
25	253 (12)	186	1.36x	0	0	1 (16.7)
50	664 (31)	186	3.57x	0	0	1 (16.7)
100	877 (42)	186	4.72x	0	0	0

Azetukalner[2,a]

Dose (mg)	Cmax (ng/mL)	MES EC_{50}[3] (ng/mL)	Cmax: MES EC_{50}	Nervous System AEs, n (%)		
				Somnolence	Dizziness	Headache
25	45.8 (14.3)	81	0.57x	2 (33.3)	3 (50.0)	0

1. Awsare B, et al. AES 2023. Poster 3.265. 2. Aycardi. AES 2018. Poster 3.282. 3. Dean. AES 2020. Poster 654. AES 2020.
a. Dosed fasted

Multiple Doses of BHV-7000 ER Exceed MES EC_{50} Over Entire Dosing Interval and Are Well-Tolerated in Healthy Volunteers

Kv7

BHV-7000

QD x 7 days (mg)	Cmax (ng/mL)	Ctau (ng/mL)	MES EC_{50} (ng/mL)	Cmax: MES EC_{50}	Ctau: MES EC_{50}	Nervous System AEs[1]		
						Somnolence	Dizziness	Headache
50	406 (21.8)	265 (26.0)	186	2.18x	1.42x	0	0	0

Azetukalner[2,a]

QD x 10 days (mg)	Cmax (ng/mL)	Ctau[3] (ng/mL)	MES EC_{50}[4] (ng/mL)	Cmax: MES EC_{50}	Ctau: MES EC_{50}	Nervous System AEs, n (%)		
						Somnolence	Dizziness	Headache
25	96.7 (8.6)	59.5	81	1.19x	0.73x	4 (66.7)	2 (33.3)	3 (50.0)

1. Awsare B, et al. AES 2024. Poster 486. 2. Aycardi, AES 2018. Poster 3.282, AES 2018. 3. Digitized estimate from Aycardi, AES 2018. Poster 3.282. 4. Dean, AES 2020. Poster 654.
a. Dosed fed

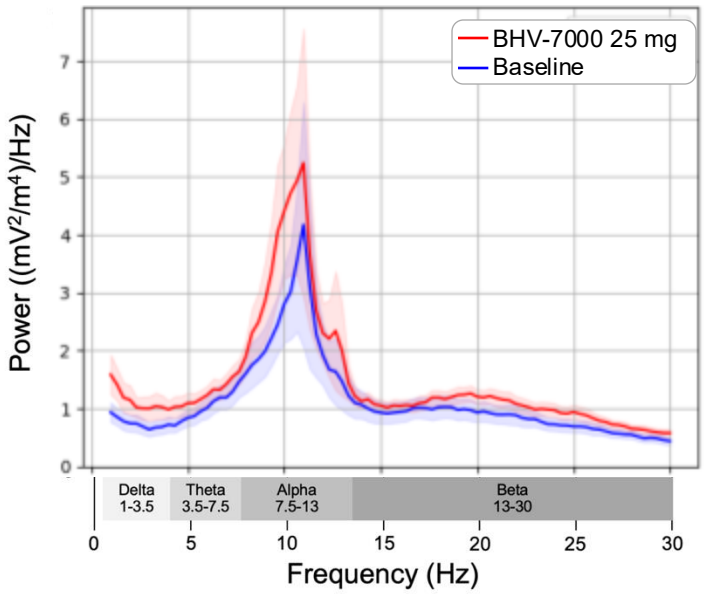
KEY POINT

In contrast to BHV-7000, azetukalner exhibits dose-limiting CNS tolerability issues in healthy volunteers at exposures predicted to be effective by preclinical MES data

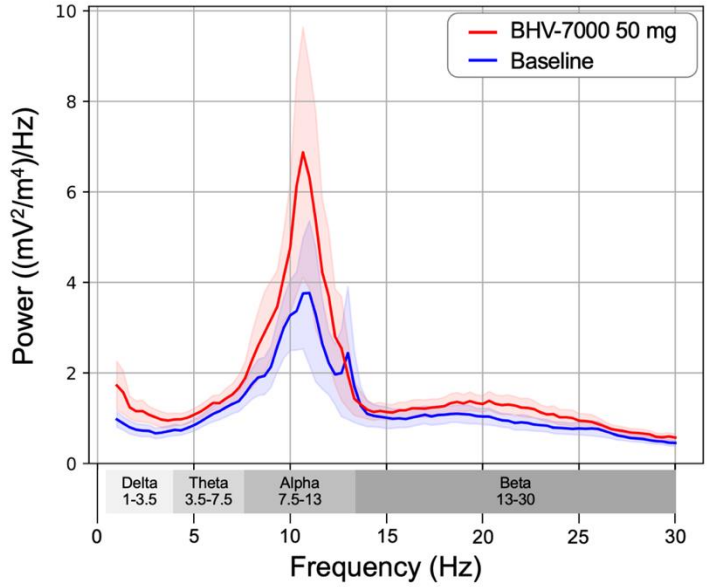
Dose-Response BHV-7000 CNS Activity Demonstrated in EEG Study

Kv7

Spectrum at Broadband Max Response BHV-7000 25 mg vs Baseline[1]



Spectrum at Broadband Max Response BHV-7000 50 mg vs Baseline[1]



		Nervous System AEs		
Single Dose (mg)	Cmax (ng/mL)	Somnolence	Dizziness	Headache
25	309 (35.7)	0	0	0
50	537 (36.4)	0	0	0

1. Lerner J, et al. AES 2023. Poster 2.510.

Excellent CNS Tolerability Observed in Ongoing Phase 2/3 Focal Epilepsy Studies (Blinded Data) Consistent With Phase 1 Profile

Kv7

BHV-7000

	Nervous System AEs, %		
Doses (mg)	Somnolence	Dizziness	Headache
25/50/75	1.7	1.1	3.3

No AEs observed at > 5% in any SOC; studies are still ongoing

Azetukalner[1]

	Nervous System AEs, %		
Doses (mg)	Somnolence	Dizziness	Headache
10/20/25	15.6	24.6	10.0

1. French JA, et al. *JAMA Neurol.* 2023;80(11):1145-1154.

KEY POINT

BHV-7000 well-tolerated in focal epilepsy at exposures predicted to be effective based on preclinical data and associated with CNS activity on EEG in healthy volunteers

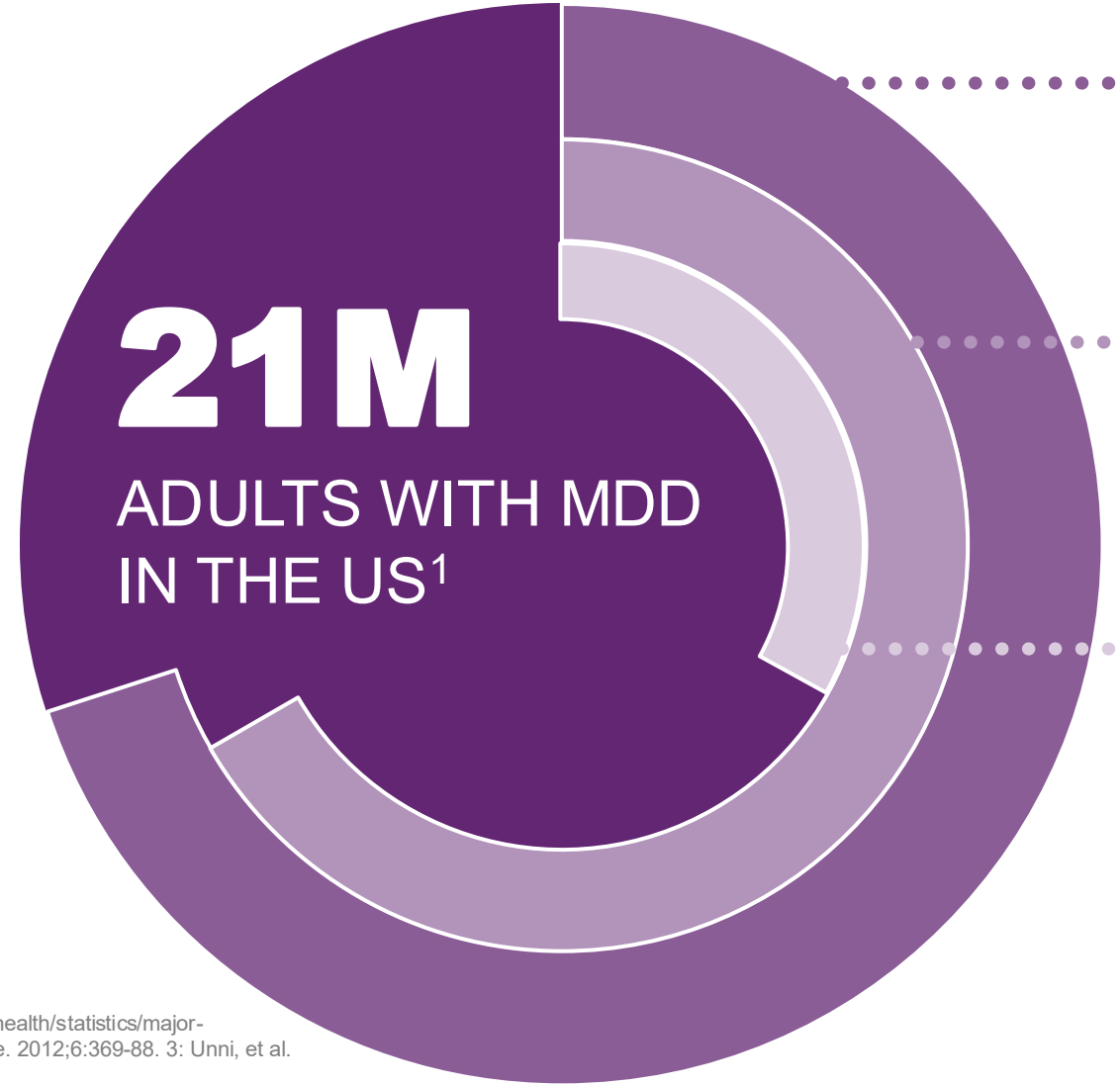
John H. Krystal, MD
Robert L. McNeil, Jr. Professor of Translational Research; Chair, Department of Psychiatry
Yale SCHOOL OF MEDICINE
Chief of Psychiatry
YaleNewHavenHealth
Yale New Haven Hospital

Kv7 for the Treatment of Depression

biohaven®

Major Depressive Disorder Is a Prevalent Illness With Treatments That Are Limited by Side Effects and Suboptimal Efficacy

Kv7



70%
fail to respond to 1st line SSRIs[2]

60%
are medication nonadherent most commonly due to side effects[3]

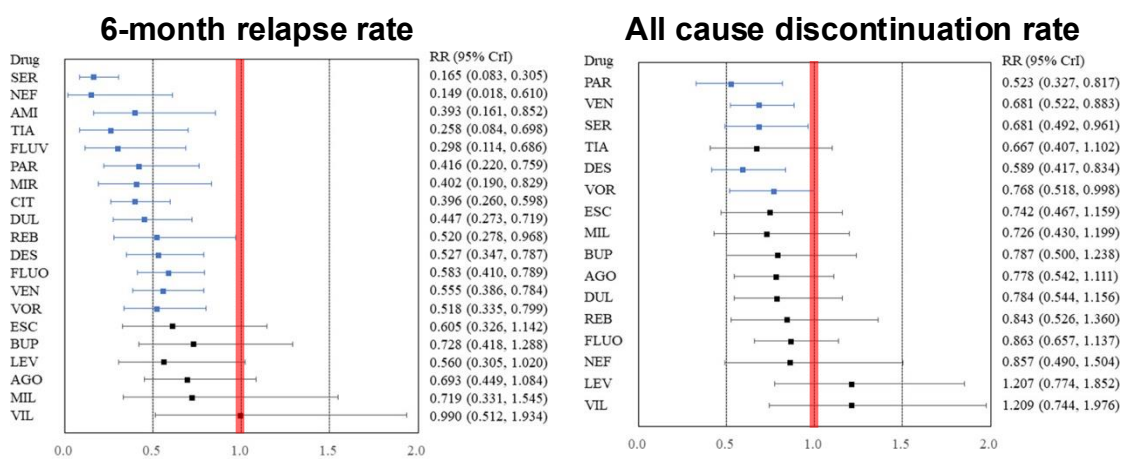
33%
remain refractory to 2nd and 3rd line[2]

1. NIH. Accessed May 25, 2025. www.nimh.nih.gov/health/statistics/major-depression. 2: Al-Harbi KS. Patient Prefer Adherence. 2012;6:369-88. 3: Unni, et al. *Journal of Affective Disorders*, 344, 446-450.

Antidepressant CNS Side Effects Are a Major Cause of Early Discontinuation and Inadequate Treatment

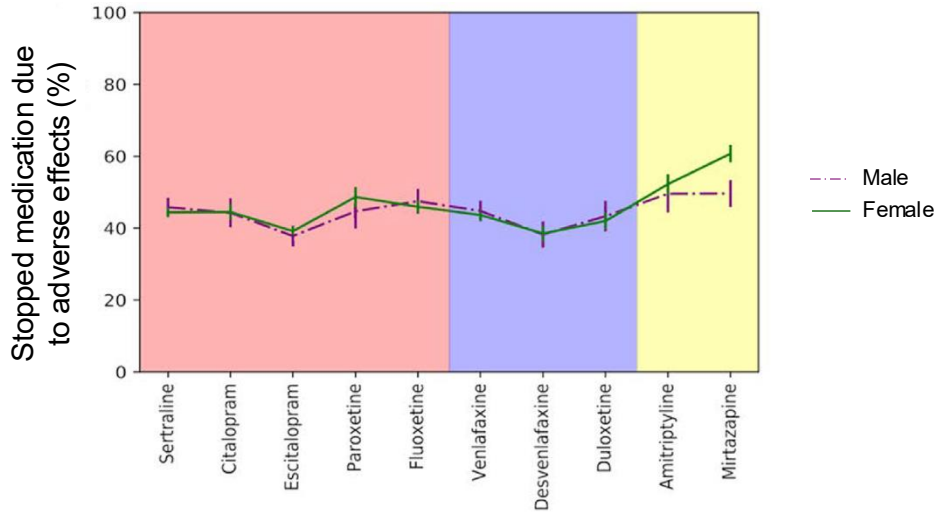
Kv7

Antidepressants for long-term treatment of MDD across 34 studies with 9,384 patients[1]



- Lower risk of CNS AEs (dizziness) results in MDD patients staying on treatments longer with lower 6-month relapse rates

Discontinuation of antidepressants in 20,000 MDD patients[2]



- High AE-related discontinuation rates are seen with commonly used antidepressants (40-60% discontinuation rate)
- CNS AEs (dizziness, drowsiness) lead to frequent and early treatment discontinuation

1. Iwata N, et al. *Mol Psychiatry*. 2023 Jan;28(1):402-409. 2. Campos AI, et al. *Ann Gen Psychiatry*. 2023 Nov 24;22(1):49.

KEY POINT

BHV-7000 is potentially a paradigm shifting antidepressant with excellent CNS tolerability

Available Antidepressants Have Limited Efficacy for Anhedonia

ANHEDONIA

Inability to experience pleasure

a major unmet need in MDD

- Represents one of two core symptom domains of MDD[1]
- Affects 70% of MDD patients[2]
- Can persist even when medications treat depressive symptoms effectively[3]

Anhedonia Predicts[1,3]

- Higher depression severity
- Longer episode duration
- Increased suicidality
- Poor QoL
- Poor treatment response

1: Khazanov GK et al. *Br J Clin Psychol*. 2022 Jun;61(2):255-280. 2: Current Topics in Behavioral Neurosciences, Anhedonia…; Springer, 2022. 3: Luca, A et al. *Int J Neuropsychopharmacol*. 2024 Dec 1;27(12):pyae055.

KEY POINT

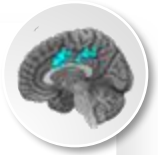
Kv7 activation is a novel antidepressant mechanism showing promise for treating anhedonia

Increasing Clinical Evidence Supports Potential of Kv7 Activation in MDD

Kv7

2020

Ezogabine OL pilot study[1]

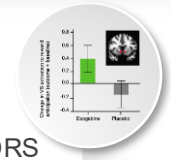


Reduction of depressive and anhedonic symptoms: MADRS (-13.7, p<.001) and SHAPS (-6.1, p<.001)

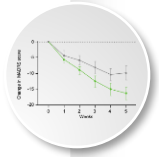
Changes in reward pathway neurocircuitry: decreased functional connectivity on f-MRI in reward-related regions (vCa, MCC, PCC)

2021

Ezogabine RCT[2]



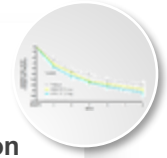
Reduction of depressive and anhedonic symptoms vs pbo: MADRS (-7.9, p<.001) and SHAPS (-6.9, p<.001)



Changes in reward pathway neurocircuitry: numerical increase in VS response to reward anticipation on fMRI

2023

Azetukalner RCT[3]



Rapid-onset, dose-related reduction of depressive and anhedonic symptoms vs pbo: MADRS (-3, p=.135) and SHAPS (-2.5, p<.05) in 20 mg group

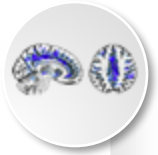
Efficacy not optimized likely due to dose limiting tolerability concerns: CNS AEs (43%) including dizziness (18%) in 20 mg group

2025

Ezogabine fMRI Analysis[4]

Kv7 activation normalizes reward pathway neurocircuitry abnormalities associated with depression: reduced VTA hyperactivity on fMRI

Ezogabine fMRI Analysis[5]



Antidepressant effects mediated through reward pathway neurocircuitry: decreased striatal-middle/posterior cingulate connectivity on fMRI

2H 2025

BHV-7000 MDD Study Topline Expected

Azetukalner Mt Sinai IST[6]

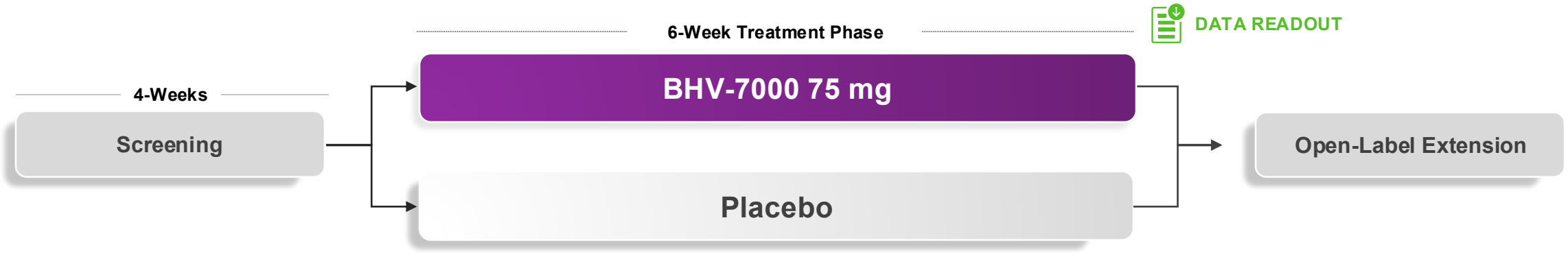
Reduction of depressive and anhedonic symptoms: numerical improvements in MADRS and SHAPS

SHAPS, Snaith-Hamilton Pleasure Scale; **MADRS**, Montgomery Åsberg Depression Rating Scale; **OL**, Open-Label; **RCT**, Randomized Control Trial; **fMRI**, Functional Magnetic Resonance Imaging; **IST**, Investigator Sponsored Trial.

1. Tan, et al. *Mol Psychiatry*. 2020 Jun;25(6):1323-1333; 2. Costi, et al. *Am J Psychiatry*. 2021 May 1;178(5):437-446; 3. Butterfield N, et al. ASCP 2024. Poster W67. 4. Morris, et al. *Mol Psychiatry*. 2025 Mar 25; 5. Chowdhury, et al. *Biol Psychiatry*. 2025 Mar 4:S0006-3223(25)01011-X. 6. Xenon Press Release May 12, 2025.

Pivotal Phase 2 Study in Major Depressive Disorder Ongoing

Kv7



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Subjects with Major Depressive Disorder (MDD) with at least one prior depressive episode who are currently experiencing a depressive episode with anhedonia (HAM-D ≥ 20, SHAPS ≥ 20)
SAMPLE SIZE	300 subjects (randomized 1:1)
TREATMENT	BHV-7000 vs placebo
TREATMENT DURATION	6-weeks
ENDPOINTS	MADRS (primary), SHAPS, CGI-S, Q-LES-Q-SF

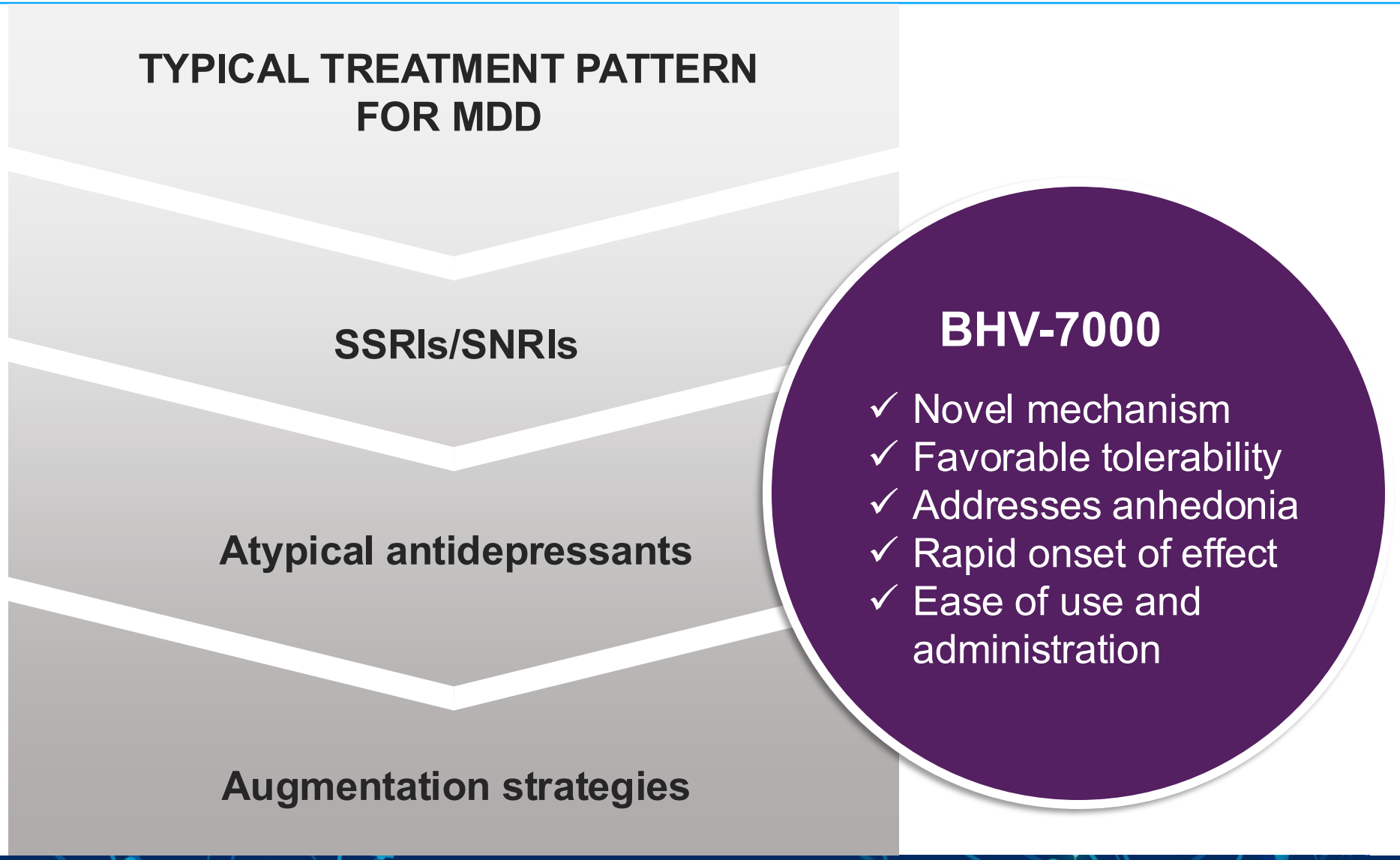
SHAPS, Snaith-Hamilton Pleasure Scale; **MADRS**, Montgomery Åsberg Depression Rating Scale; **CGI-S**, Clinical Global Impression Scale – Severity; **Q-LES-Q-SF**, Quality of Life Enjoyment and Satisfaction Questionnaire.

KEY POINT

Topline results expected 2H 2025

BHV-7000 Has Potential to Overcome Limitations of Existing Therapies

Kv7



Professor Thomas Voets

Laboratory of Ion Channel Research
VIB Center for Brain and Disease Research

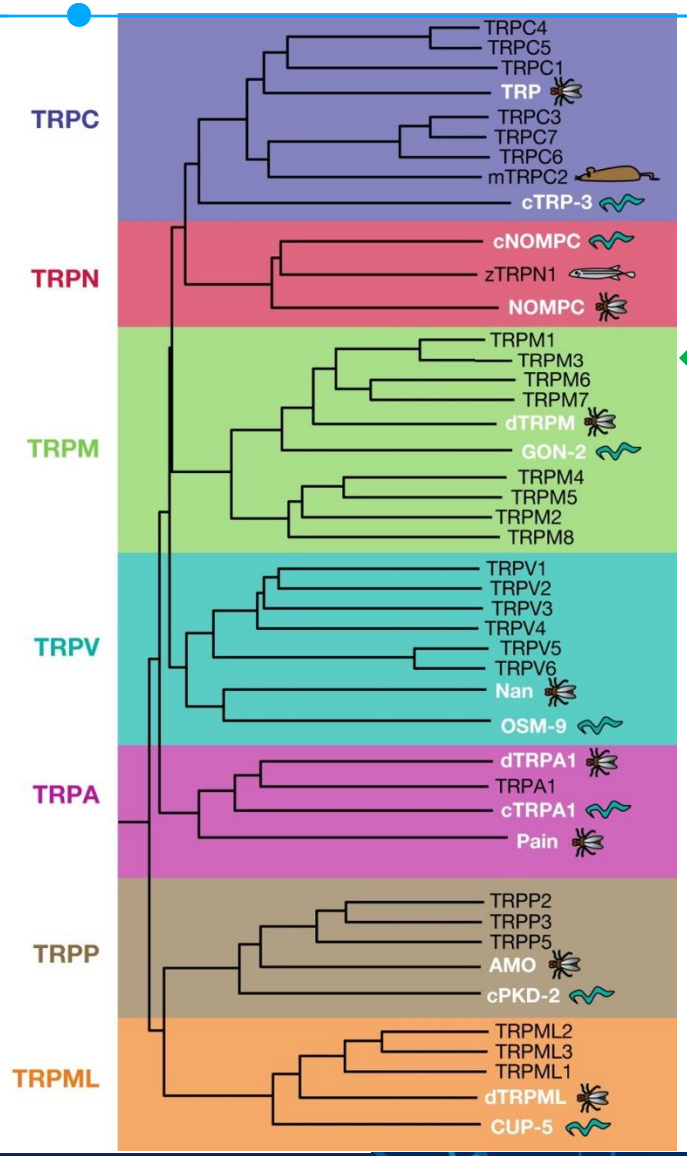
KU LEUVEN

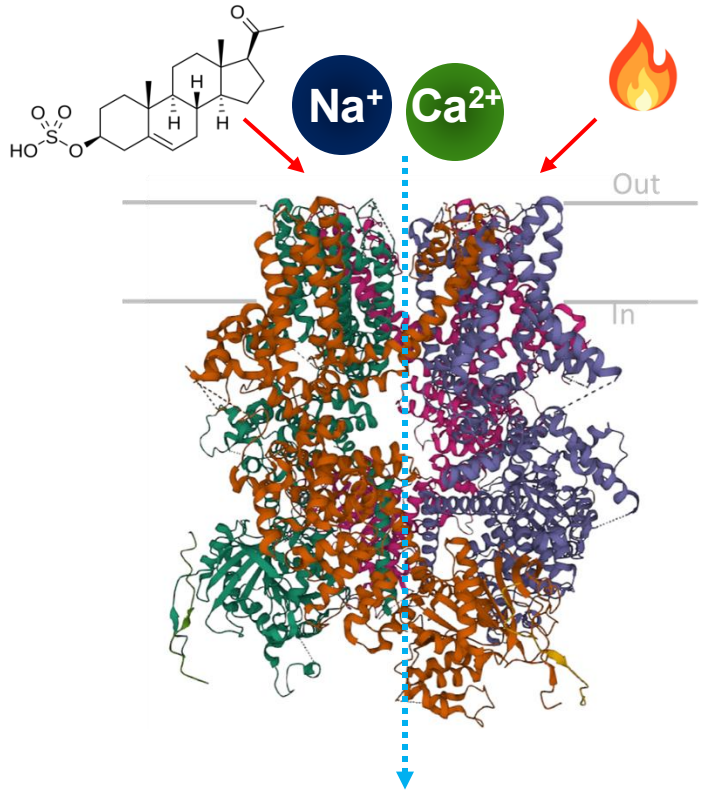
Evolving Landscape of TRPM3 in the Treatment of Chronic Pain and Epilepsy

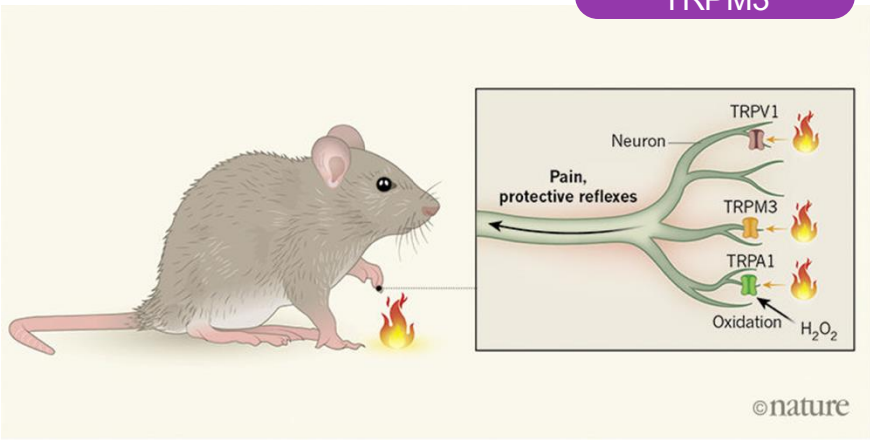
biohaven®

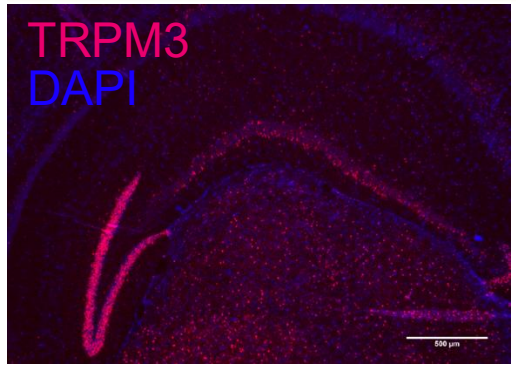
TRPM3 — Member of the Transient Receptor Potential Superfamily

TRPM3









- Tetrameric ion channel in plasma membrane, permeable to Na^+ and Ca^{2+}
- Directly activated by heat and by neurosteroids like pregnenolone sulfate
- Expressed in nociceptor neurons, including terminals in skin and meninges
- One of three redundant sensors for noxious heat
- Expressed in CNS, including excitatory neurons in cortex, hippocampus and cerebellum

TRPM3 Platform Offers Potential to Treat an Expanding Range of Diseases

TRPM3

PERIPHERAL NERVOUS SYSTEM
Pain Disorders

- Genetic analyses link TRPM3 to pain disorders (migraine, trigeminal neuralgia, neuropathic and nociceptive pain)
- TRPM3 is upregulated in preclinical pain models of inflammatory and neuropathic pain
- TRPM3 activation causes pain and CGRP release
- TRPM3 inhibition reverses pain/hypersensitivity

Peripherally restricted TRPM3 antagonists (BHV-2100)

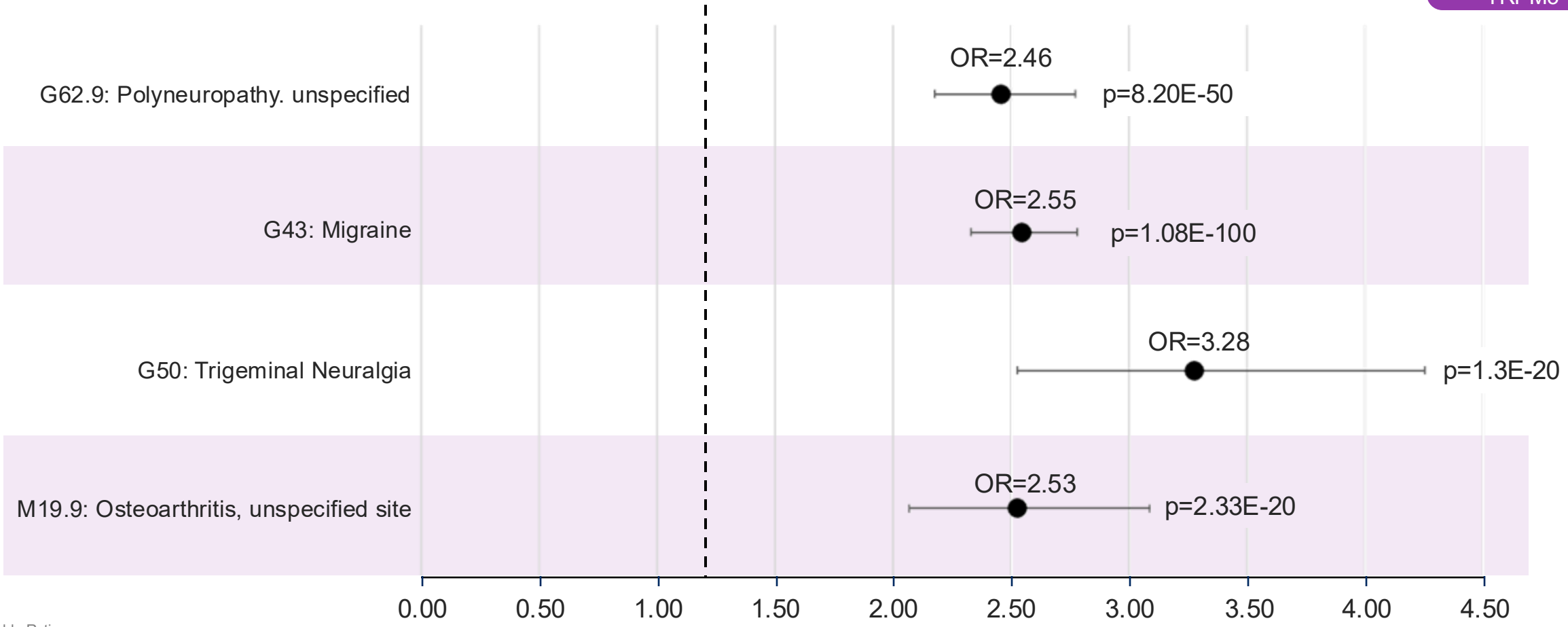
CENTRAL NERVOUS SYSTEM
Pain and Other Brain Disorders

- Gain-of-function variants in TRPM3 cause developmental and epileptic encephalopathies
- TRPM3 activation causes seizures in mice
- TRPM3 inhibition has potent antiseizure efficacy in preclinical models
- Brain-penetrant TRPM3 antagonists have the potential to treat a range of pain disorders

Brain-penetrant TRPM3 antagonists (preclinical)

UK Biobank Analysis Provides Human Genetic Validation for TRPM3

TRPM3



OR: Odds Ratio.
p value claculated using the Benjamini-Hoschberg procedure for False Discovery Rate; error bars represent 95% confidence intervals

KEY POINT

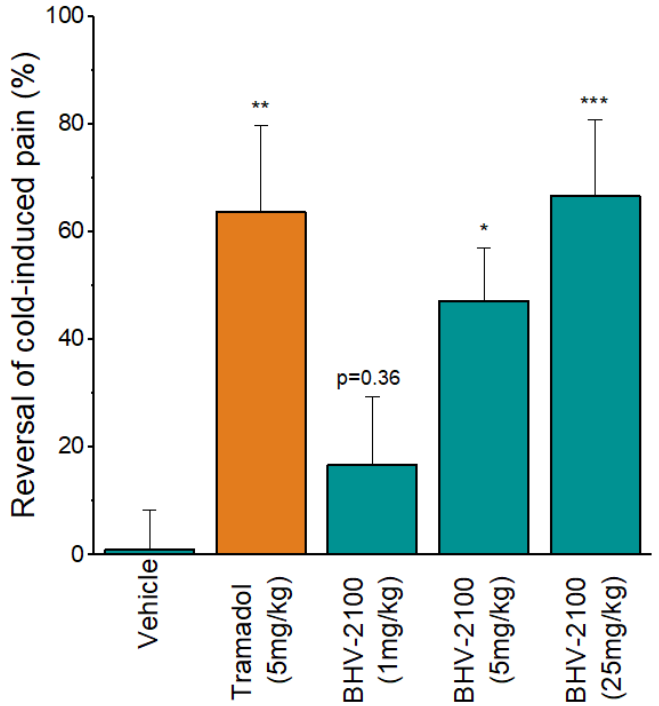
TRPM3 variants increase the risk for neuropathic pain, migraine, trigeminal neuralgia, and osteoarthritis, further corroborating with preclinical experiments

biohaven

Peripheral TRPM3 Antagonism Reverses Pain in Multiple Neuropathic Pain Models

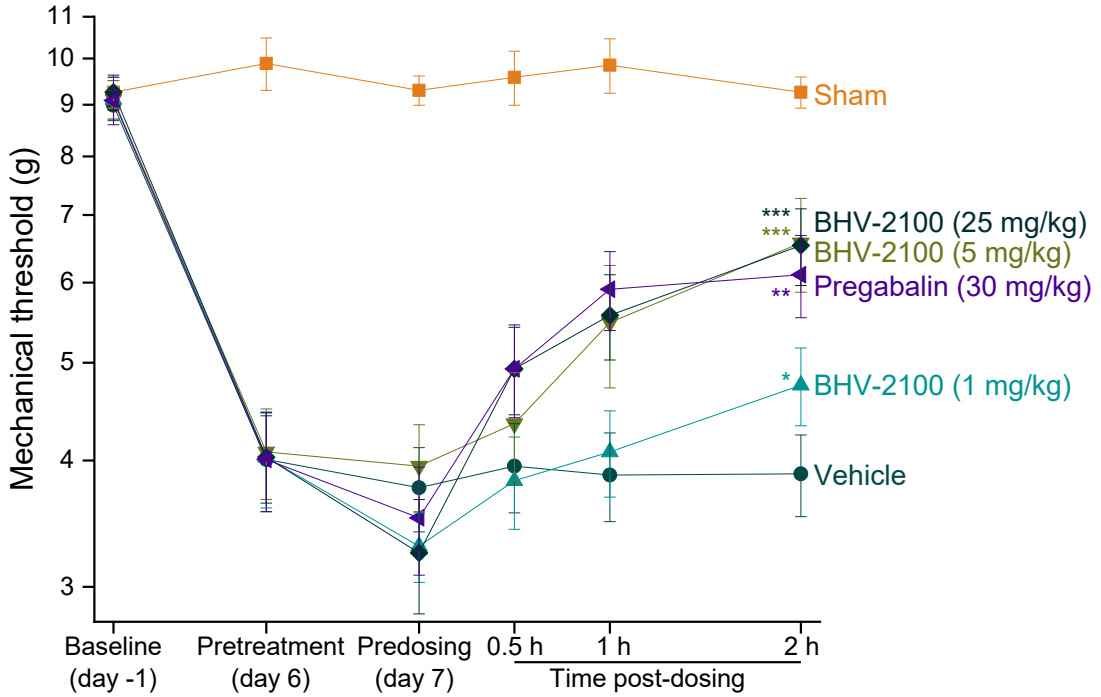
TRPM3

Chemotherapy-Induced Neuropathic Pain Model[1]



Mouse oxaliplatin model

Diabetic Neuropathy Model[1]



Rat streptozotocin (STZ) model

* P<0.05. ** P<0.01. *** P<0.001

1. Vriens J, et al. IASP 2024. Poster WE727

KEY POINT

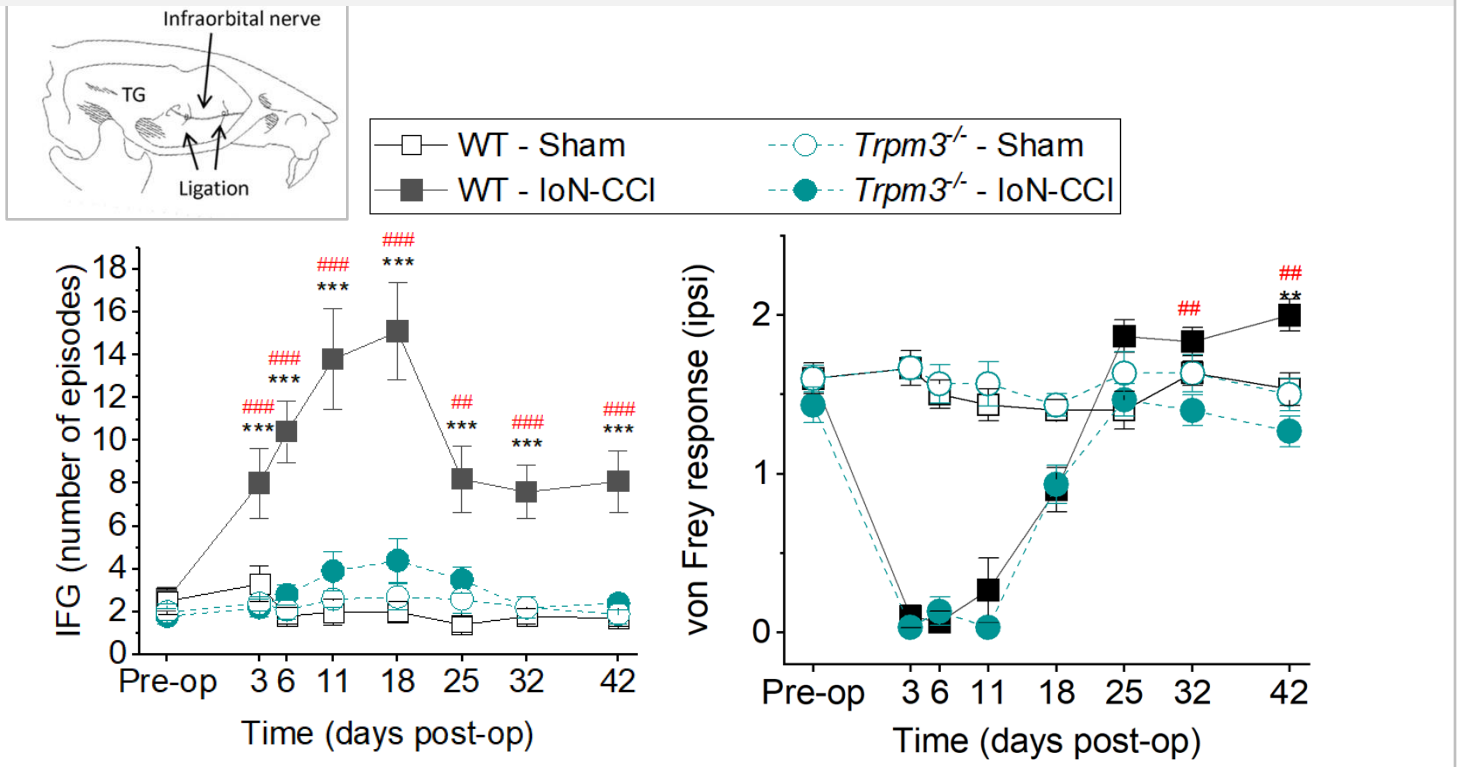
Comparable analgesic efficacy as tramadol or pregabalin, but without sedative side-effects

biohaven

TRPM3 Deficiency and Antagonism in Mouse Trigeminal Neuropathic Pain Models

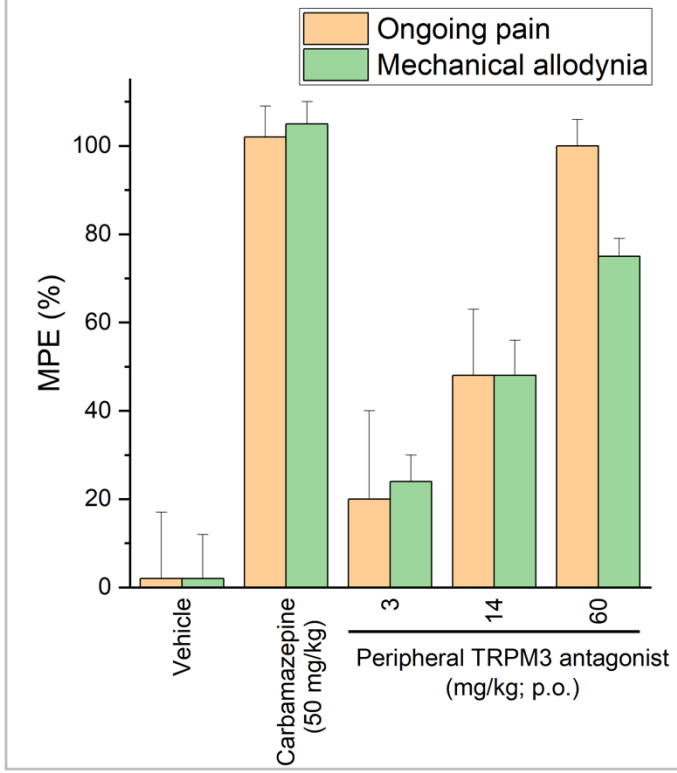
TRPM3

Trigeminal Neuropathy Model: TRPM3 Knockout



** p<0.01, *** p<0.001 for the comparison WT - IoN-CCI versus WT – Sham
p<0.01, ### p<0.001 for the comparison Trpm3$^{-/-}$ - IoN-CCI versus WT - IoN-CCI

Trigeminal Neuropathy Model: TRPM3 Antagonist



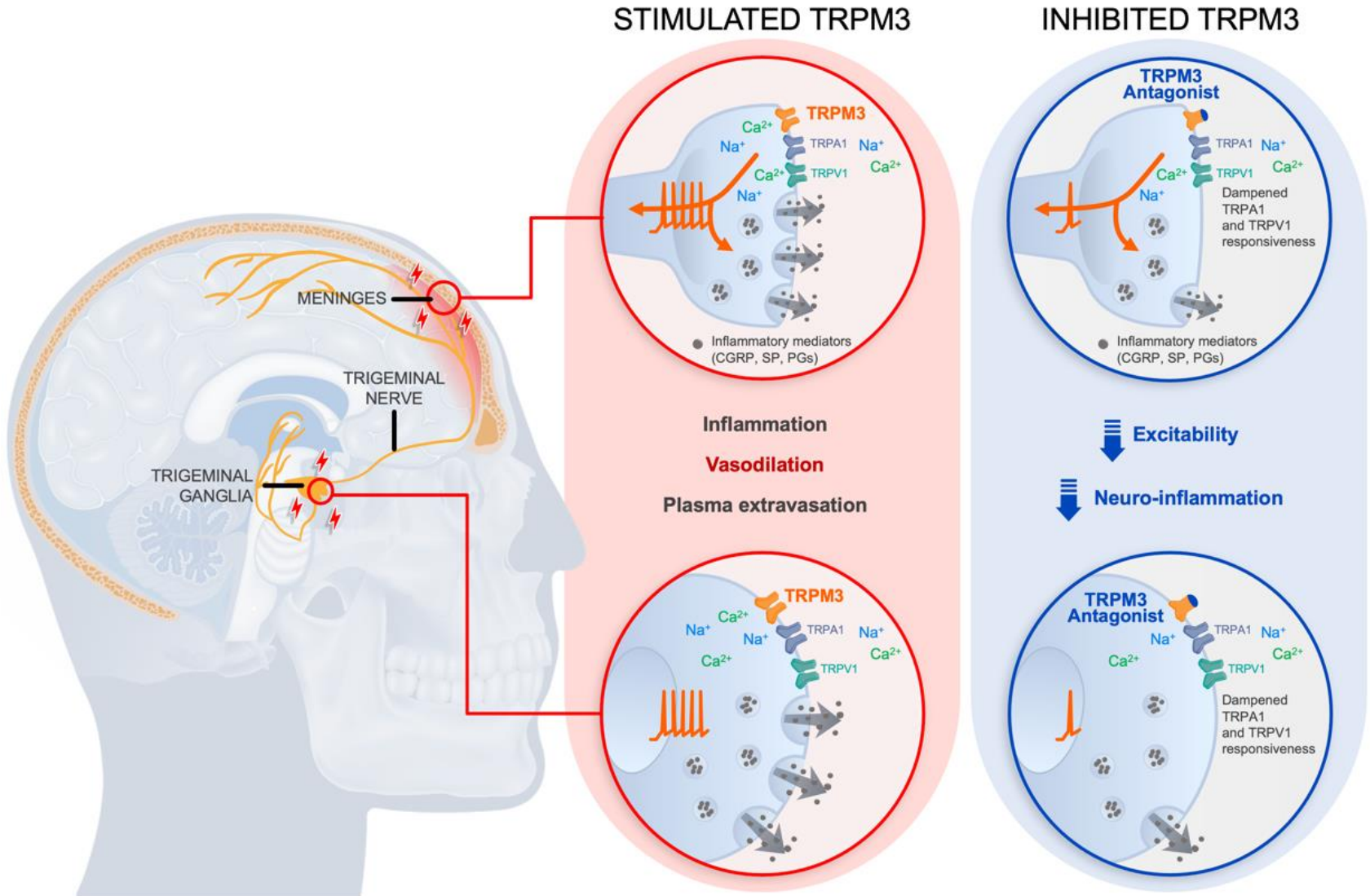
IFG, Isolated Face Grooming; **MPE**, Maximal Possible Effect

KEY POINT

Absence or inhibition of TRPM3 provides sustained pain reversal

biohaven

Mechanistic Rationale for TRPM3 Antagonism to Treat Migraine



TRPM3 Platform Offers Potential to Treat an Expanding Range of Diseases

TRPM3

PERIPHERAL NERVOUS SYSTEM
Pain Disorders

- Genetic analyses link TRPM3 to pain disorders (migraine, trigeminal neuralgia, neuropathic and nociceptive pain)
- TRPM3 is upregulated in preclinical pain models of inflammatory and neuropathic pain
- TRPM3 activation causes pain and CGRP release
- TRPM3 inhibition reverses pain/hypersensitivity

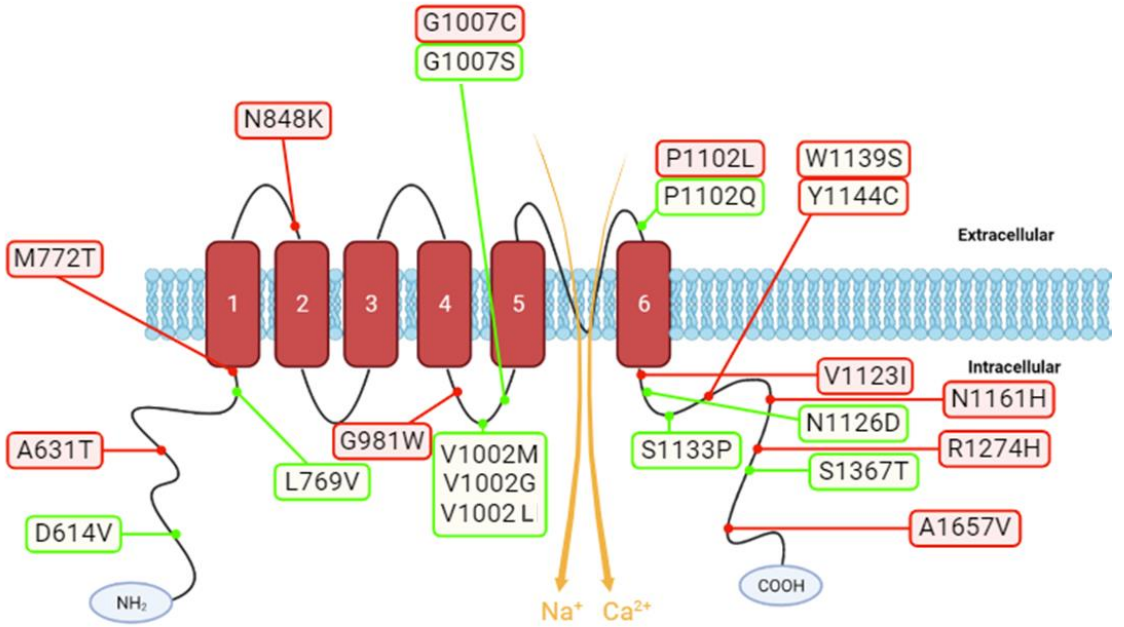
Peripherally restricted TRPM3 antagonists (BHV-2100)

CENTRAL NERVOUS SYSTEM
Pain and Other Brain Disorders

- Gain-of-function variants in TRPM3 cause developmental and epileptic encephalopathies
- TRPM3 activation causes seizures in mice
- TRPM3 inhibition has potent antiseizure efficacy in preclinical models
- Brain-penetrant TRPM3 antagonists have the potential to treat a range of pain disorders

Brain-penetrant TRPM3 antagonists (preclinical)

Rare Genetic Disorder Links TRPM3 to Epilepsy and Neurodevelopment

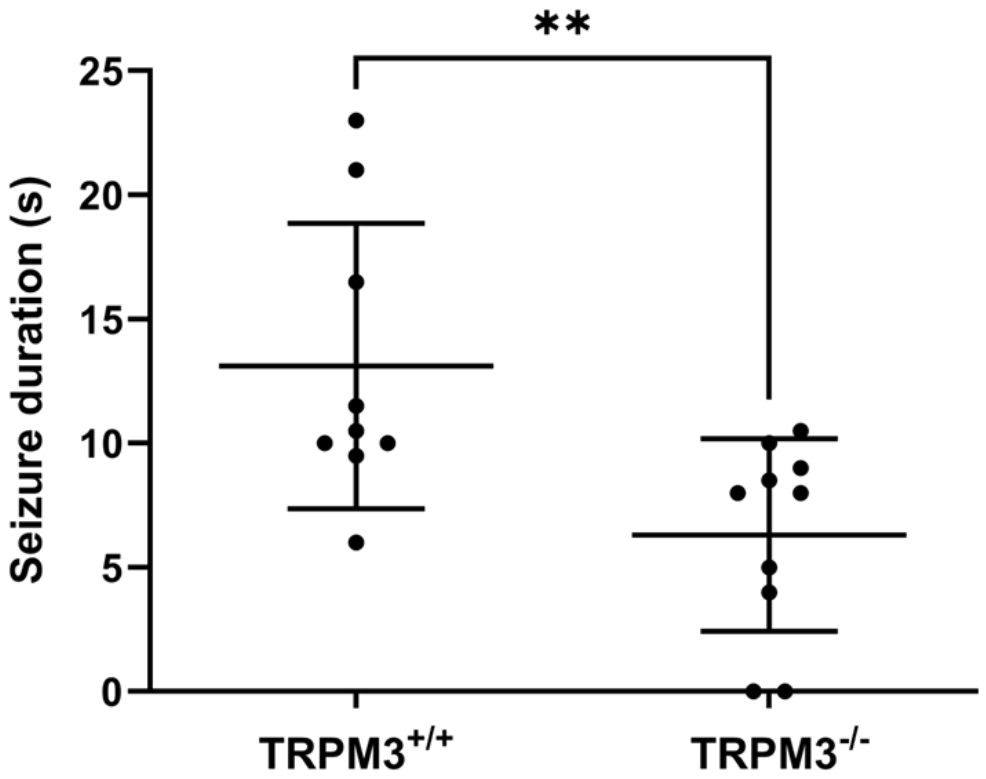


- Patients carry Gain-of-Function mutations in TRPM3
- Complex phenotype with epilepsy, neurodevelopmental delay, cerebellar degeneration and sensory disturbances
- Treatment with primidone (non-selective TRPM3 antagonist) provide improvement, but side-effects limit usage

TRPM3 in the CNS Determines Seizure Susceptibility

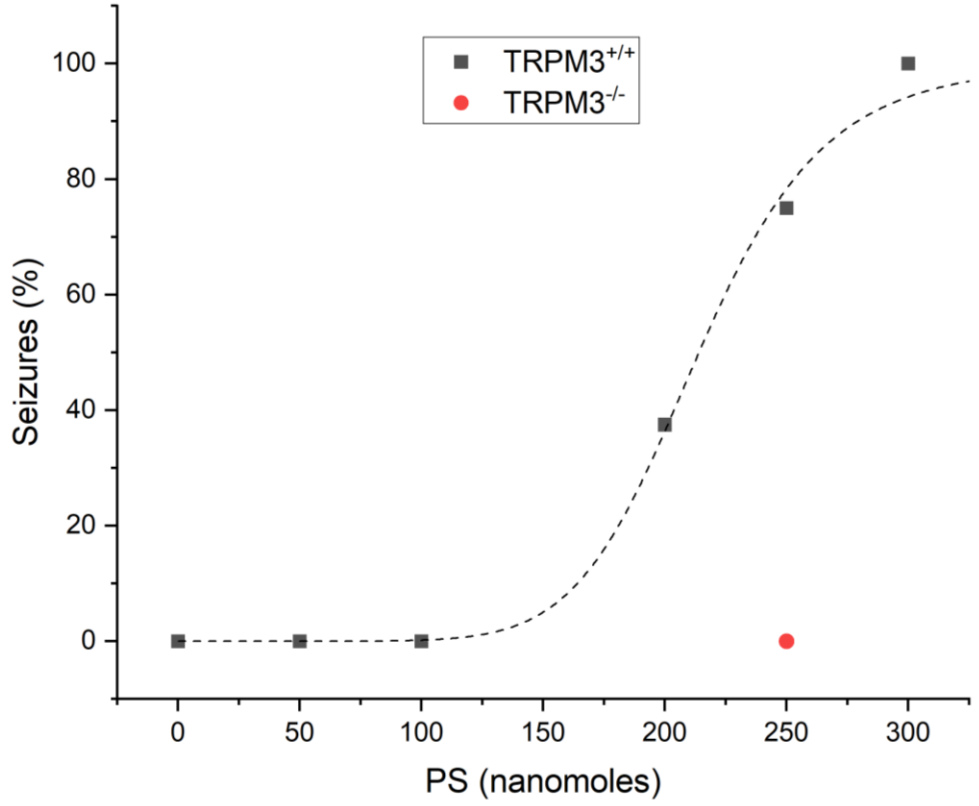
TRPM3

6Hz Seizure Model: TRPM3 Knockout



**: p< 0.01 for the comparison WT versus Trpm3-/-

PS-Induced Seizure Model: TRPM3 Knockout



Pregnenolone sulfate (PS) is a TRPM3 agonist

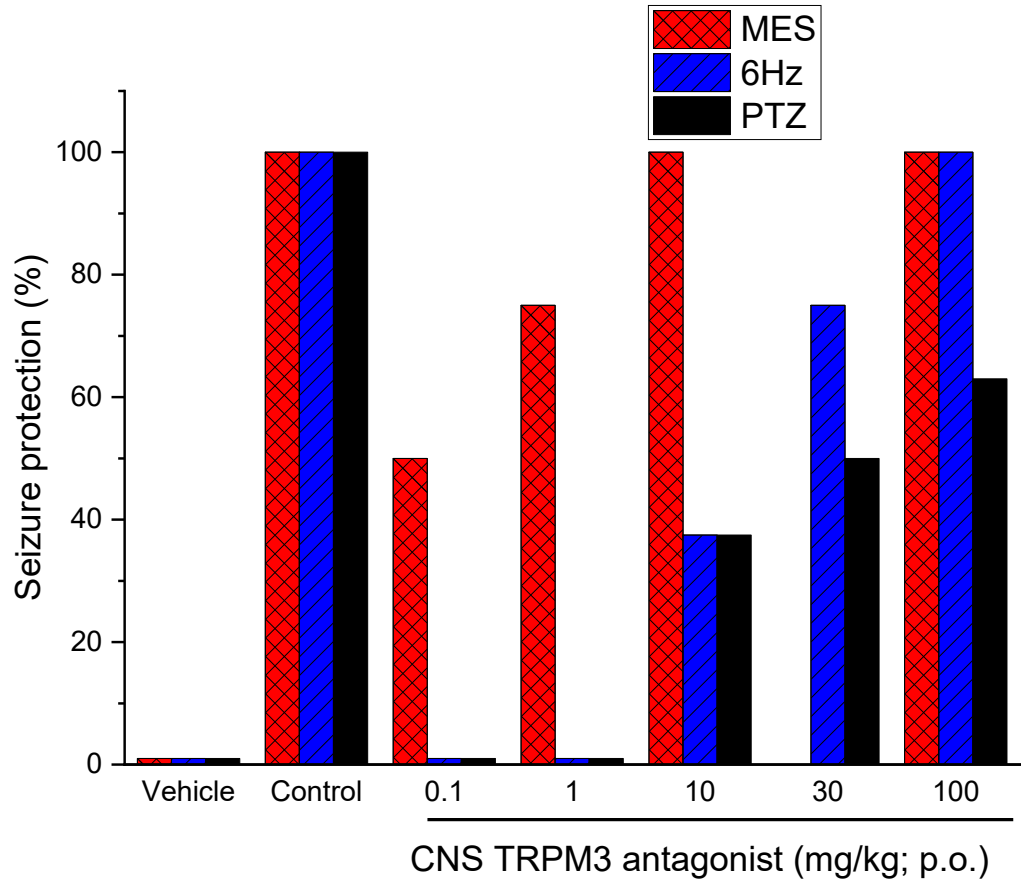
KEY POINT

Absence of TRPM3 provides seizure protection

Selective Brain-Penetrant TRPM3 Antagonists Are Potent Anticonvulsants

TRPM3

Brain-Penetrant TRPM3 Antagonist Across Validated Epilepsy Models



- Biohaven has pre-clinical candidates with potent TRPM3 antagonism, high selectivity and good brain permeability
- Brain-permeant TRPM3 antagonist is active in multiple rodent (mouse and rat) seizure models
- Highly potent: ED_{50} ~0.1mg/kg
  Prolonged (>8h) activity
- No preclinical signs of central side-effects

MES, Maximal Electroshock Seizure Model; **PTZ,** Pentylenetetrazol Model

Volkan Granit, MD, MSc
Senior Medical Director &
Head of Neuromuscular Disease

biohaven®

BHV-2100 Program Overview and Clinical Proof of Concept in Pain

biohaven®

First-in-Clinic TRPM3 Antagonist — Novel Mechanism for the Treatment of Pain

- BHV-2100 is an orally administered, peripherally-restricted and selective TRPM3 antagonist
- Preclinical data shows robust efficacy in pain models
- Highly differentiated from programs that target TRPV1 and TRPA1, avoids TRP family liabilities

Phase 1 Study Data Supports Evaluation in Pain

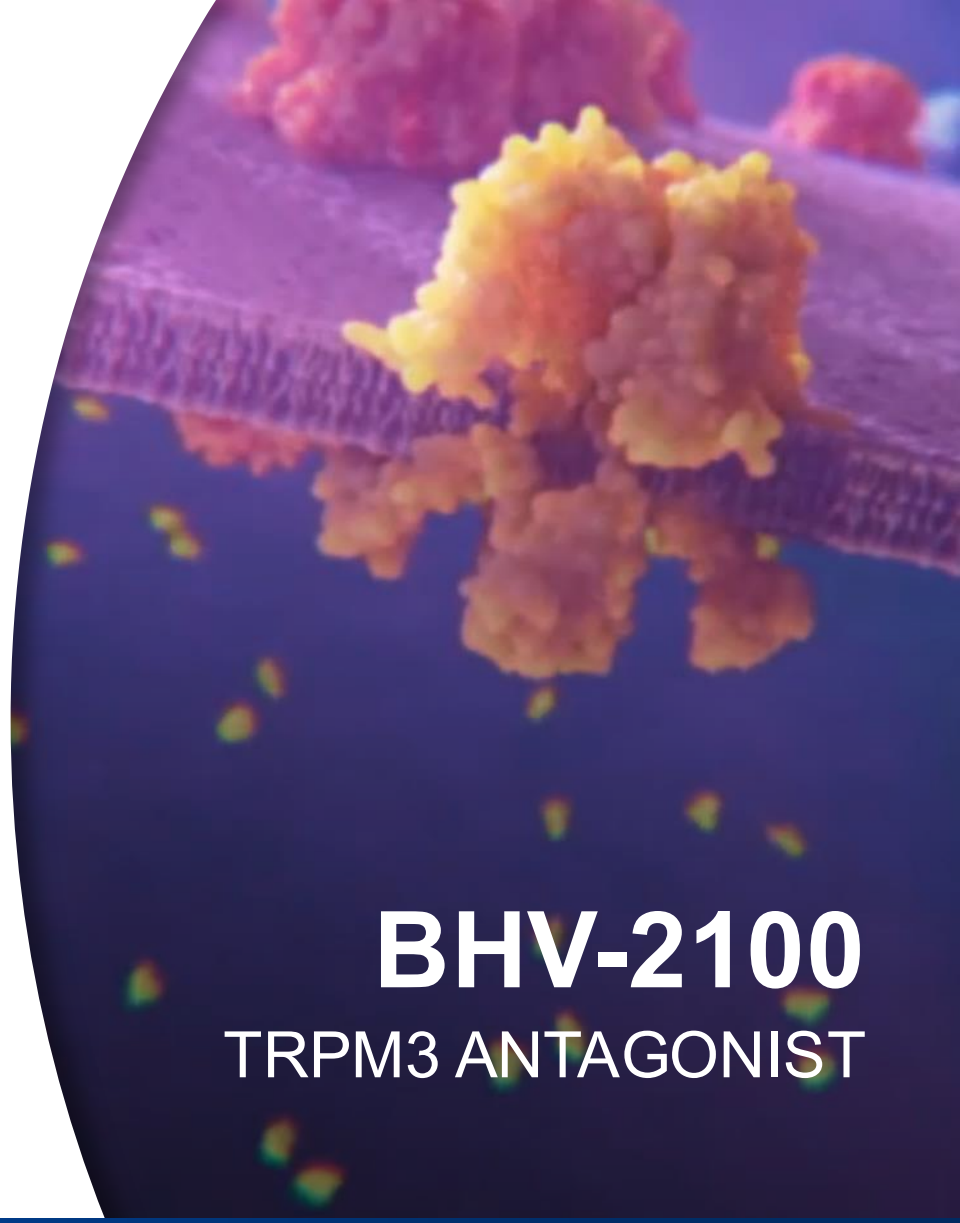
- BHV-2100 demonstrated excellent safety/tolerability and favorable PK
- Proof of concept demonstrated for pain

The Therapeutic Landscape of TRPM3-Targeted Therapies Is Evolving

- Emerging data support the potential for targeting TRPM3 in nociceptive pain conditions
- Non-clinical data support Biohaven's brain-penetrant TRPM3 program in epilepsy, as well as pain

Milestones Achieved

- Laser-evoked pain proof-of-concept trial completed
- Proof-of-concept trial for acute treatment of migraine ongoing



KEY POINT

Proof of concept for pain demonstrated; program advancing to later stage pain trials

BHV-2100: Laser Evoked Pain Proof-of-Concept Study Demonstrates Anti-Nociceptive and Anti-Hyperalgesic Effects

TRPM3

Laser-evoked pain on UV-inflamed skin

Multiple methods to assess pain:

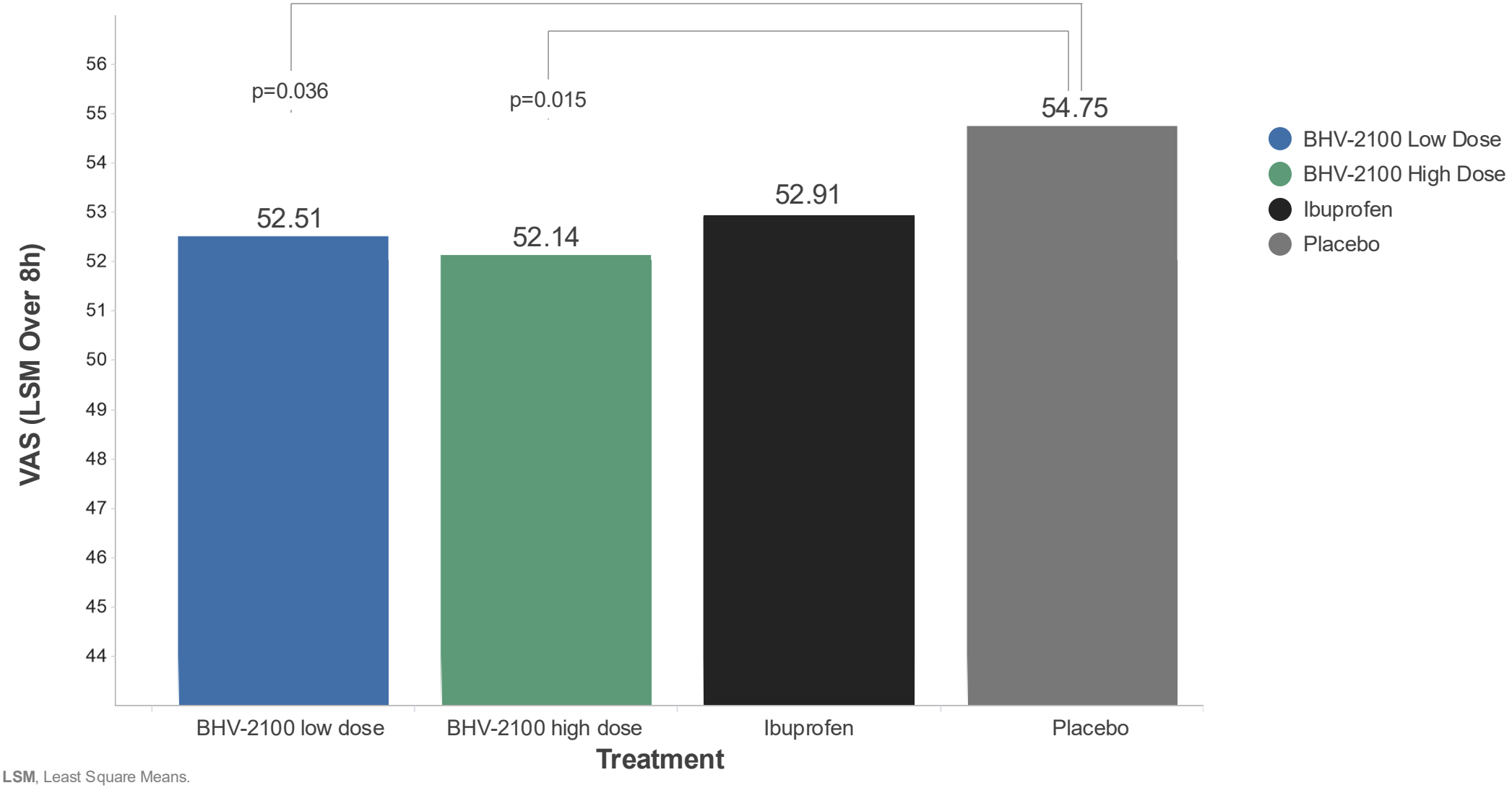
- Visual analog scale (VAS)
- Mechanical pain (weighted needle)
- Inflammation (skin reflection spectroscopy)

KEY POINT

First indication of potential clinical efficacy in pain with novel TRPM3 antagonist BHV-2100

BHV-2100: Statistically Significant Pain Reduction in Inflamed Skin

TRPM3

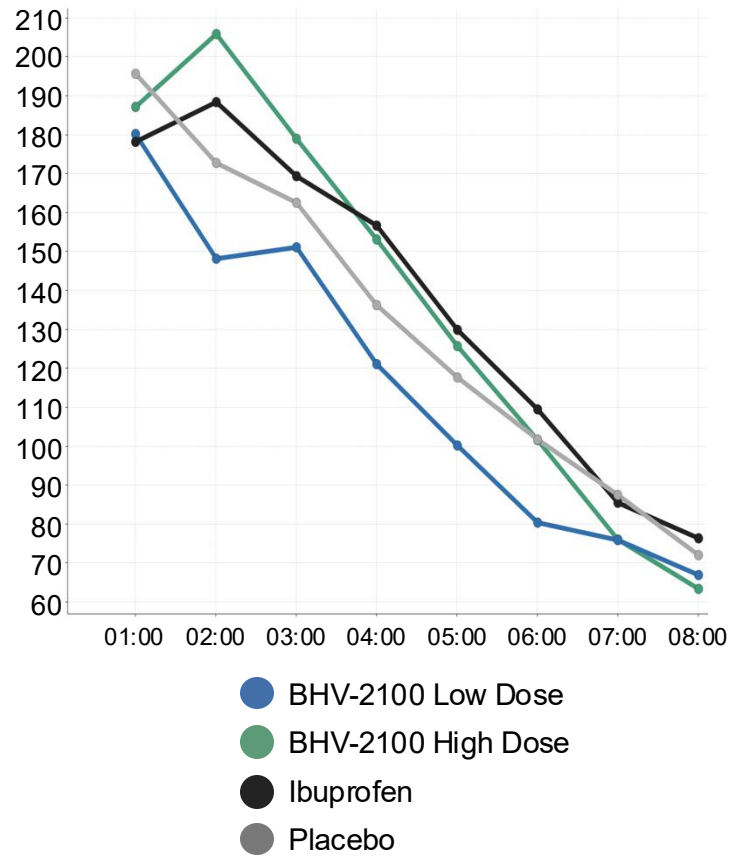


VAS, Visual Analog Scale; **LSM**, Least Square Means.
Data shown represents LSM over 8h post-dose

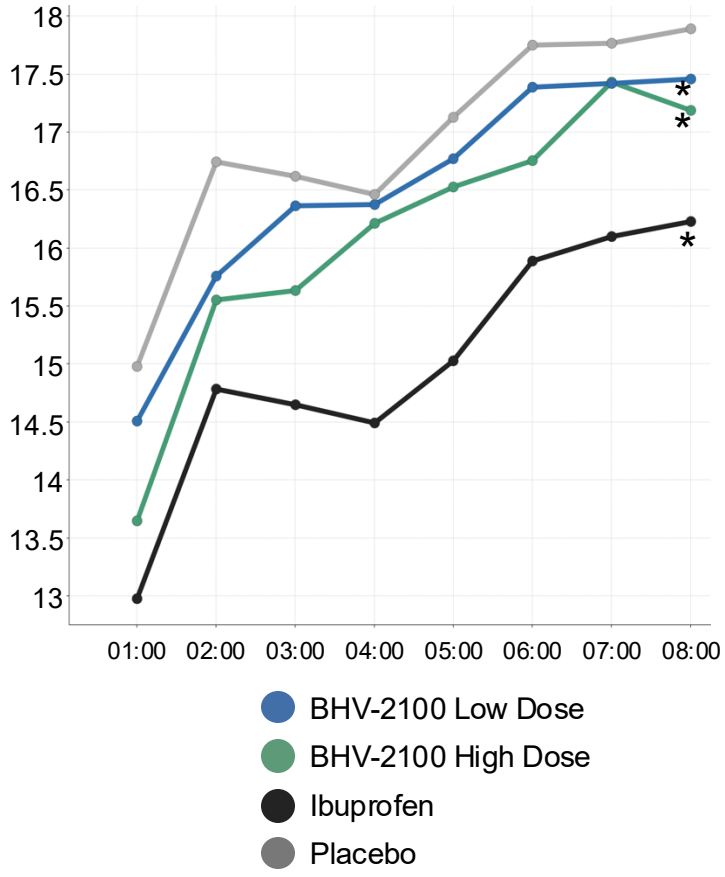
Weighted Needle Threshold and Skin Reflection Spectroscopy on UVB-Inflamed Skin Over 8 Hours

TRPM3

Weighted Needle Threshold (mN)



Skin Reflection Spectroscopy



BHV-2100 numerically increased the Weighted Needle Threshold (higher threshold suggests less mechanical pain)

TRPM3 antagonism reduces cellular excitability

↓

Reduced release of inflammatory cytokines

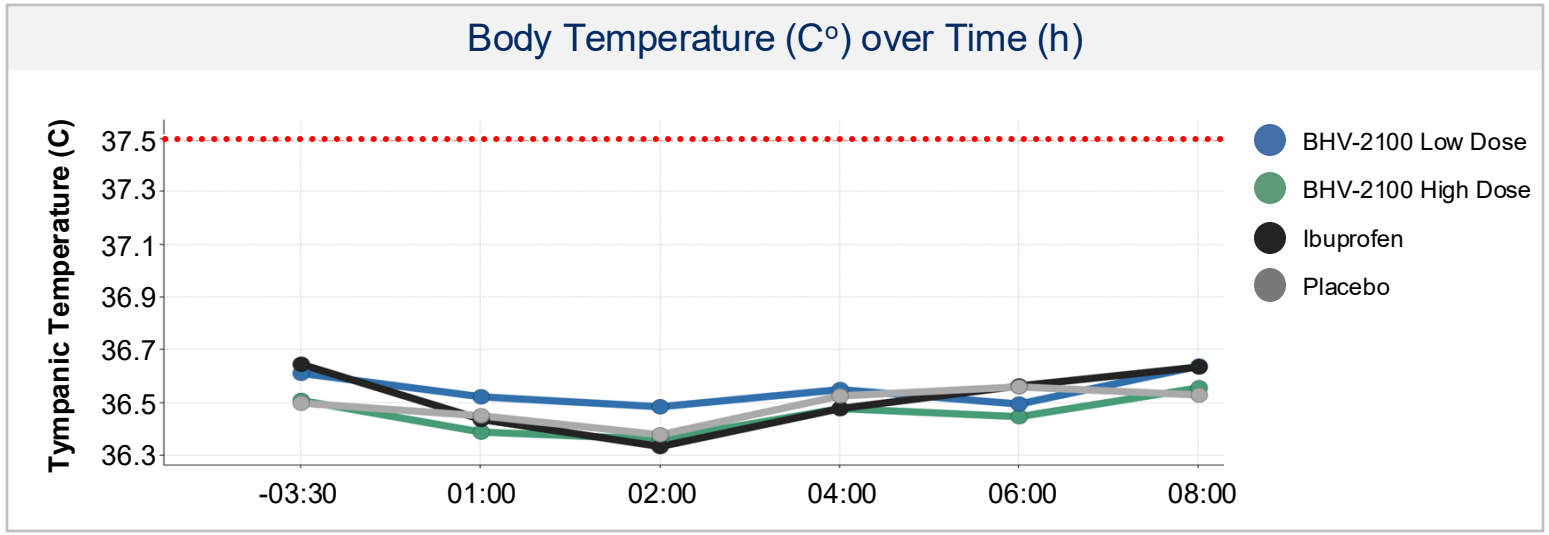
↓

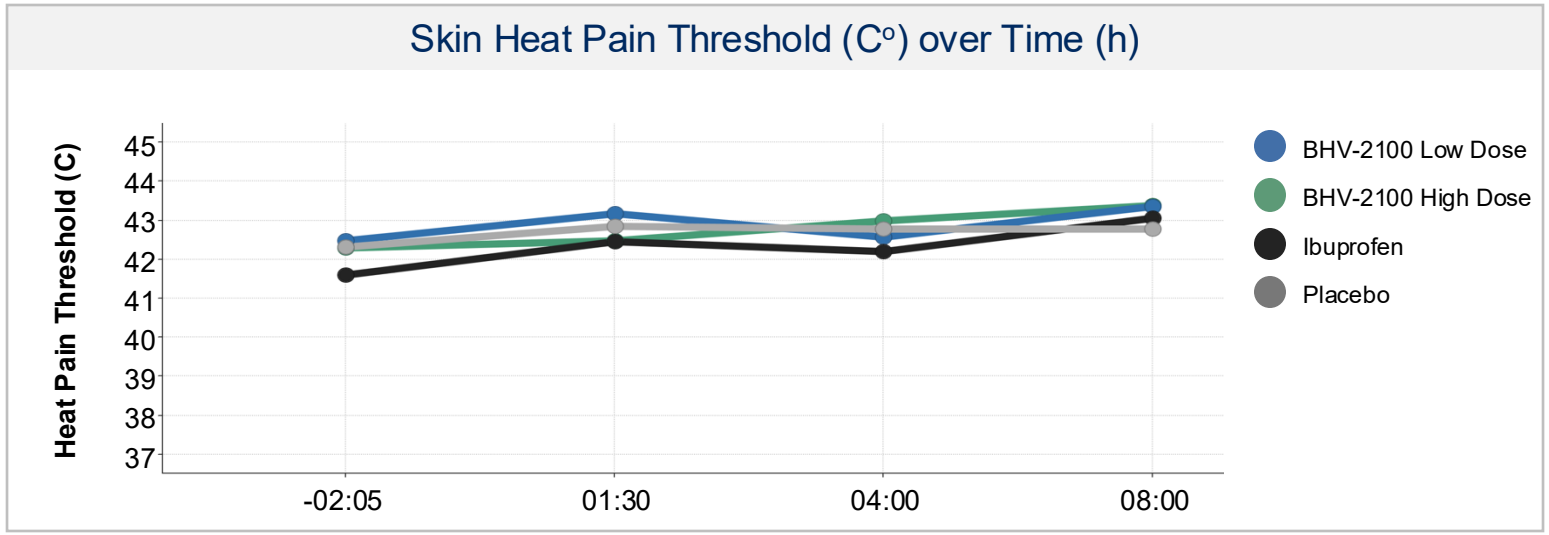
Reduced skin redness in SRS

Comparison was made for each dose level vs. placebo (Least Square Means over 8h)
* P<0.05

BHV-2100 Had No Effect on Body Temperature or Heat Pain Threshold

TRPM3



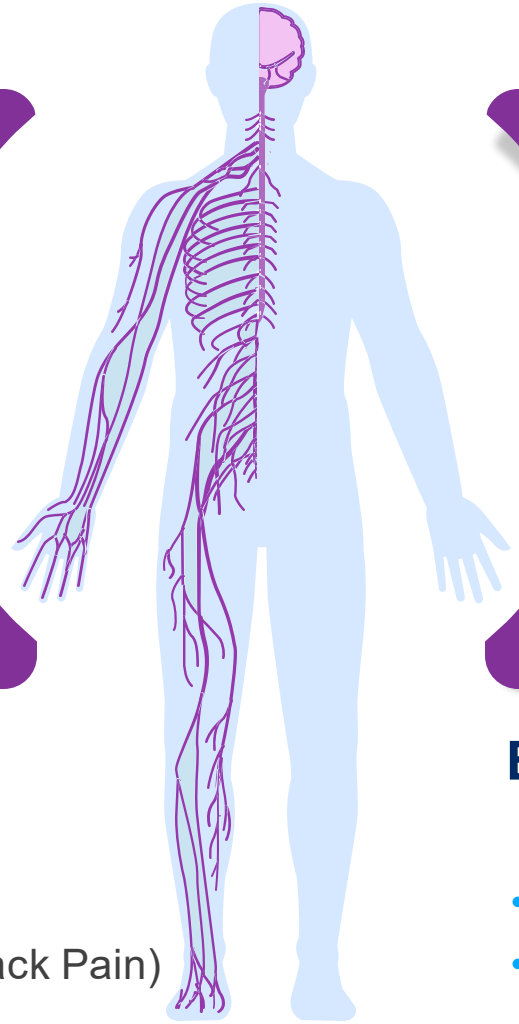


TRPM3 Platform Offers Potential to Treat an Expanding Range of Diseases

TRPM3

PERIPHERAL NERVOUS SYSTEM
Pain Disorders

- ✓ Mechanistic Data
- ✓ Human Genetic Validation
- ✓ Safety and Tolerability
- ✓ Human Proof of Concept



CENTRAL NERVOUS SYSTEM
Pain and Other Brain Disorders

- ✓ Mechanistic Data
- ✓ Preclinical Proof of Concept

BHV-2100

- Chronic Neuropathic Pain
- Nociceptive Pain (Osteoarthritis)
- Mixed Neuropathic and Nociceptive Pain (Back Pain)
- Migraine
- Acute Pain

Brain-Penetrant TRPM3 antagonists (preclinical)

- Acute and Chronic Pain Disorders
- Epilepsy

Panel

MODERATOR

Jason Gerberry

Equity Analyst

BANK OF AMERICA

PANELISTS

Raman Sankar, MD, PhD, FAAN, FAES
Emeritus Professor of Neurology and Pediatrics, Emeritus Chief of Pediatric Neurology
David Geffen School of Medicine at UCLA

Irfan Qureshi, MD
Chief Medical Officer

John H. Krystal, MD
Robert L. McNeil, Jr. Professor of Translational Research; Chair, Department of Psychiatry;
Yale University School of Medicine
Chief of Psychiatry, Yale-New Haven Hospital

Professor Thomas Voets
Laboratory of Ion Channel Research, VIB Center for Brain and Disease Research,
Ku Leuven, Department of Cellular and Molecular Medicine

Volkan Granit, MD, MSc
Senior Medical Director, Head of Neuromuscular Disease
Biohaven

BHVN LISTED NYSE

David A. Hafler, MD

William S. and Lois Stiles Edgerly Professor of Neurology and Professor of Immunobiology

Yale SCHOOL OF MEDICINE

Peter Ackerman, MD

Senior Vice President, Clinical Development

biohaven®

Karl Kieburtz, MD, MPH

Professor of Neurology, Univ. of Rochester
Managing Principal, Clintrex Research LLC, A BlueRidge Life Sciences company

CLINTREX

BHV-8000: Neuroinflammation

biohaven®

David A. Hafler, MD

William S. and Lois Stiles Edgerly Professor of Neurology and Professor of Immunobiology

Yale SCHOOL OF MEDICINE

Therapeutic Targeting of Inflammatory Pathways in Early Parkinson's Disease

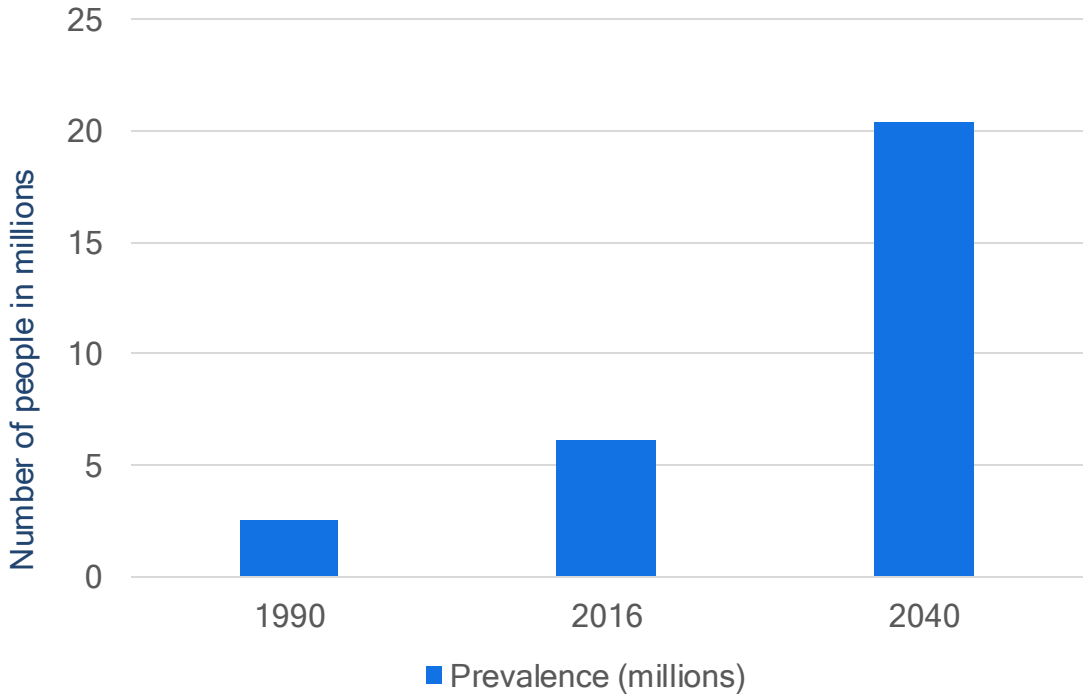
biohaven®

Therapeutic Targeting of Inflammatory Pathways in Early Parkinson's Disease

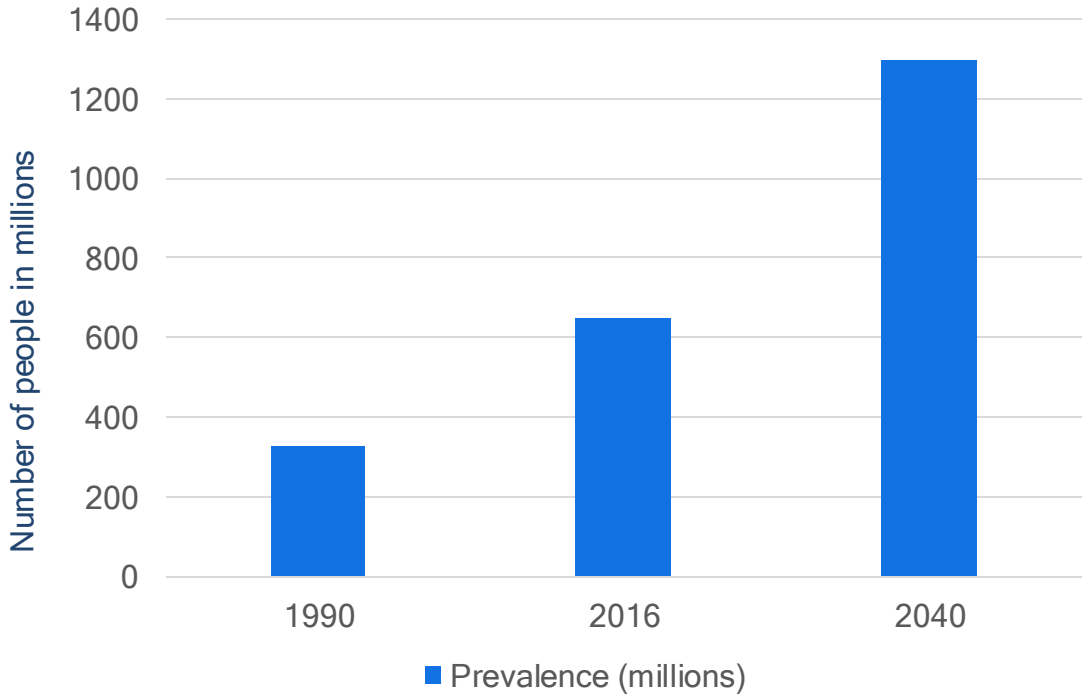
David A. Hafler, M.D.
William and Lois Stiles Edgerly
Professor of Neurology and Immunobiology
Associate Member, Broad Institute of
MIT and Harvard

Prevalence of Parkinson's Disease is Increasing Out of Proportion to the Aging Population

Global Prevalence of Parkinson's Disease[1-3]

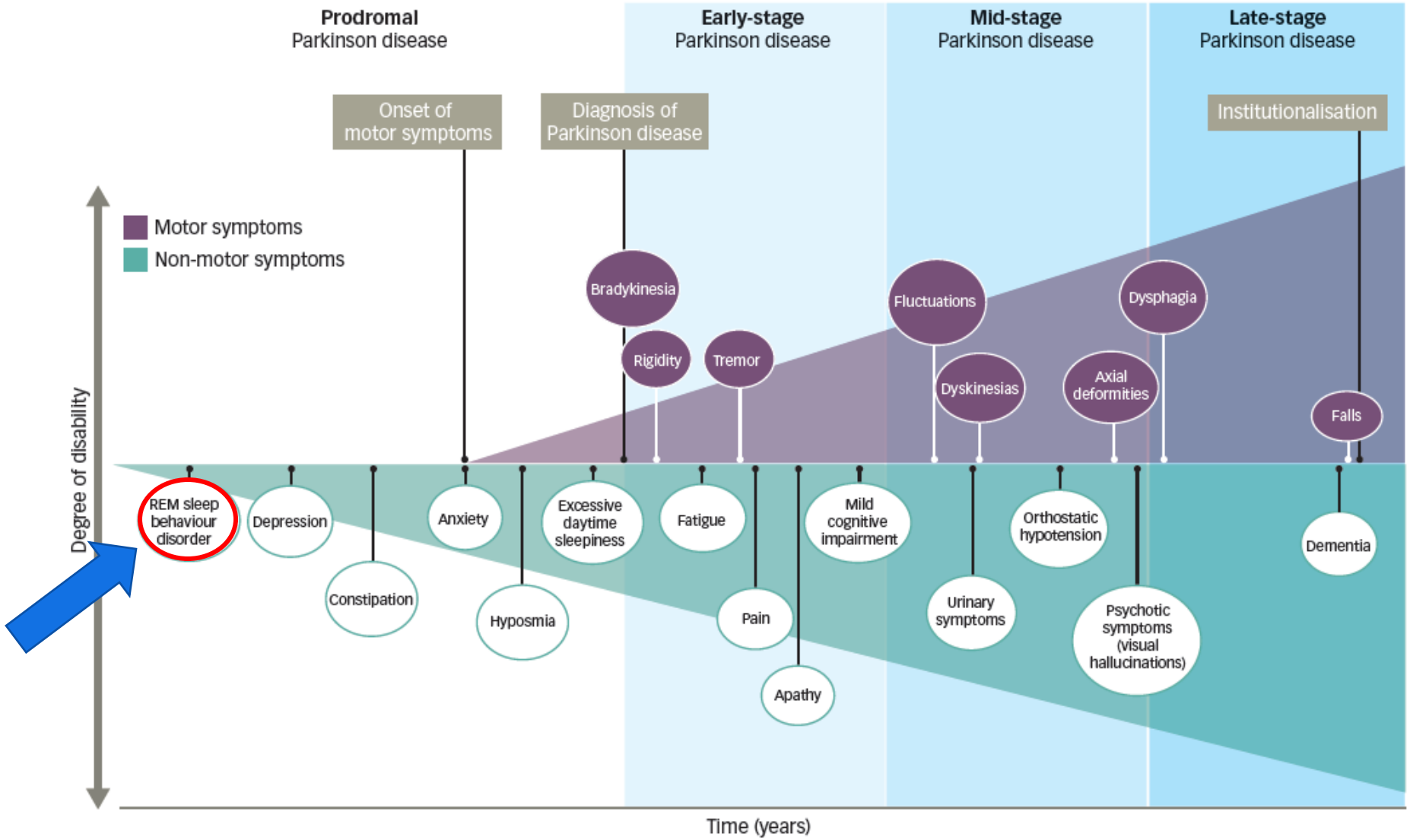


Global Population Aged 65 and Older[4-5]



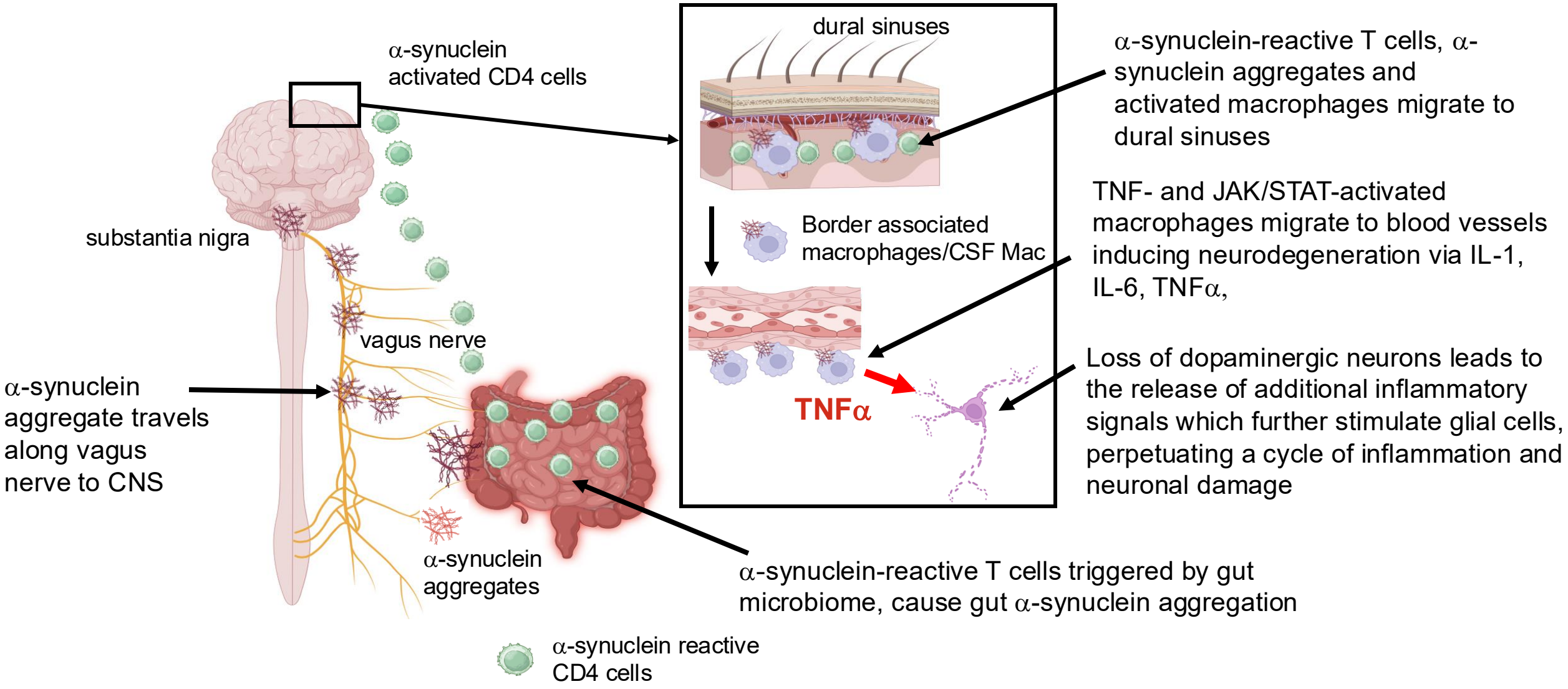
[1]Cheng, PLoS Med 2020; [2]He, et al. An Aging World: 2015. https://www.census.gov/library/publications/2016/demo/P95-16-1.html US Census Bureau. Updated 8OCT2021; Accessed 11MAY2025; [3]Li, BMJ Open 2025; [4]GBD 2016 Neurology Collaborators, *Lancet Neurol* 2019; [5]Carey, P. Parkinson's disease cases forecast to top 25 million worldwide by 2050. https://www.thenationalnews.com/health/2025/03/06/parkinsons-disease-cases-forecast-to-top-25-million-worldwide-by-2050/ The National. Updated 6MAR2025; Accessed 11MAY2025.

Evolution of Parkinson's Disease



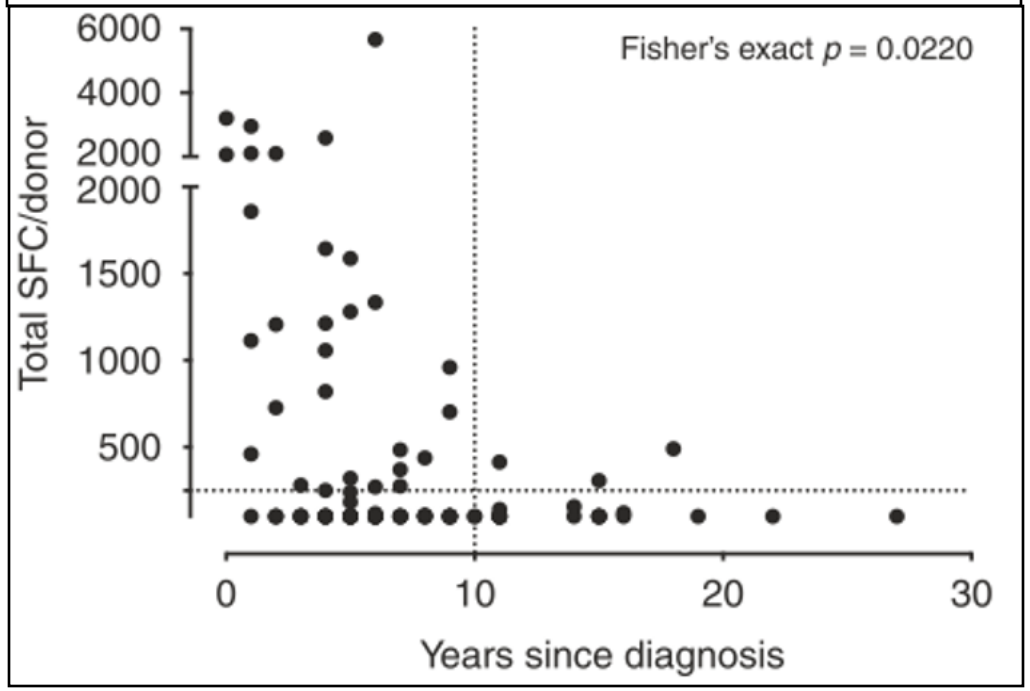
REM Sleep Behavior Disorder (RBD) is a prodromal form of Parkinson's disease in which patients act out their dreams, often violently

Integrated Autoimmune Hypothesis



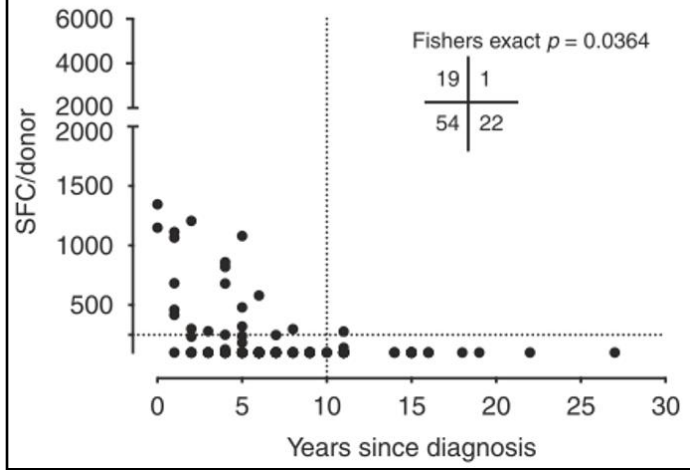
Immune-Modulatory Therapy for PD May be Most Effective Early in the Disease Course

T cell Reactivity and Time Since PD Diagnosis

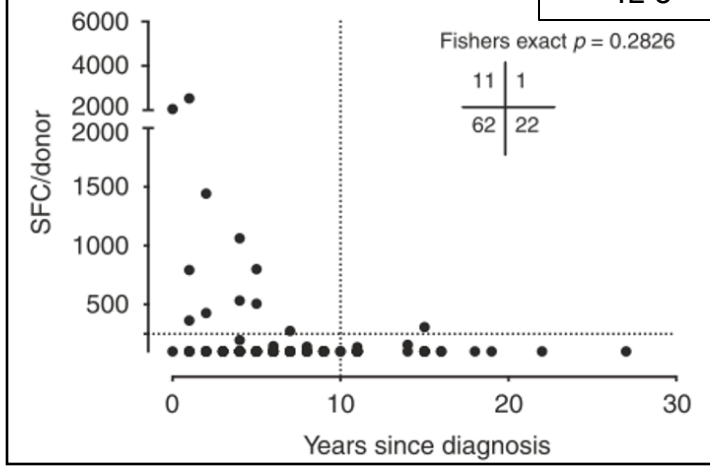


Inflammatory Cytokines Since PD Diagnosis

IFNɣ



IL-5



[1]Lindestam Arlehamn CS et al. Nature Communications 2020
SFC – Spot-Forming Cells

Parkinson’s Disease and the Gut-Brain Interface

- Single Cell nuc seq atlas of Parkinson’s Disease brain: more T cells observed in PD
- Single Cell RNA seq analysis of CSF in prodromal PD
- PRISMS study in prodromal PD

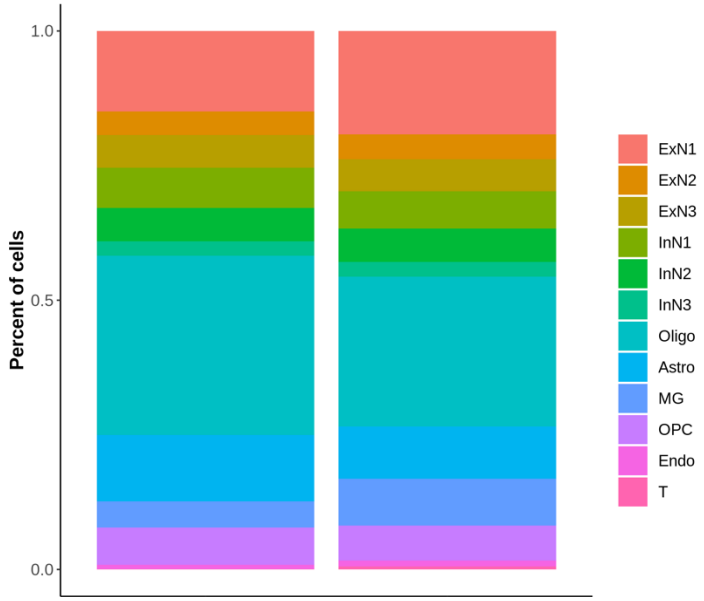
Parkinson’s Disease and the Gut-Brain Interface

- Single Cell nuc seq atlas of Parkinson’s Disease brain: more T cells observed in PD
- Single Cell RNA seq analysis of CSF in prodromal PD
- PRISMS study in prodromal PD

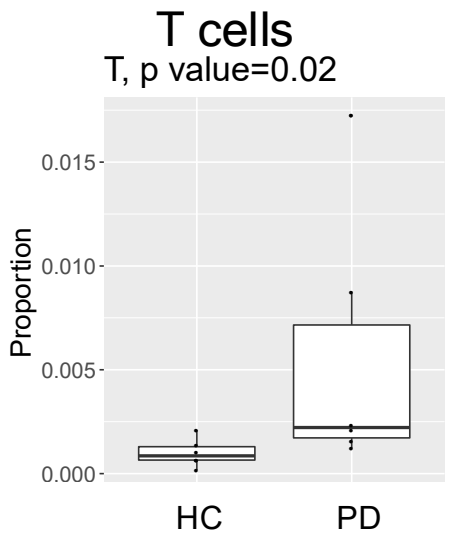
T cells Identified in Human PD Brain by snRNA-seq

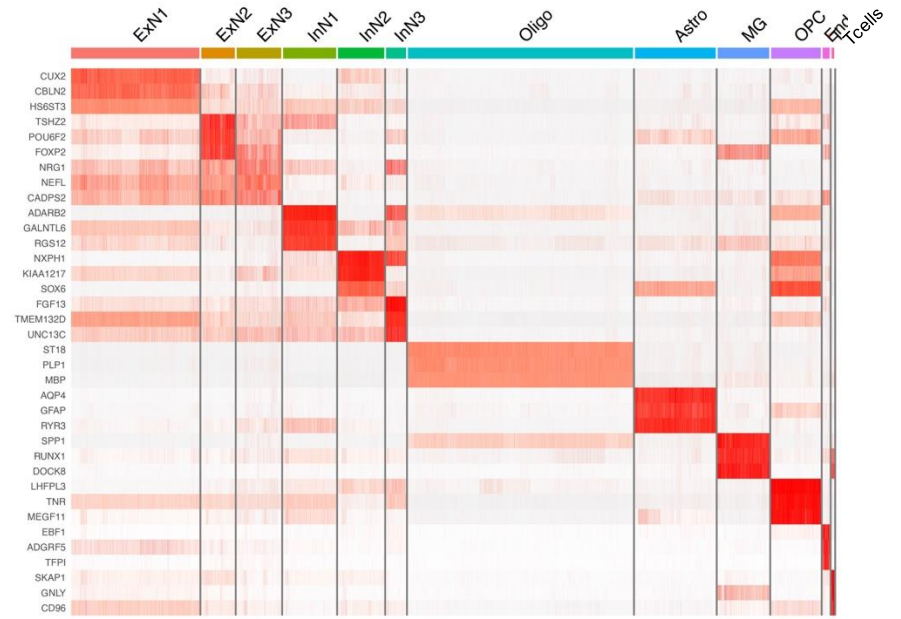
Slight increase in T cells in prefrontal cortex of PD brain, but distinctly fewer than in MS

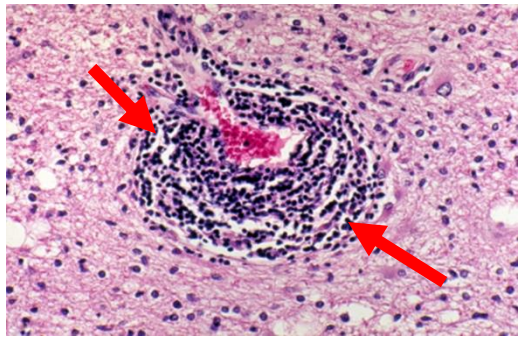
- 77,384 brain nuclei after QC
- 2,598 genes & 5,639 UMI per cell
- 100K sequencing reads per cell



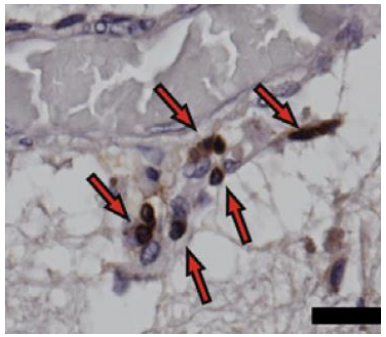
Zhu, et al. *Sci Transl Med.* 2024







Multiple sclerosis



Parkinson's

Parkinson’s Disease and the Gut-Brain Interface

- Single Cell nuc seq atlas of Parkinson’s Disease brain: more T cells observed in PD
- Single Cell RNA seq analysis of CSF in prodromal PD
- PRISMS study in prodromal PD

Inflammatory Signature for PD Synucleinopathy Discovered

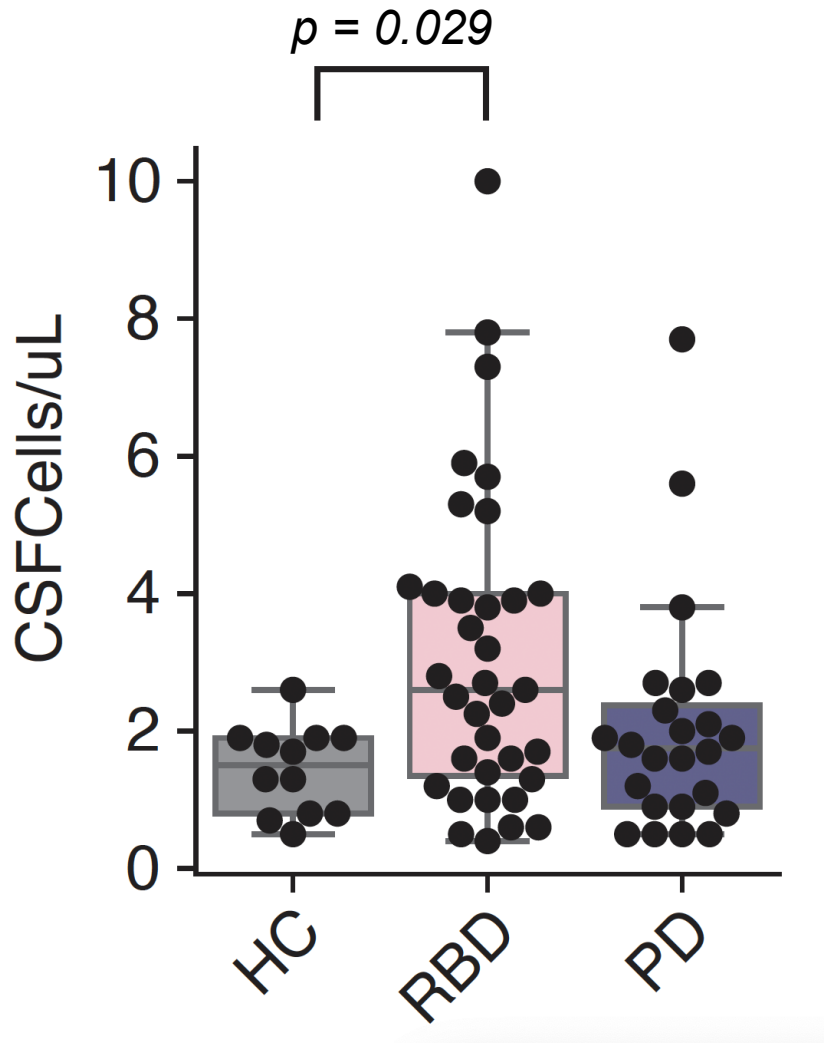
- Summary of findings in prodromal Parkinson's Disease:
  - Mild increase in inflammatory cells in CSF
  - Increased frequency of microglia-like macrophages in CSF
  - Increases in myeloid JAK/STAT, IL-6, and TNFα expression

Demographics of PD Cohorts and Healthy Control Subjects

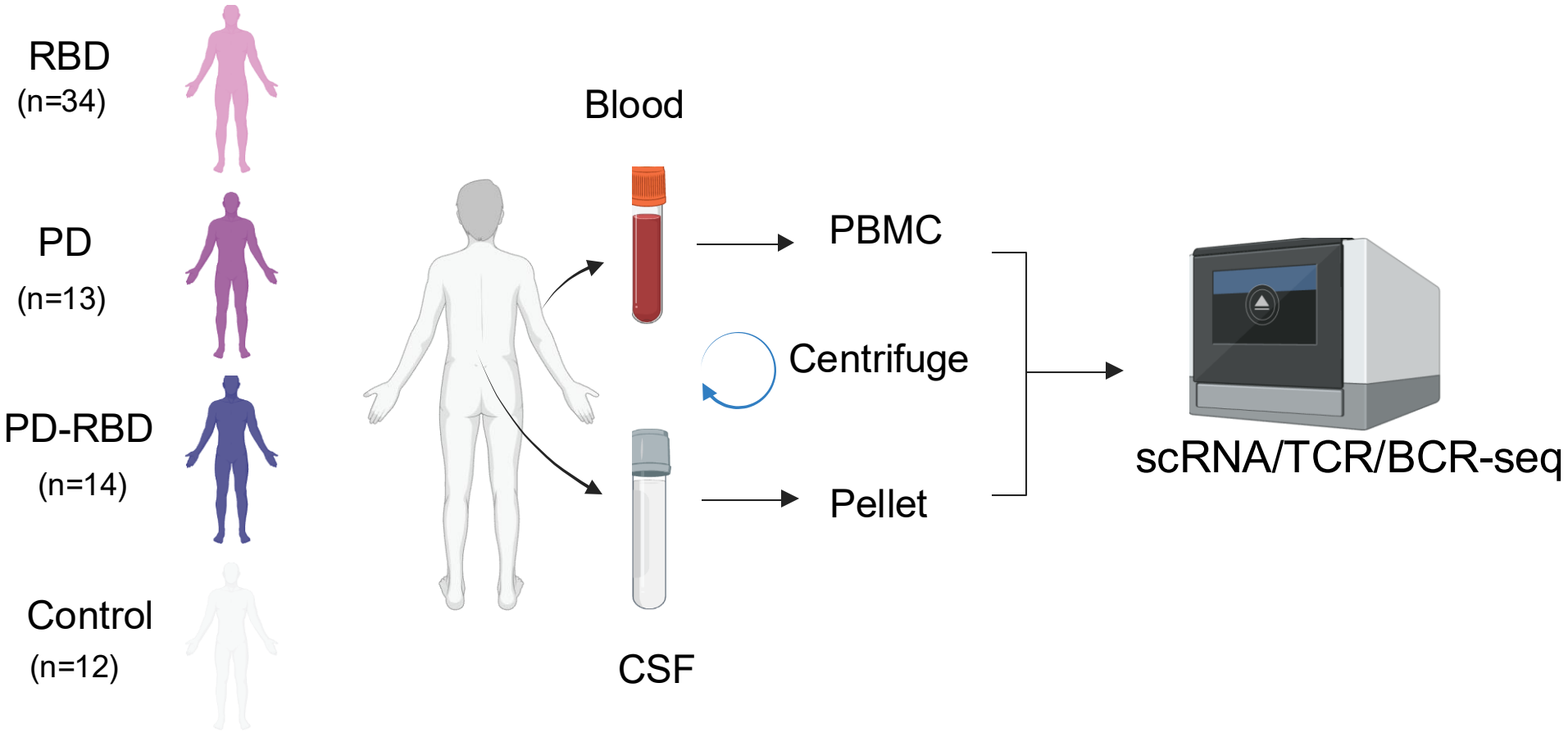
	HC N=15	PD N=15	PD RBD N=18	RBD N=36	ANOVA p value
Age (SD)	64.4 (1.75)	68.5 (1.75)	67.0 (1.59)	68.9 (1.13)	0.1780
Sex					
Female (n, %)	2 (13.3%)	4 (26.7%)	2 (11.1%)	11 (30.6%)	0.63
Male (n, %)	13 (86.7%)	11 (73.3%)	16 (88.9%)	25 (69.4%)	
Race					
White (n, %)	12 (80.0%)	13 (86.7%)	18 (100%)	36 (100%)	0.19
Other (n, %)	3 (20.0%)	2 (13.3%)	0 (0%)	0 (0%)	
Non-Motor Assessments					
MOCA	27.13 ± 1.41	27.87 ± 2.20	27.17 ± 2.43	25.89 ± 3.34	0.16
UPSIT Percentile	50.5 ± 32.6	27.2 ± 21.1	19.8 ± 25.8	31.5 ± 32.7	0.0088
NMSS	12.1 ± 15.5	26.6 ±17.9	41.6 ± 30.8	36. 8 ± 30.3	0.0020
SCOPA	5.6 ± 6.5	11.7 ± 5.5	12.9 ± 7.0	12.9 ± 6.3	0.0026
Constipation*	0.6 ± 1.4	1.6 ± 1.6	2.9 ± 1.8	1.9 ± 1.7	0.0025
ESS	4.5 ± 3.33	7.6 ± 3.4	8.4 ± 4.2	6.0 ± 3.4	0.0154
Motor Assessments					
10-Item Motor Sx	0.20 ±0.6	3.4 ± 2.4	5.1 ± 2.3	1.3 ± 2.001	<0.0001
MDS-UPDRS I	2.50 ± 2.59	5.36 ± 3.86	7.88 ± 4.30	7.36 ± 4.36	0.0005
MDS-UPDRS II	0.7 ± 1.9	4.9 ± 3.3	8.1 ± 5.0	3.6 ± 6.111	<0.0001
MDS-UPDRS III	3.0 ± 3.4	22.0 ± 9.2	25.8 ± 9.2	6.4 ± 6.7	<0.0001
MDS-UPDRS Total	6.2± 6.0	32.3 ± 13.1	41.73 ± 13.4	17.3 ± 17.3	<0.0001
Biomarkers					
Mean Striatal SBR					
% SAA Positive		5/6(83%)		6/18(67%)	

Mean duration RBD = 2.8 years

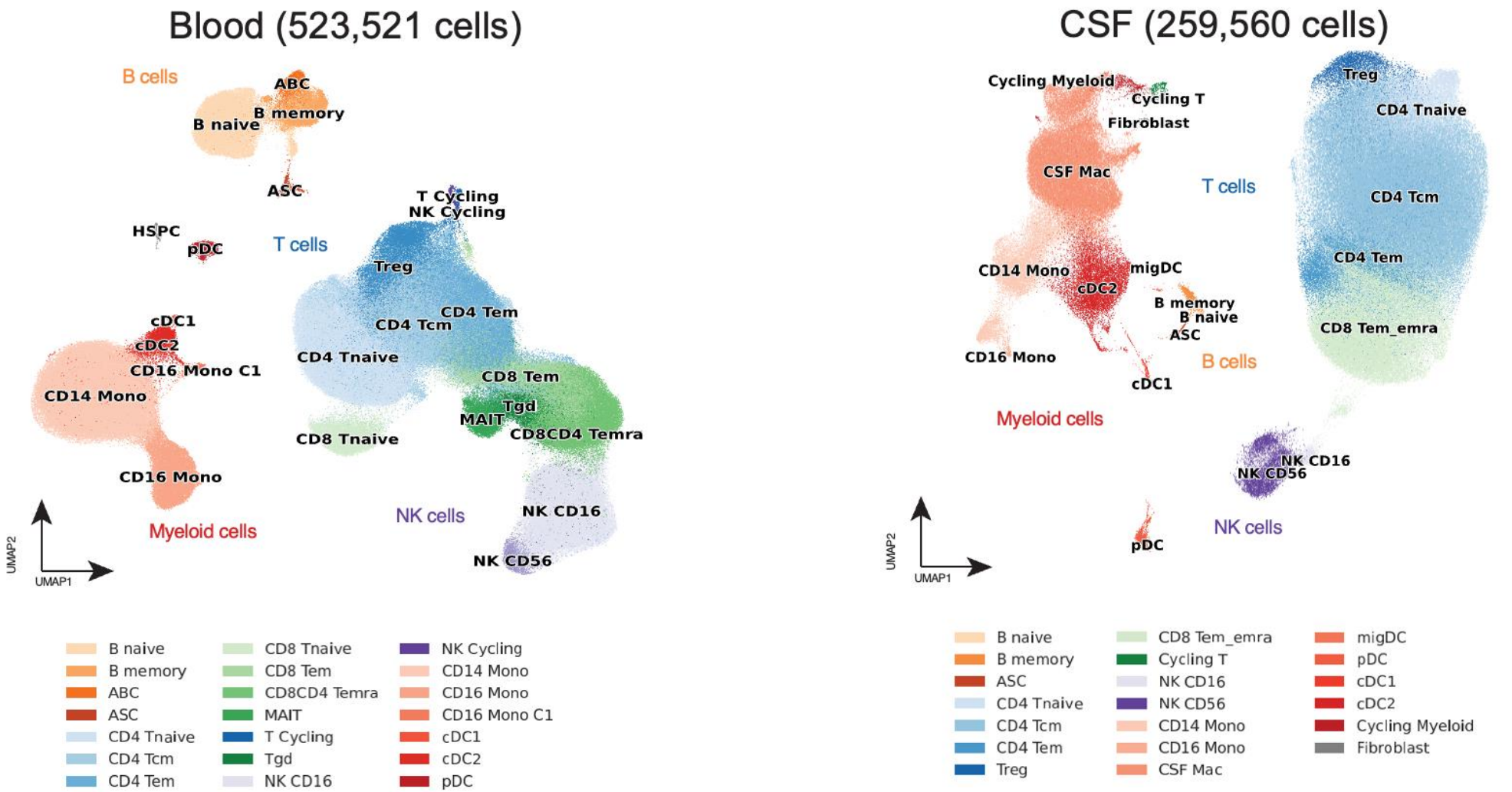
Lymphocytic Pleocytosis in Prodromal PD



Parkinson’s Disease Blood/CSF Immune Cell Atlas

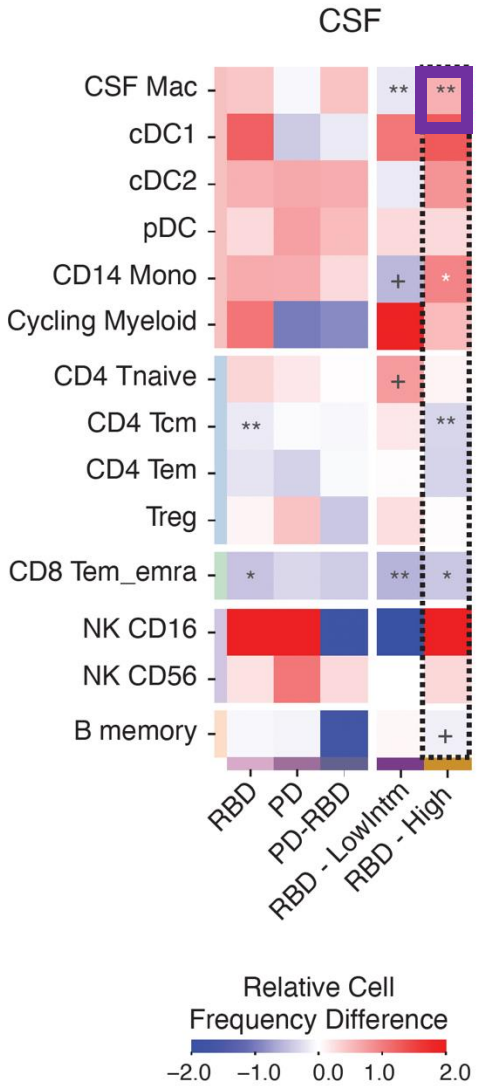


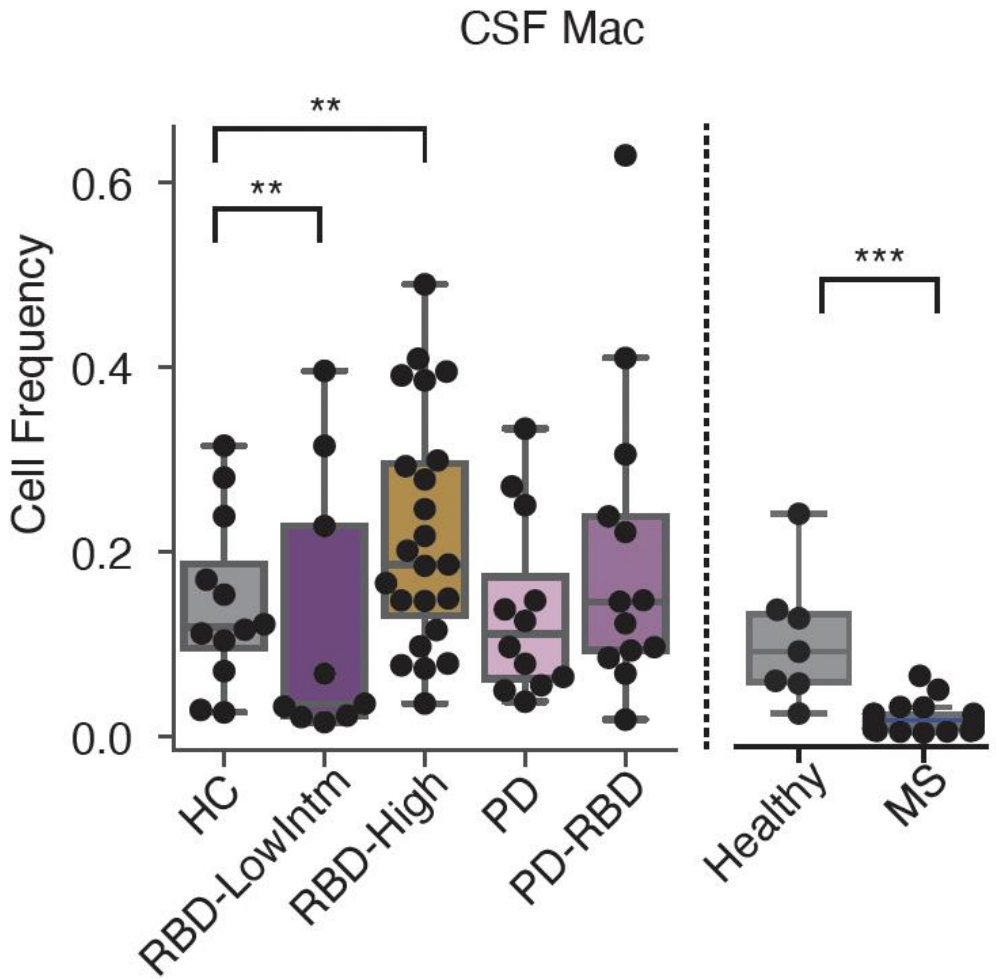
Mapping Immune Cells in Blood and CSF of PD Patients

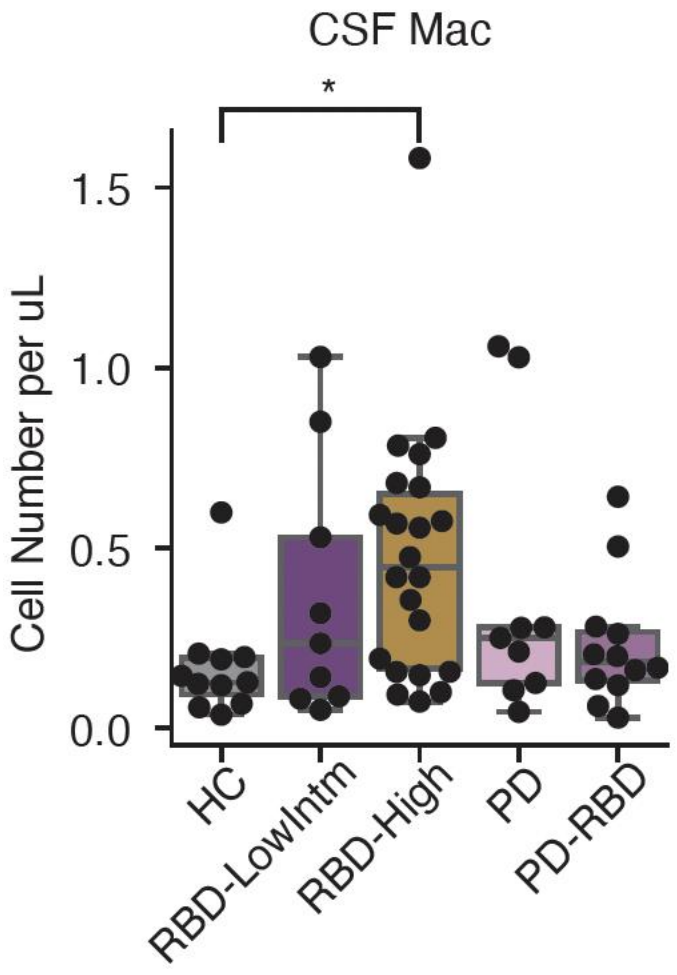


ASC: Antibody Secreting Cells, ABC: Atypical B Cells

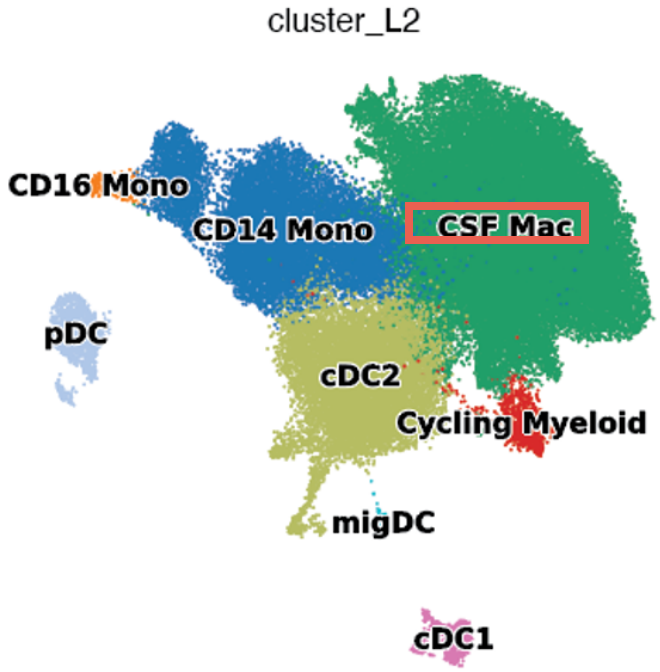
Mac Population is Increased in CSF of Prodromal Parkinson's Disease

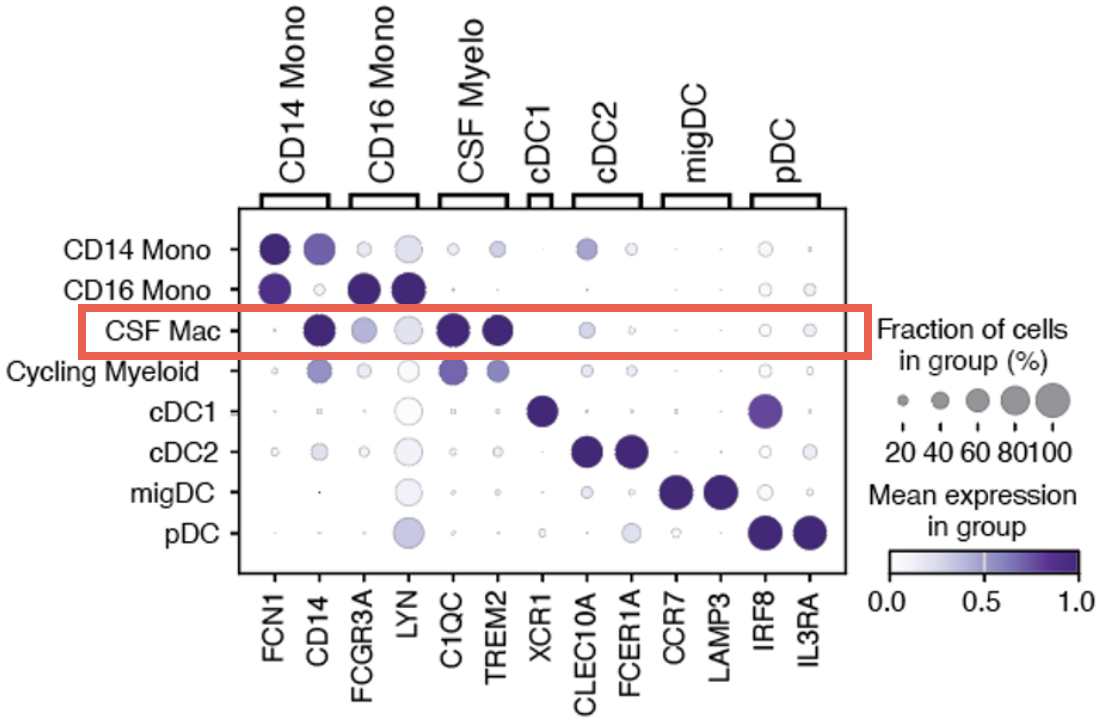




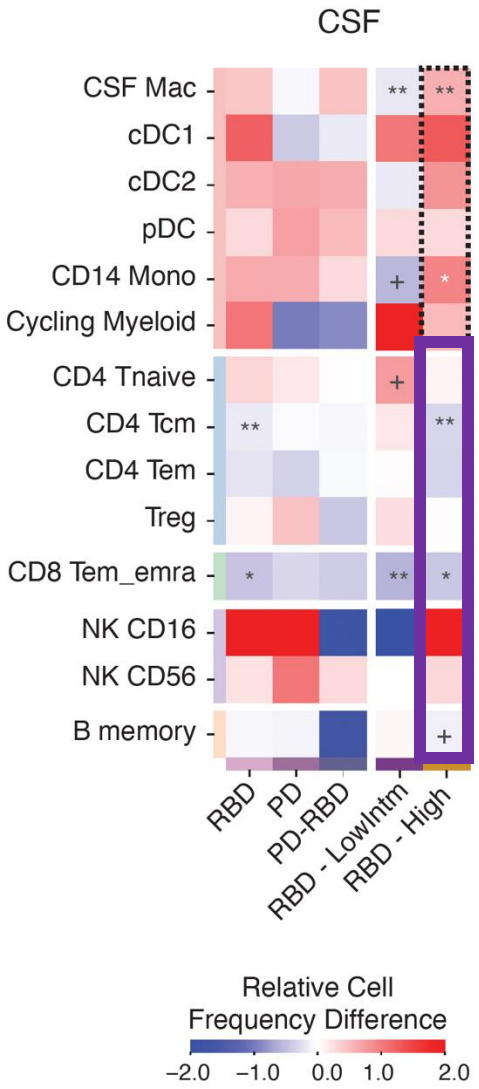


In Prodromal PD, CSF-like Macrophages (Mac) Highly Express Microglia and Monocyte Genes

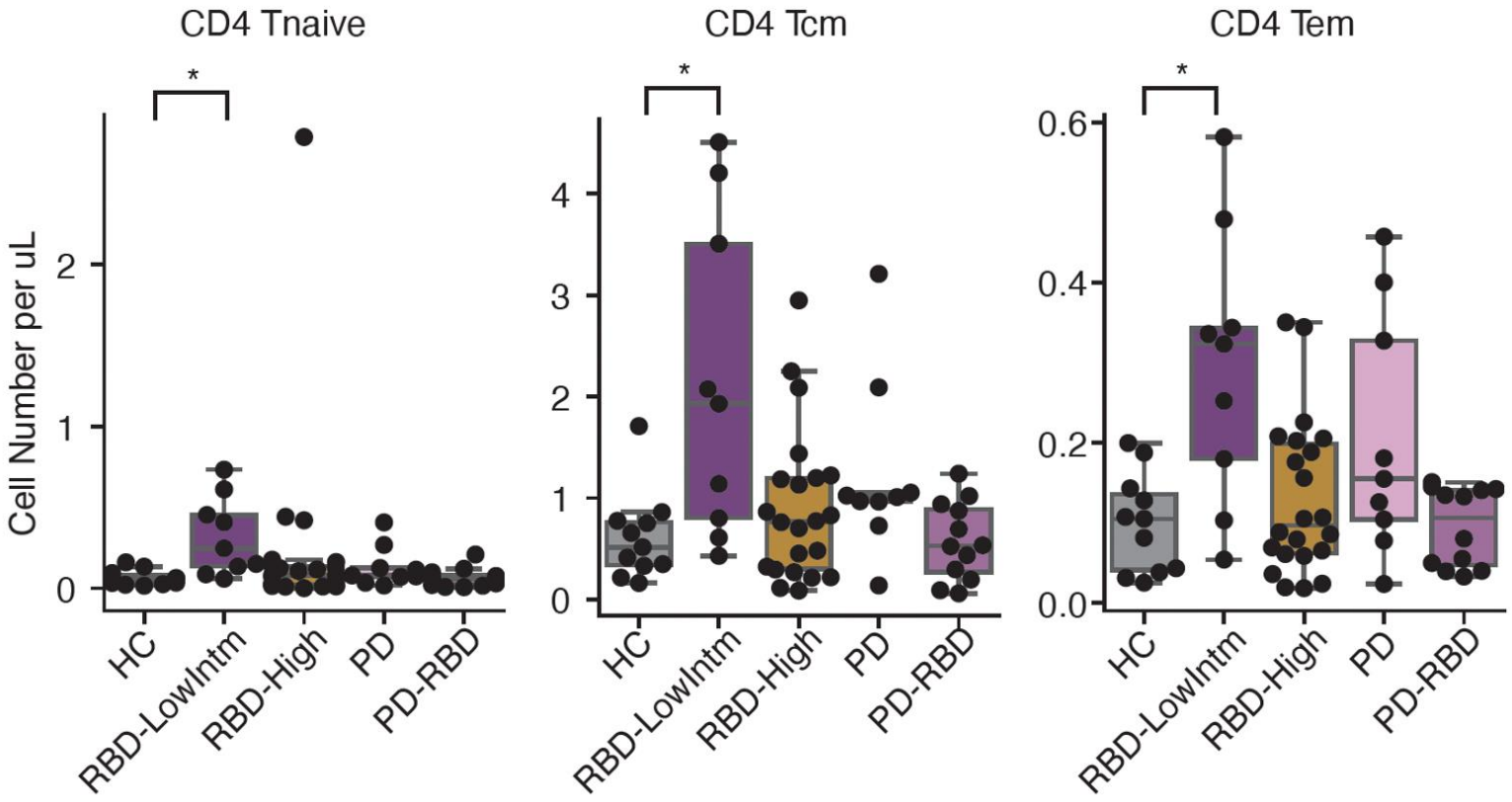




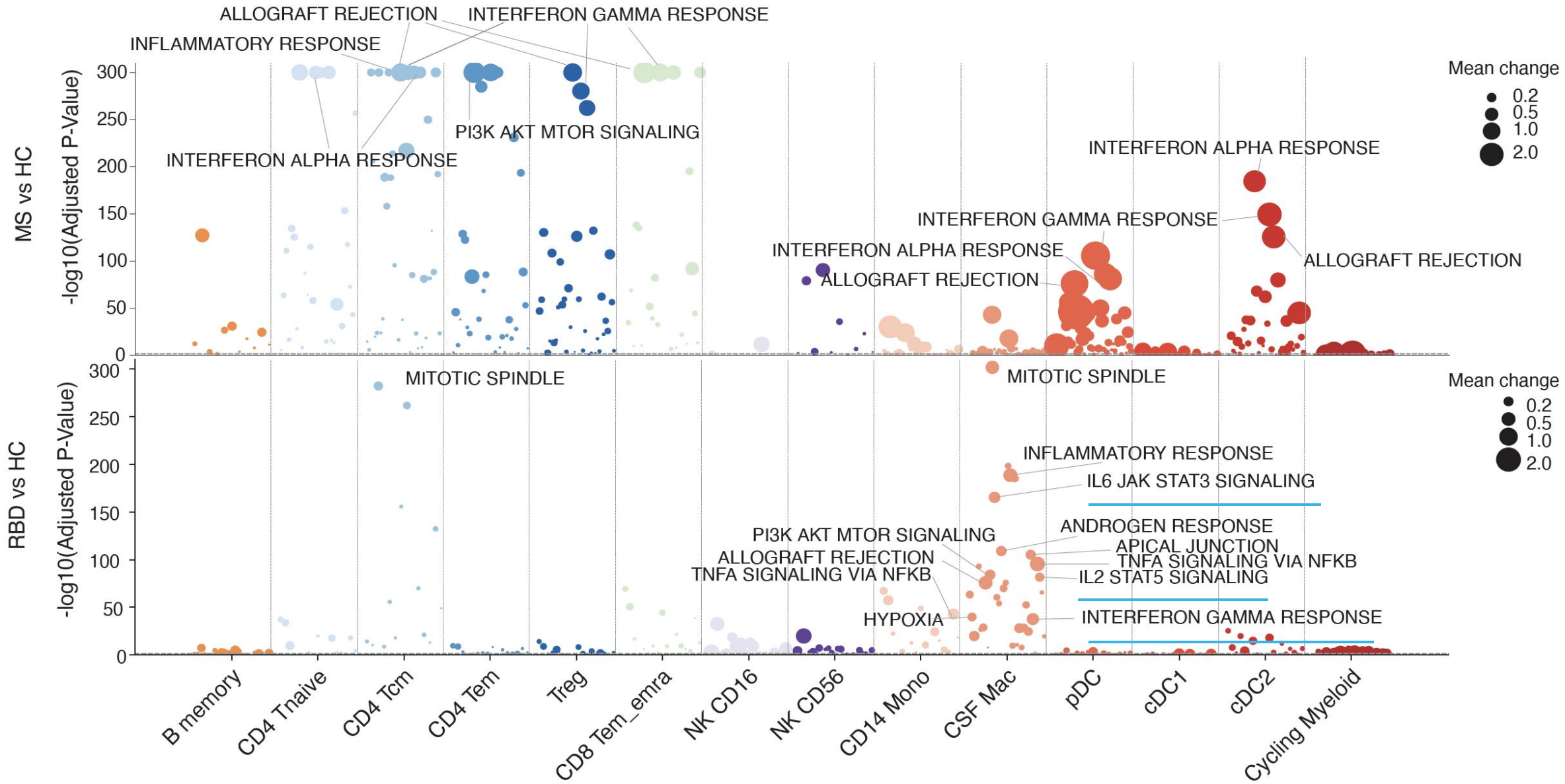
Increased Cell Number of Myeloid Cells in CSF of Prodromal PD Patients



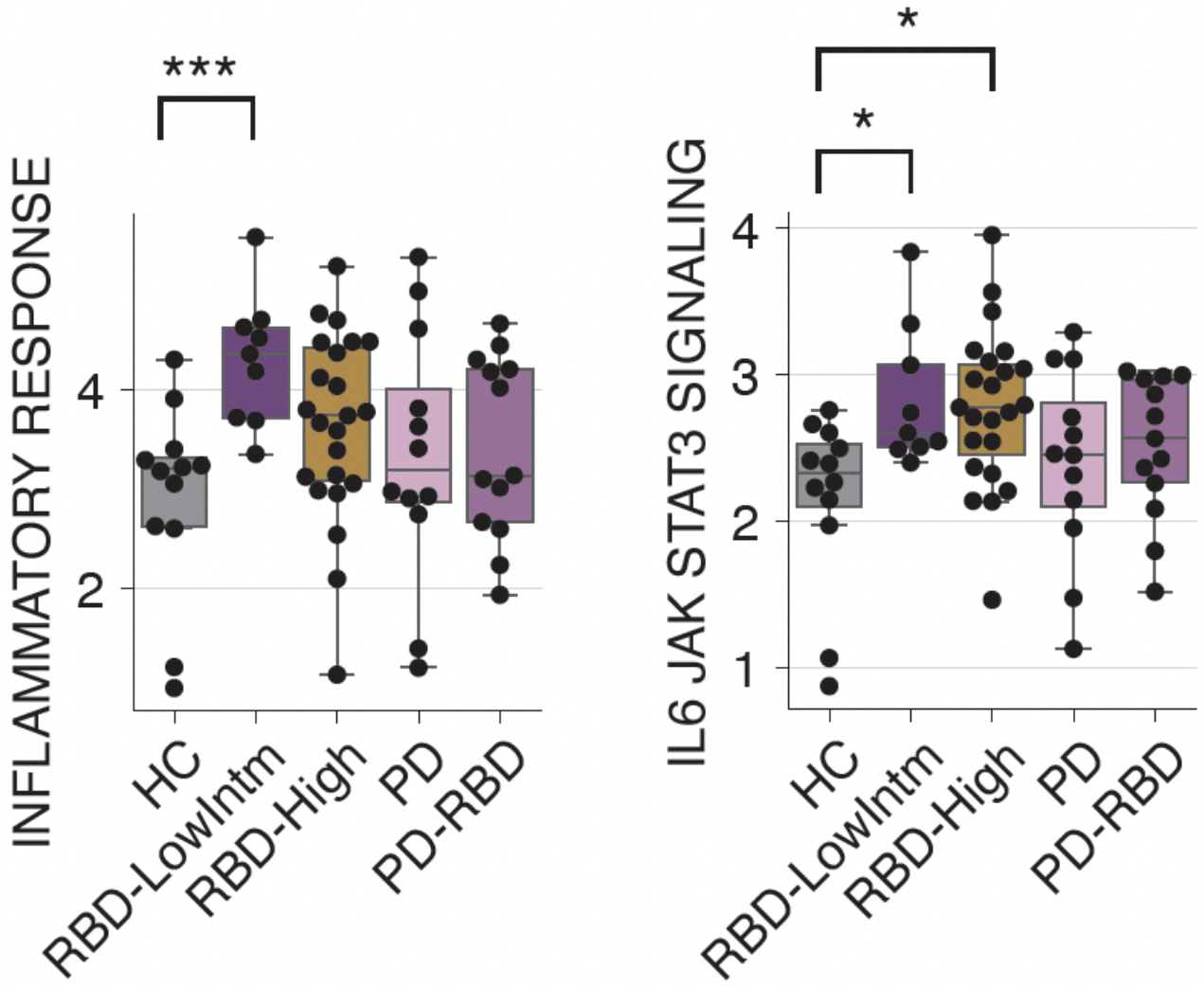
Relative Decrease in Number of CD4 T-memory and T-effector Cells



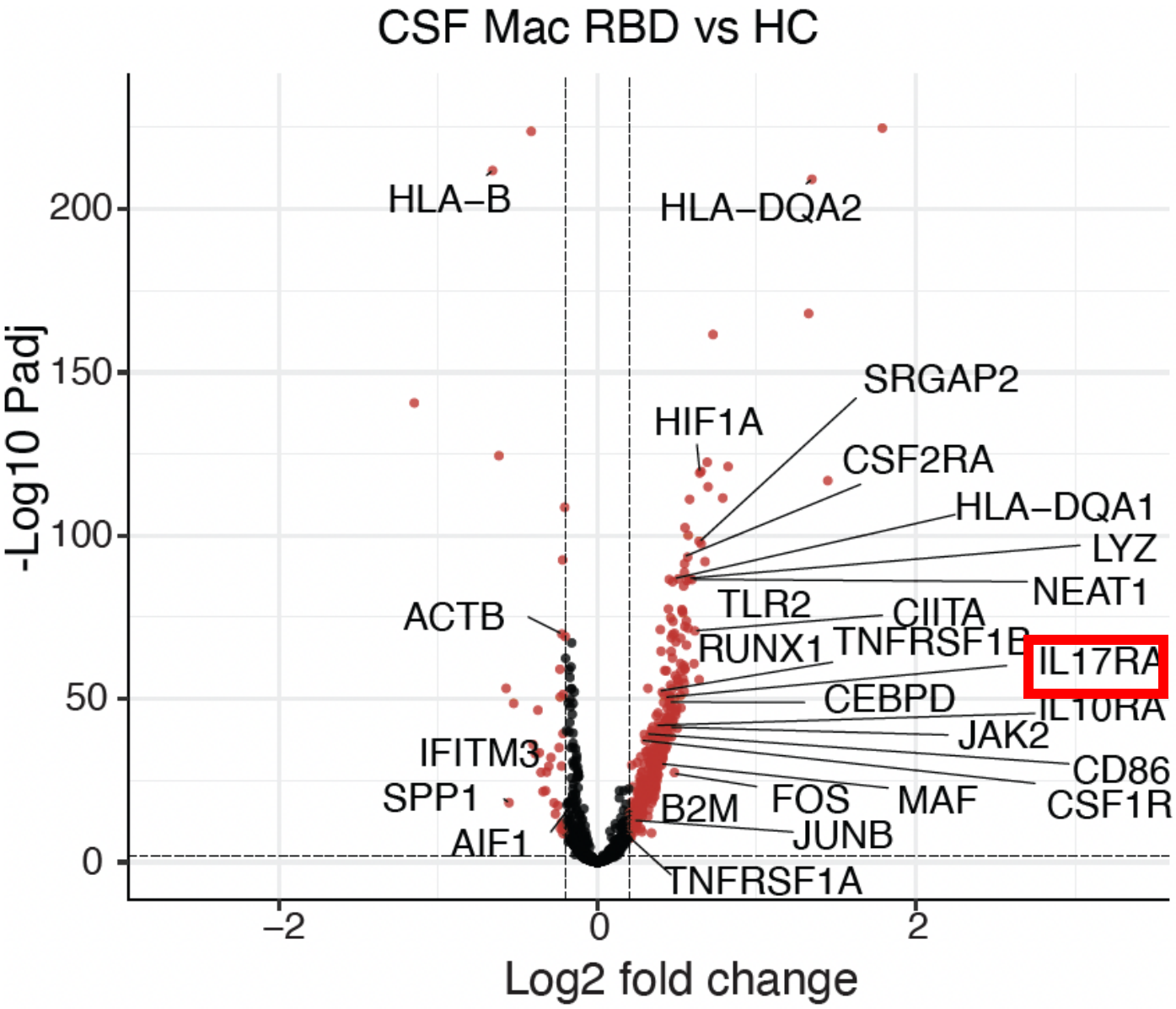
TNFα and JAK-STAT Signaling Were Upregulated in CSF Mac Population of Prodromal PD Patients



Mac Population in CSF of Patients with Prodromal PD has Inflammatory Signature that Includes Increased JAK-STAT Signaling

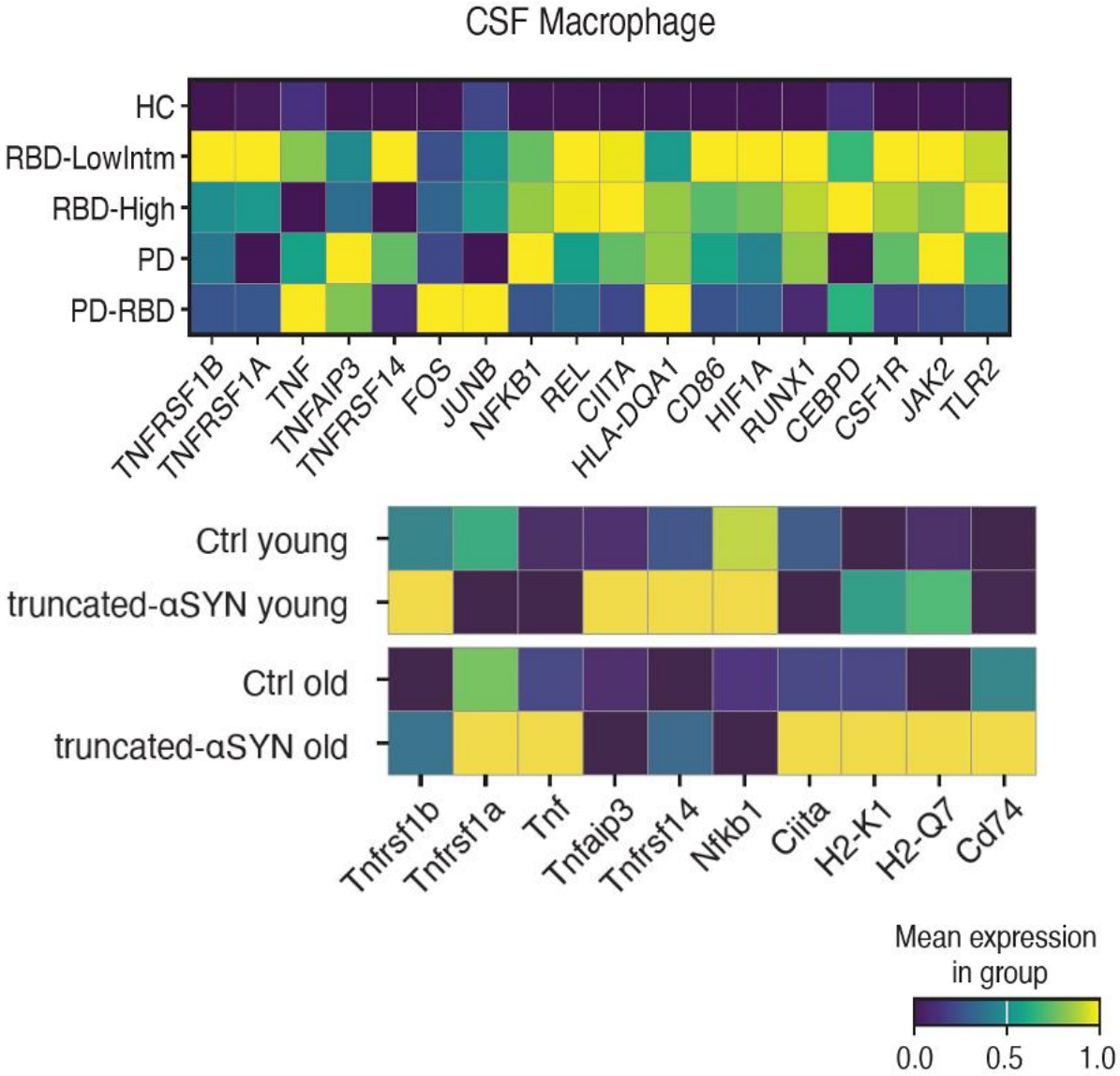


Mac Population in CSF of Patients with Prodromal PD has Inflammatory Signature that Includes Increased JAK-STAT Signaling were Observed in CSF

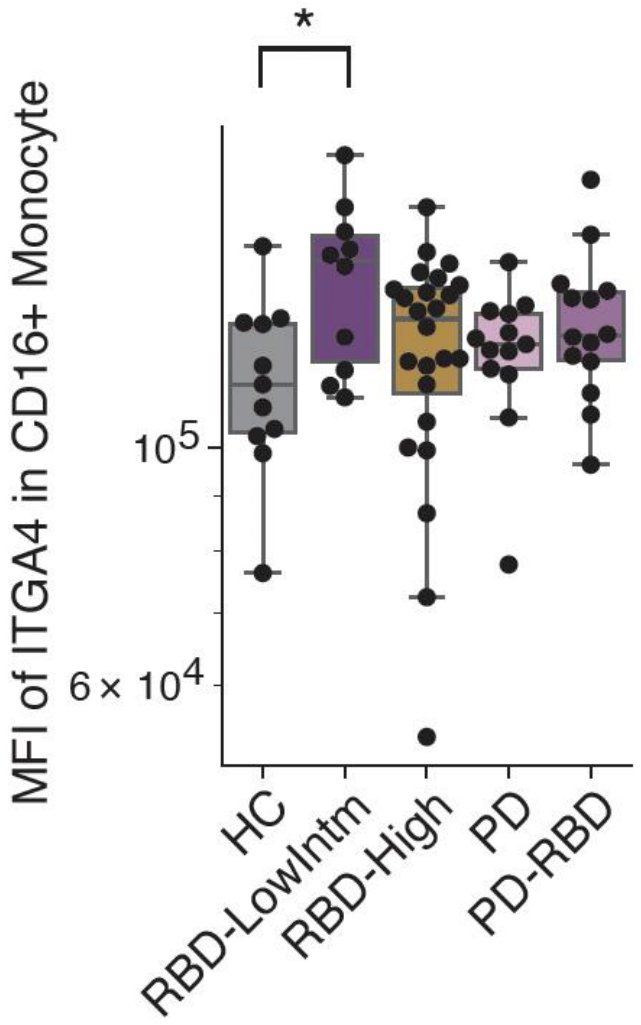


Inflammatory Response and JAK-STAT Signaling Were Highlighted in CSF Mac

- TNFα and JAK-STAT and MHC class II genes were upregulated in PD model mice, consistent with the change of CSF Mac in prodromal PD.
- Dural myeloid cells from PD model mice expressing human αSyn under the control of the tyrosine hydroxylase promoter. The dural macrophage expressed CSF Mac marker genes such as *Trem2*, *Apoe*, and *C1qc*.



Increased Trafficking of Potentially Pathogenic Macrophages into the CNS



Parkinson’s Disease and the Gut-Brain Interface

- Single Cell nuc seq atlas of Parkinson’s Disease brain: more T cells observed in PD
- Single Cell RNA seq analysis of CSF in prodromal PD
- PRISMS study in prodromal PD

PRISMS

AN EXPLORATORY STUDY OF THE **P**OTENTIAL FOR **R**ATIONAL **I**MMUNE **S**YSTEM **M**ANIPULATION TO PREVENT EMERGENCE OF **S**YNUCLEINOPATHY MANIFESTATIONS IN PERSONS WITH REM SLEEP BEHAVIOR DISORDER (RBD)

Yale University
School of Medicine

PSG

Real-World Analytics of Large Healthcare Database Show Parkinson's Disease Risk Reduction With TNF/IL-17 Targeting Therapies

- Biohaven conducted analysis using Komodo Health database (over 320 million patients since 2012) examining treatment with anti-TNF or anti-IL-17 and incidence of PD
- Millions of patients over 8+ years of dosing captured key epidemiologic confirmation of the neuroinflammatory hypothesis
- Results support rationale for the effectiveness of BHV-8000 in treating PD

Treatment	PD Events	Person-years	Rate (per 100 person-years)	Adjusted IRR (95% CI)	P-value
Anti-TNF or Anti-IL-17 exposure	2,957	393,114	**0.66**	0.77 (0.74 - 0.80)	<0.0001
No Treatment	50,562	5,328,307	0.95		
Anti-TNF exposure	2,471	371,867	**0.66**	0.64 (0.52 - 0.80)	<0.0001
No Treatment	50,562	5,328,307	0.95		
Anti-IL-17 exposure	81	15,598	**0.52**	0.77 (0.78 - 0.81)	<0.0001
No Treatment	50,562	5,328,307	0.95		

Slide courtesy of Biohaven

Inflammatory Signature for PD Synucleinopathy Discovered

- Summary of findings in prodromal Parkinson's Disease:
  - Mild increase in inflammatory cells in CSF
  - Increased frequency of microglia-like macrophages in CSF
  - Increases in myeloid JAK/STAT, IL-6, and TNFα expression
- Signature consistent with that of autoimmune disease

Departments of Neurology and Immunobiology Yale School of Medicine

Lab Team

Yoshiaki Yasumizu
Le Zhang
Tomomi Yoshida
Aurelie Hanin
Benjamin Lu
Biqing Zhu
Tomokazu Sumida
Nick Buitrago
Jeonghyeon Moon
Nardos Cheru
Joseph Walewski
Nikhil Lele
Haowei Wang
Joseph Walewski
Minh Pham
Hande Sutova
Alice Yi
Oksana Goroshchuk
Sarah Reeves
Jack Coburn

Clinical Team

Jesse Cedarbaum
Brian Koo
John Seibyl
Kara Mead
Erika Renkl
Shreya Reddy
Sapna Patel
Samantha Esposito

YALE Neuroinflammation Group

https://medicine.yale.edu/lab/hafler/

david.hafler@yale.edu

Peter Ackerman, MD

Senior Vice President,
Clinical Development

biohaven®

BHV-8000:
Brain-Penetrant TYK2/JAK1 Inhibitor

biohaven®

First-in-Clinic, Brain-Penetrant, Selective TYK2/JAK1 Inhibitor for the Treatment of Neuroinflammatory and Neurodegenerative Diseases

- TYK2 and JAK1 inhibition target key inflammatory signaling pathways
- Selectivity profile avoids safety liabilities of JAK2/3 inhibition

Breaks Cycle of Central and Peripheral Inflammation

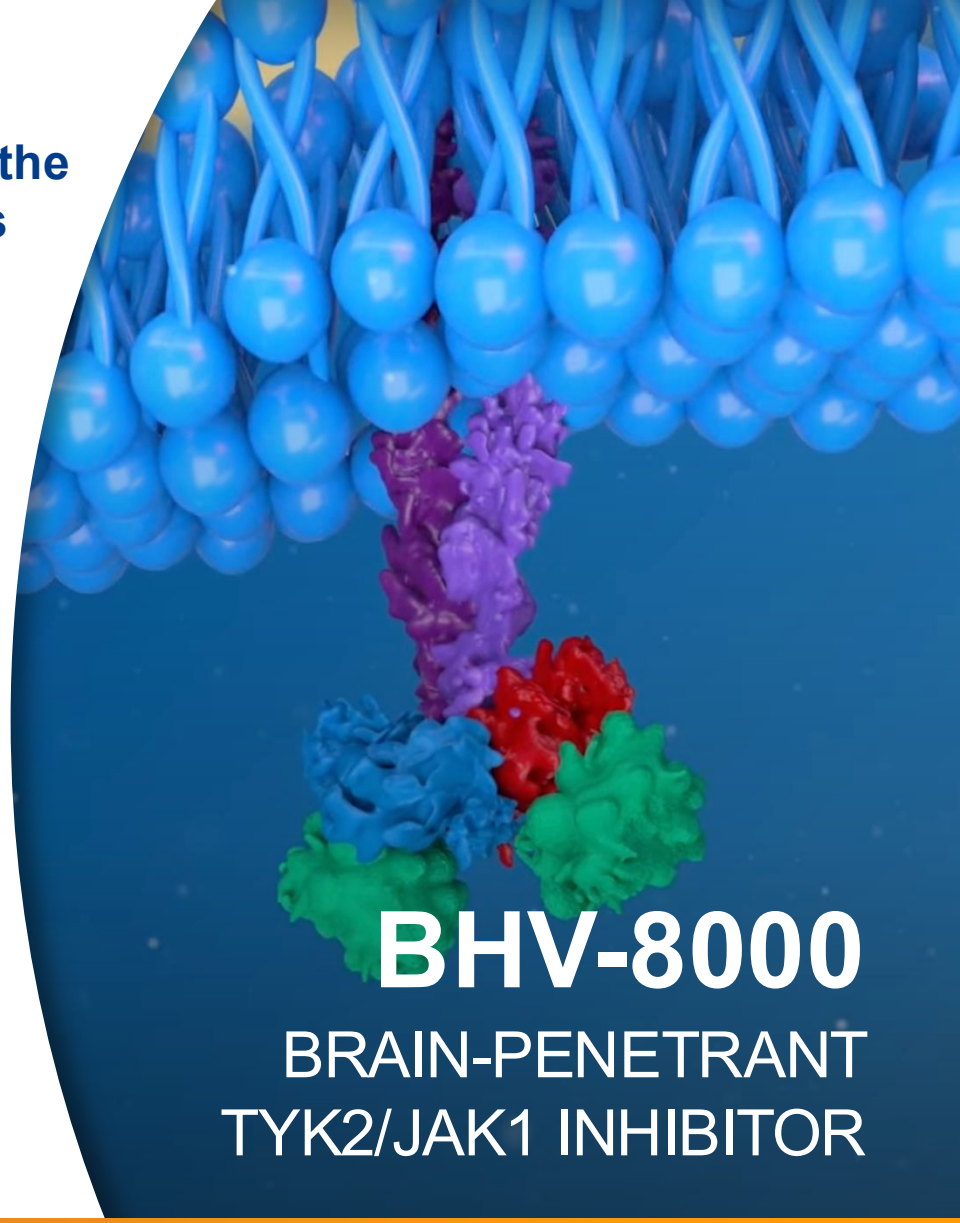
- Autoimmunity plays key role in Parkinson's and is novel therapeutic target
- TYK2/JAK1 inhibition reduces inflammatory impact of activated microglia and astrocytes in the CNS, and infiltrating T lymphocytes

Encouraging Results from Phase 1

- Well-tolerated
- Achieves target engagement
- Robust brain penetration

Phase 2/3 Parkinson's Disease Study Ongoing

Innovative study design optimized for efficiency and sensitivity in detecting clinically meaningful change



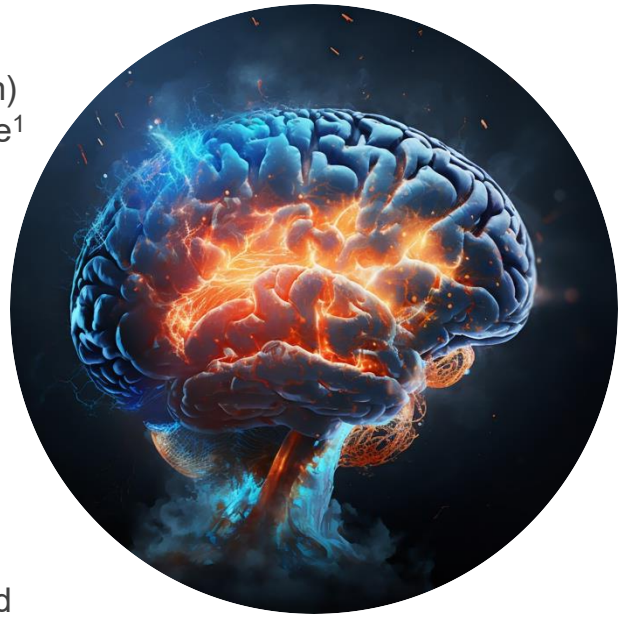
BREAKING NEWS

Phase 2/3 Parkinson's study initiated May 2025

Parkinson’s Disease Is an Autoimmune Disorder

PD meets criteria for autoimmunity based on pathophysiology and genetics

- Misidentification of self-proteins (α-synuclein) as foreign antigen triggers immune response[1]
- GWAS studies link PD risk to HLA gene variants involved in antigen presentation[2]



Epidemiology reveals increased risk of PD in individuals with other autoimmune diseases[3]

- Epi studies suggest immune dysfunction and inflammation are key to the development of PD[4]
- Reduction in rates of PD have been seen when this population is exposed to immune-modulating therapies[5]

PD animal models demonstrate immune dysregulation drives neurodegeneration[6]

- In mouse models, T cells specific to α-synuclein peptides can induce dopaminergic neuronal loss[7]
- Manipulation of immune components (T cells) affect α-synuclein-induced neurodegeneration[8]

PD patient samples and imaging exhibit characteristic proinflammatory signatures[9,10]

- Proinflammatory cytokines (e.g., IL-6, TNF-α, IFNɣ) are found in CSF and blood of PD patients[11]
- PD brains express high levels of HLA-DR+ reactive microglia[12]

1. Sulzer, *Nature* 2017; 2. Wissemann, *Am J Hum Genet* 2013; 3. Li, *Front Immunol* 2023; 4. Tansey, *Nat Rev Immunol* 2022; 5. Potashman, *Parkinsonism Relat Disord* 2025; 6. Roodveldt, *Brain* 2024; 7. Karikari, Brain Behav Immun 2022; 8. Williams, *Brain* 2021; 9. Yacoubian, *Mov Disord* 2023; 10. Pajares, *Cells* 2020; 11. Qu, *Nature* 2023; 12. McGeer, *Neurology* 1988.

biohaven

Real-World Analytics of Large Healthcare Database Show Parkinson's Disease Risk Reduction With TNF/IL-17 Targeting Therapies

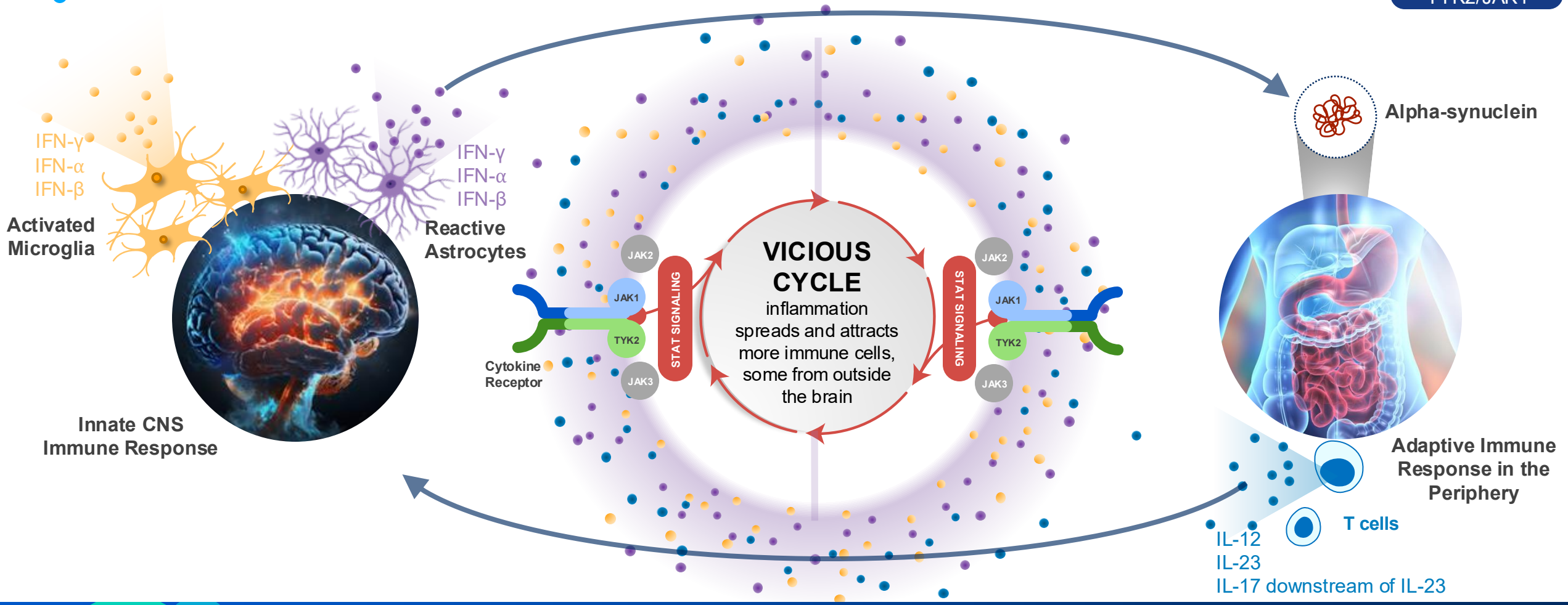
TYK2/JAK1

Treatment	PD Events	Person-years	Rate (per 100 person-years)	Adjusted IRR (95% CI)	P-value
Anti-TNF or Anti-IL-17 exposure	2,957	393,114	**0.66**	0.77 (0.74 – 0.80)	<0.0001
No Treatment	50,562	5,328,307	0.95		
Anti-TNF exposure	2,471	371,867	**0.66**	0.64 (0.52 – 0.80)	<0.0001
No Treatment	50,562	5,328,307	0.95		
Anti-IL-17 exposure	81	15,598	**0.52**	0.77 (0.78 – 0.81)	<0.0001
No Treatment	50,562	5,328,307	0.95		

IRR, incidence rate ratio; **TNF**, tumor necrosis factor.

TYK2/JAK1 Signaling Fuels Inflammation Driving Disease Progression in Parkinson's Disease

TYK2/JAK1



KEY POINT

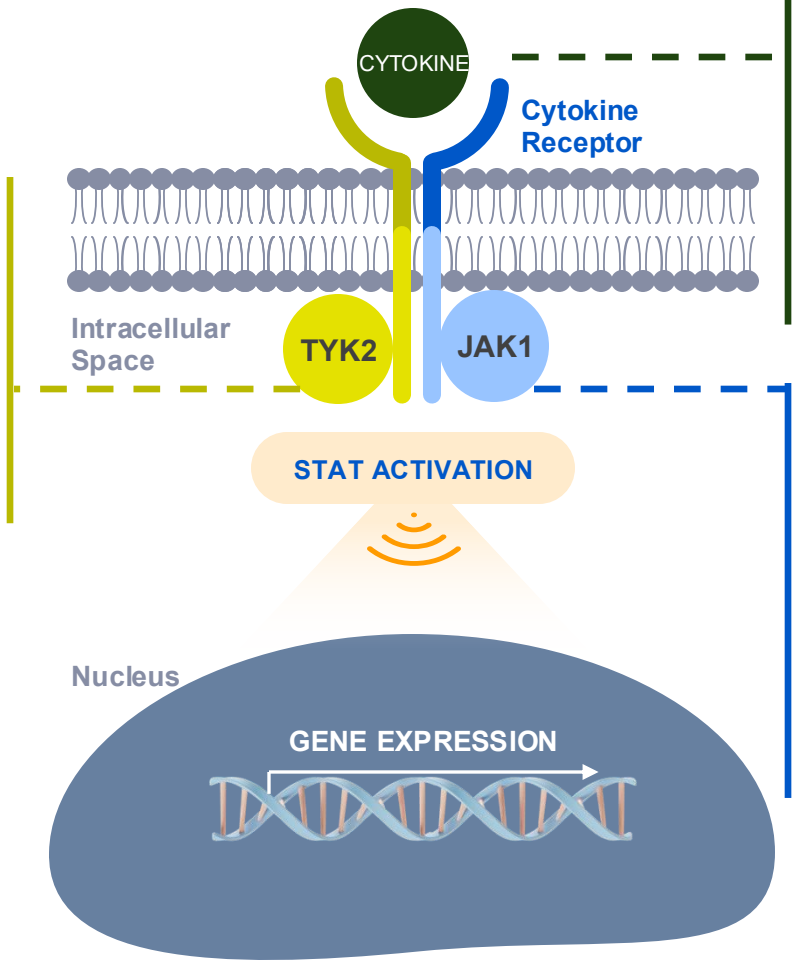
BHV-8000 treats both central and peripheral immune dysregulation underpinning Parkinson's

BHV-8000 Targets Both TYK2 and JAK1 to Control Immune Dysregulation in Parkinson's Disease

JAK-STAT SIGNALING PATHWAY

TYK2 PATHWAY
(IL-12, IL-23, etc.)

- Activates cytotoxic CD8 T cells and Th17 CD4 cells (which produce IL-17A) in the periphery
- IL-17A causes glial cell activation, release of neurotoxins such as TNFα, and disruption of the blood brain barrier[3]



SHARED TYK2 AND JAK1 PATHWAY
(IL-6, IFNα, IFNβ, etc.)

- Type-I IFN signaling is increased in post-mortem human PD brains[1]
- Type-I IFN modulates inflammatory response to α-syn in the gut, potentiating pathology along the gut-brain axis[2]

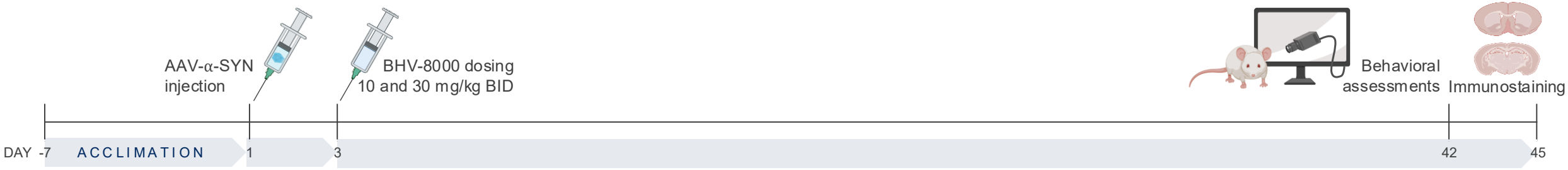
JAK1 PATHWAY
(IL-4, IFNɣ, etc.)

- Activates CNS innate immune cells (microglia and astrocytes)
- Promotes T cell infiltration and upregulation of MHC II expression on glial cells and macrophages – exacerbating immune activation in the CNS[4]

1. Main, Glia. 2016; 2. Waters, bioRxIv. Accessed May 15, 2025. https://www.biorxiv.org/content/10.1101/2024.05.05.592614v1. 3. Chen, *Front Aging Neurosci*. 2020; 4. Hong, *J Neuroinflammation*. 2024

BHV-8000 Reduces Inflammation and Improves Motor Function in AAV-α-syn Mouse Model of Parkinson's Disease

TYK2/JAK1



Improved Behavioral Assessments

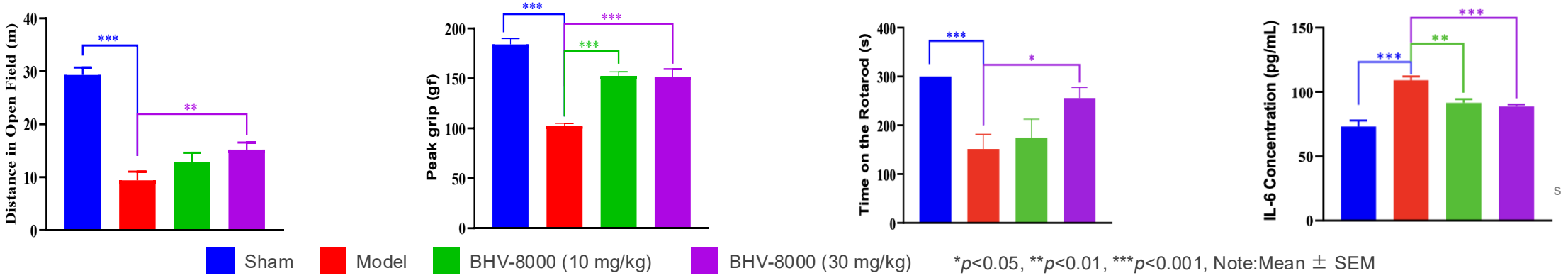
Increased Movement Distance in an Open Field by:
36.8%
61.4%

Increased Grip Strength by:
48.5%
47.5%

Increased Time on Rotarod by:
14.8%
64.4%

Alleviated Inflammatory Response

Significantly Decreased IL-6 Level in Str and SN Tissues of Mice

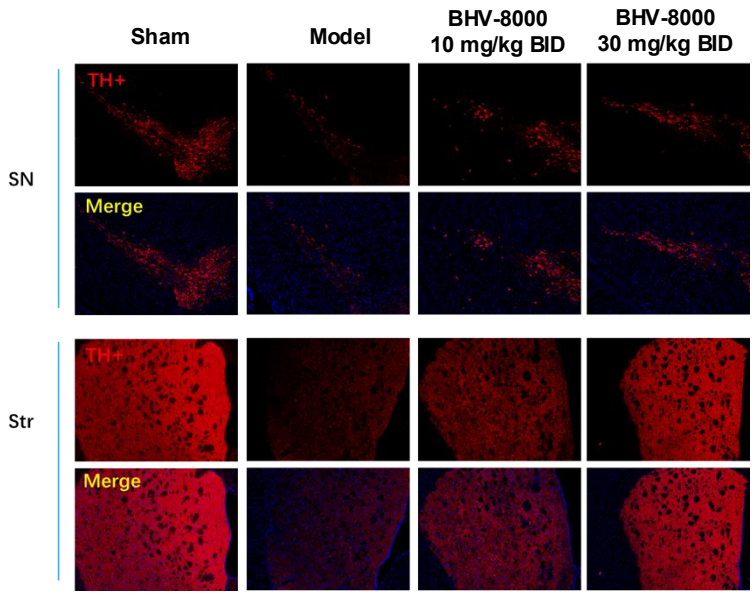


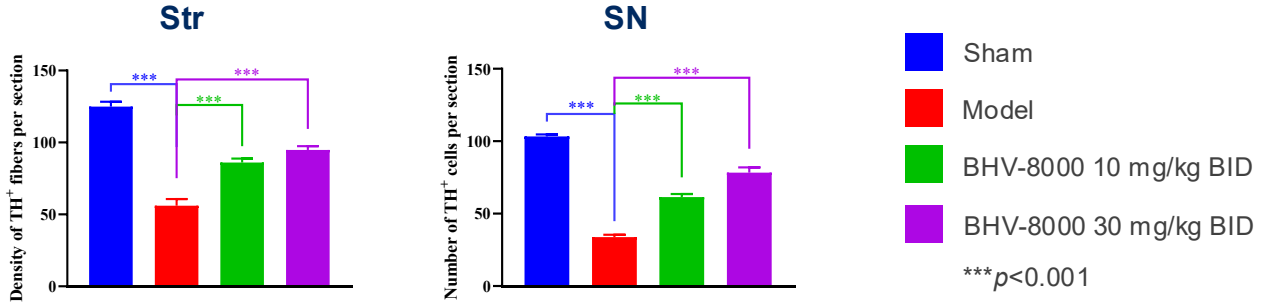
*p<0.05, **p<0.01, ***p<0.001, Note:Mean ± SEM

BHV-8000 Mitigates Microglial Activation and Prevents Neuronal Loss in AAV-α Synuclein Mouse Model

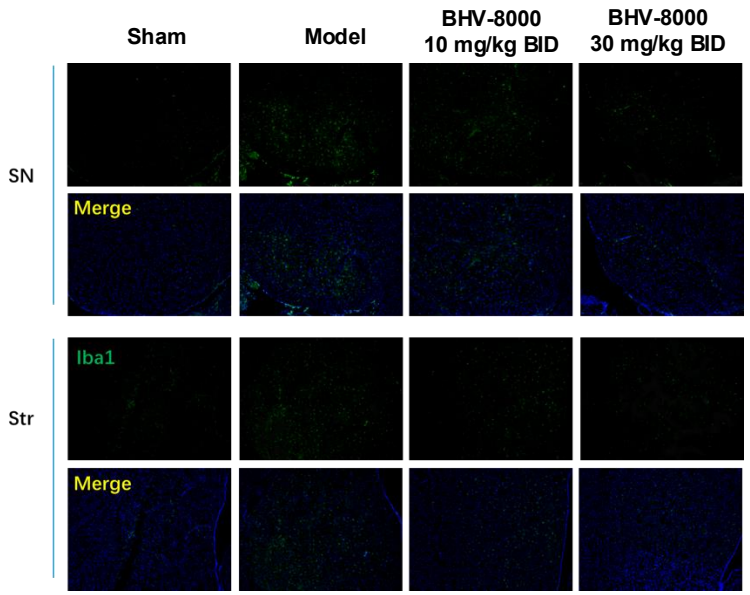
TYK2/JAK1

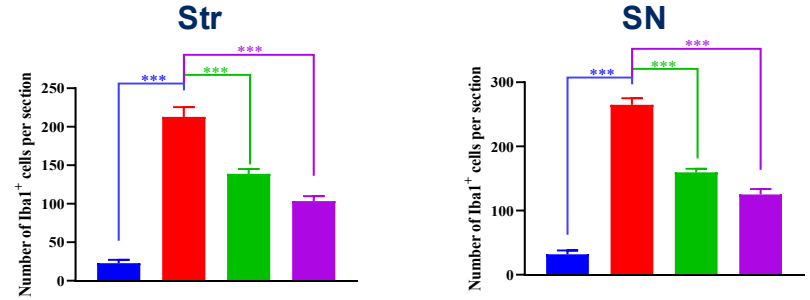
Prevented Neuron Death Indicated by Increased Counts of TH+ Neurons in SN





Mitigated Microglia Activation Represented by Reduced Numbers of Iba1+ Microglia





BHV-8000 Demonstrates a Promising Phase 1 Profile

TYK2/JAK1

Phase 1 program completed

- Includes SAD/MAD study in healthy adults

Well-tolerated

- No SAEs or severe AEs
- No adverse laboratory trends related to study drug

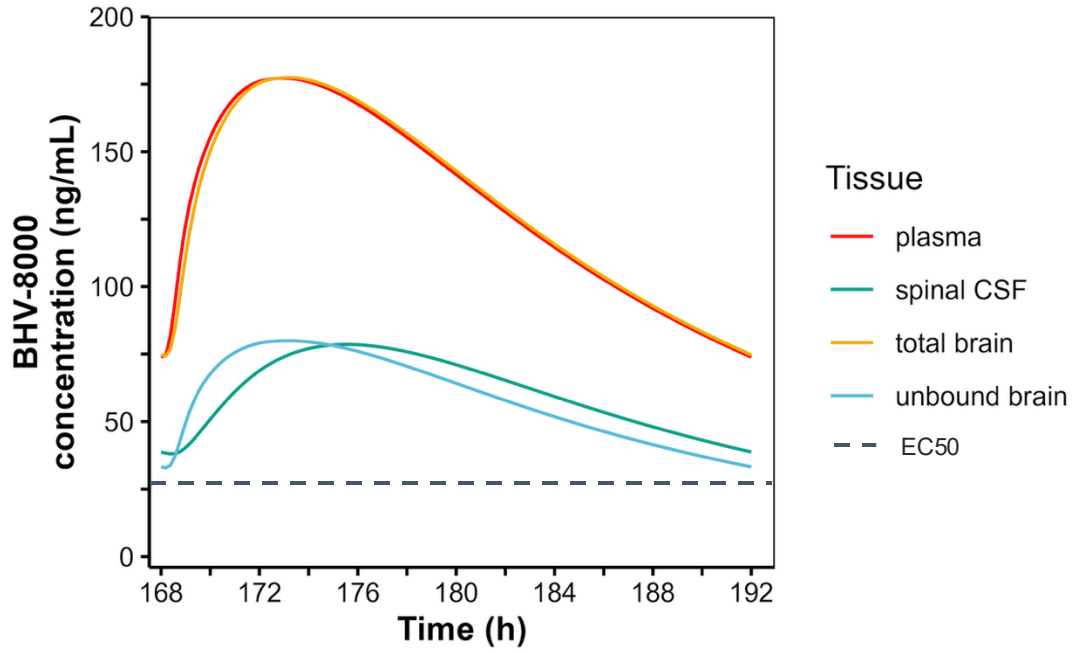
Evidence of target engagement

- Reduced plasma inflammatory cytokines downstream of TYK2 (IP-10, IFNβ) and JAK1 (hsCRP, IFNβ)

Robust brain penetration

- Exposures in CNS approximately 50% of plasma concentrations

BHV-8000 Brain Exposures at 20 mg QD



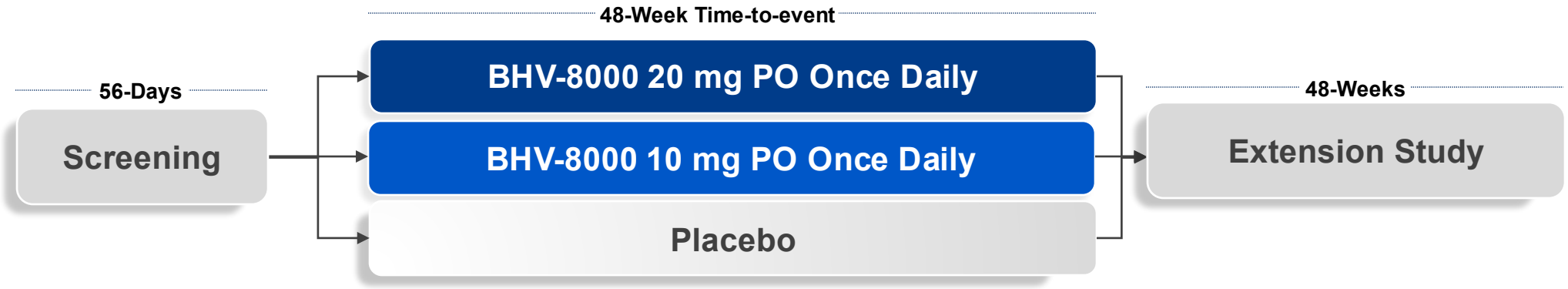
Modelling data

KEY POINT

Brain exposure sustained above target EC50s for 24 hours at clinically relevant doses

Phase 2/3 Study in Early Parkinson's Disease Initiated

TYK2/JAK1



POPULATION	Male and female adults living with early untreated PD
STUDY SIZE	550 participants randomized 1:1:1 (stratified by study site). 185 study sites across 13 countries (NA/EU)
TREATMENT	BHV-8000 10 mg or 20 mg or matching PBO PO once daily
TREATMENT DURATION	48-week double-blind treatment period. Completers to rollover into a 48-week extension study
KEY ENDPOINTS	**PRIMARY**: Time to qualifying worsening event on MDS-UPDRS Part II; **SECONDARY**: Change in MDS-UPDRS Part III, CGI-S, DaT-SPECT, PARCOMS composite scale, and Safety/tolerability

MDS-UPDRS, Movement Disorder Society – Unified Parkinson's Disease Rating Scale; **CGI-S**, Clinician Global Impression of Severity scale; **PARCOMS**, Parkinson's composite scale that includes most sensitive items from MDS-UPDRS and PDQ-39.

KEY POINT

Time-to-event primary endpoint enables fast and focused trial

Karl Kieburtz, MD, MPH
Professor of Neurology, Univ. of Rochester
Managing Principal, Clintrex Research LLC,
A BlueRidge Life Sciences company

CLINTREX
A BlueRidge Life Sciences Company

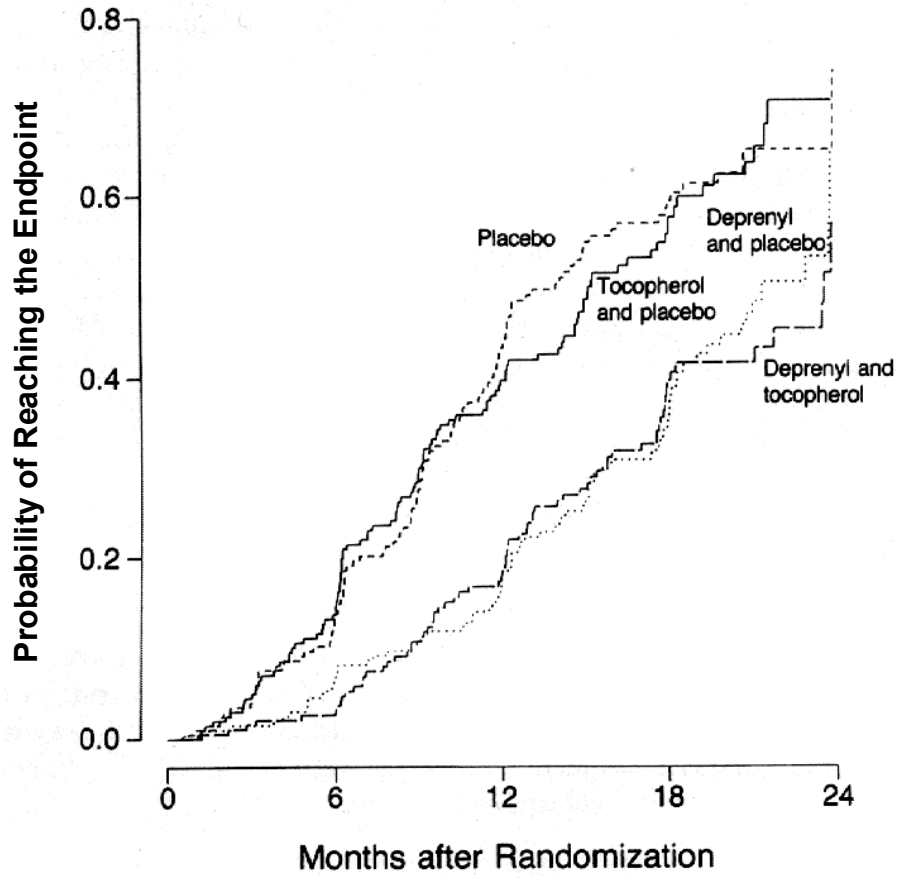
Fast and Focused —
Efficient Neurotherapeutics for Parkinson's Disease
Innovation Building on Experience

biohaven®

Effects of Tocopherol and Deprenyl on the Progression of Disability in Early Parkinson's Disease

TYK2/JAK1

Primary Endpoint Analysis (Time-to-Initiation of Levodopa) in the DATATOP Trial, Conducted in Early PD



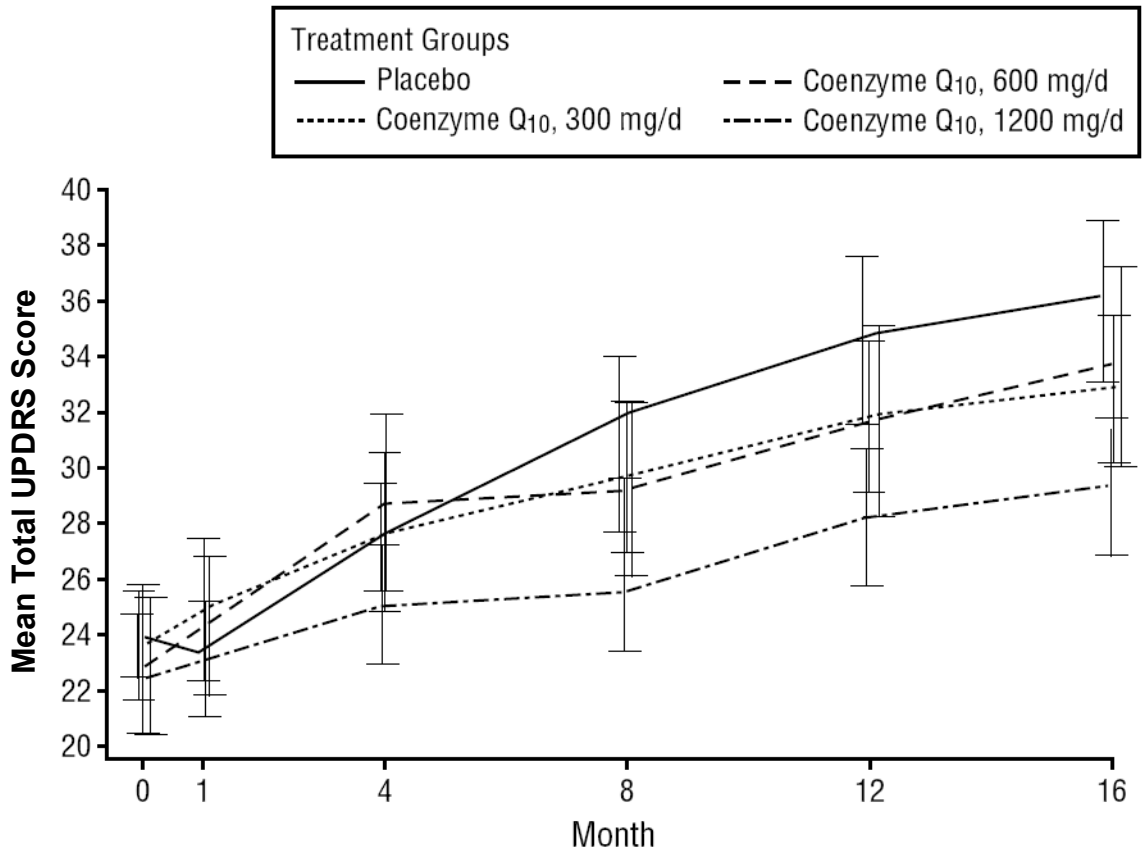
PSG. *NEJM* 1993;328:176-83; Kaplan-Meier estimate of the cumulative probability of reaching the endpoint

PSG. NEJM 1993;328:176-83

Effects of Coenzyme Q10 in Early Parkinson's Disease Evidence of Slowing of the Functional Decline

TYK2/JAK1

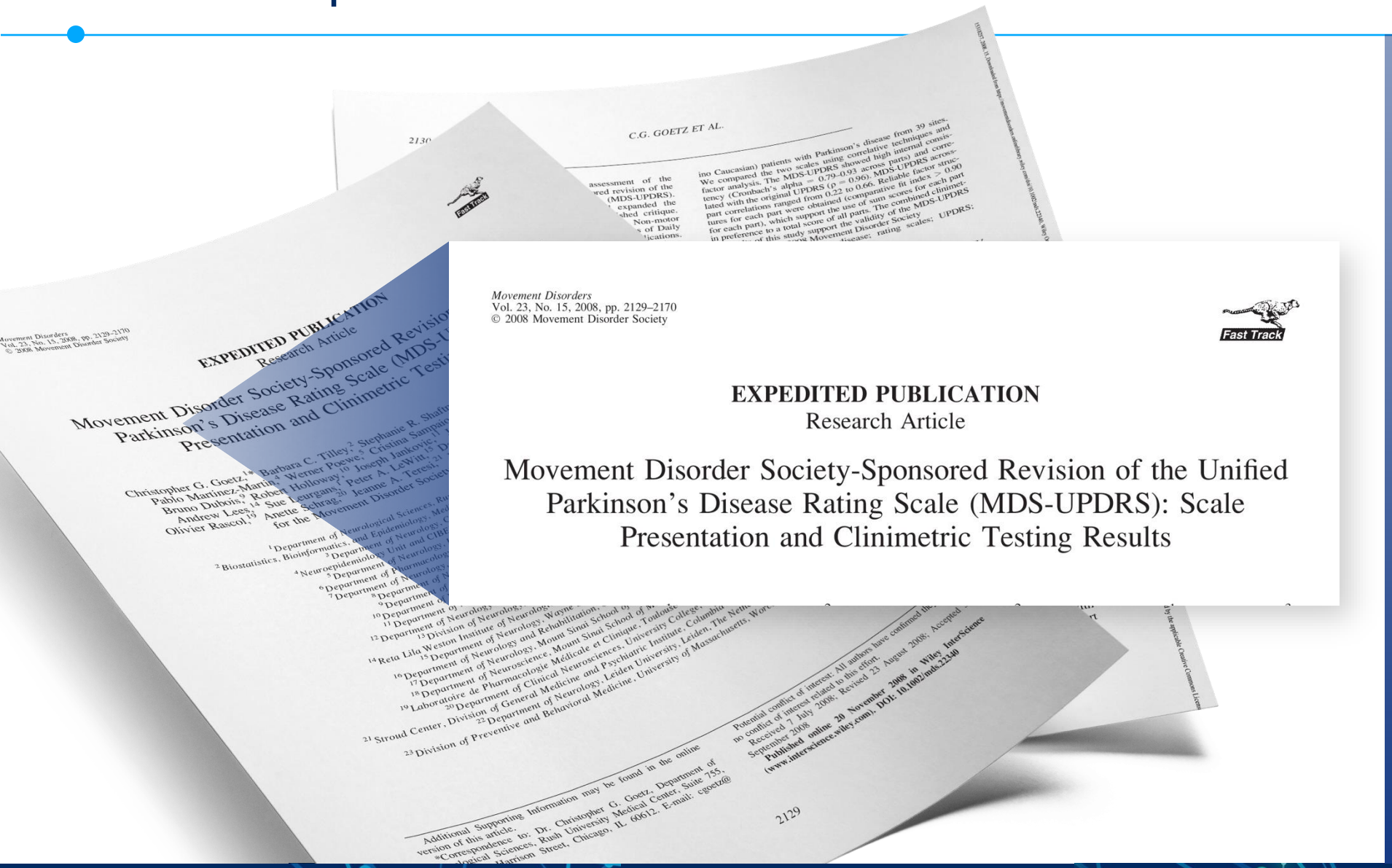
Primary Endpoint Analysis (Mean Change in UPDRS) in the Phase 2 Coenzyme Q10 Trial, Conducted in Early PD



Shults, et al. *Arch Neurol* 2002;59:1541-1550

Patient-Reported Functional Assessment Standardized

TYK2/JAK1



Part II Measures Motor Impact on Function — Meaningful to the Patients

Components of MDS-UPDRS

Part	Name	Focus	Who	Items	Time	Score
I	Non-Motor Experiences of Daily Living	Cognitive, mood, hallucinations, sleep, apathy, etc.	Clinician*	13	<15”	0–52
II	Motor Experiences of Daily Living	Speech, swallowing, handwriting, dressing, walking, etc.	Patient	13	10–15”	0–52
III	Motor Examination	Rigidity, bradykinesia, tremor, gait, posture, etc.	Clinician	33	15”	0–132
IV	Motor Complications	Dyskinesias, motor fluctuations, dystonia, etc.	Clinician	6	5”	0–24

*MDS-UPDRS Part Ia is completed by the clinician and Part Ib is completed by the patient

Design Innovation for BHV8000-301 Trial — Building on Past Experience

- Utilize a time to event design for efficiency (time and sample size)
- Choose excellent investigators, monitor emerging data
- Carefully select participants — DA deficiency and imaging
- Assess a meaningful functional decline — as reported by the study participant
- Agreement with regulatory authorities

Robust Screening Measures Are Needed to Ensure the Recruitment of Target Population

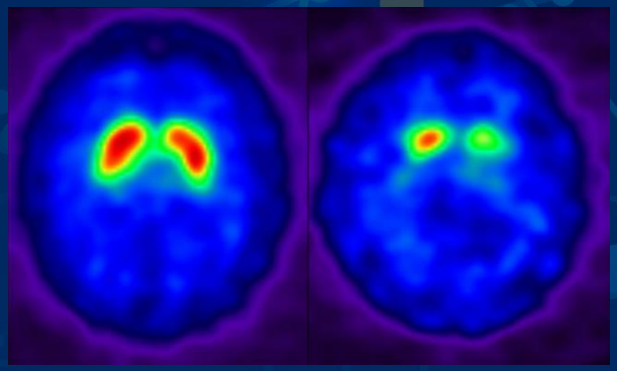
TYK2/JAK1

BHV8000-301 study utilizes a combination of history, physical examination, and diagnostic tests as Inclusion and Exclusion Criteria

- Meet the diagnostic criteria for “Probable PD” per Movement Disorder Society Clinical Diagnostic Criteria
- MDS-UPDRS total score ≥3 suggestive of at least mild disability at screening
- DaT-SPECT brain scan consistent with the diagnosis of PD — as confirmed by a central radiology service
  - DaT can detect early presynaptic dopaminergic neuron loss before significant motor symptoms
  - DaT has high sensitivity and specificity for differentiating PD from essential tremor, psychogenic disorders, and many other forms of Parkinsonism

DaT-SPECT Scanner

DaT Results in HC vs PD Patient[1]



1. Son, et al. *Sci Rep* 2016;6:38070

1Son, Sci Rep 2016

biohaven

Innovative Study Designed in Collaboration with Regulators

TYK2/JAK1

Time-to-event (≥ 2-point worsening on MDS-UPDRS-Part II) is the BHV8000-301 pre-specified primary endpoint

- Rates of decline in Part II were based on comprehensive analyses of PPMI and placebo-arm clinical trial data (C-Path)
- Addresses FDA requirement for a functional endpoint in PD trials
- Allows for fewer participants to be enrolled into the trial than a traditional design based on a mean change in MDS-UPDRS-Part II, and may also shorten timelines

Outcome Measure Innovation

TYK2/JAK1

1. MDS UPDRS Part II has acceptance by regulators and investigators but may be insensitive in early PD

2. Selection of specific elements and combination with other self-report elements (from PDQ-39) may improve operating characteristics in early PD

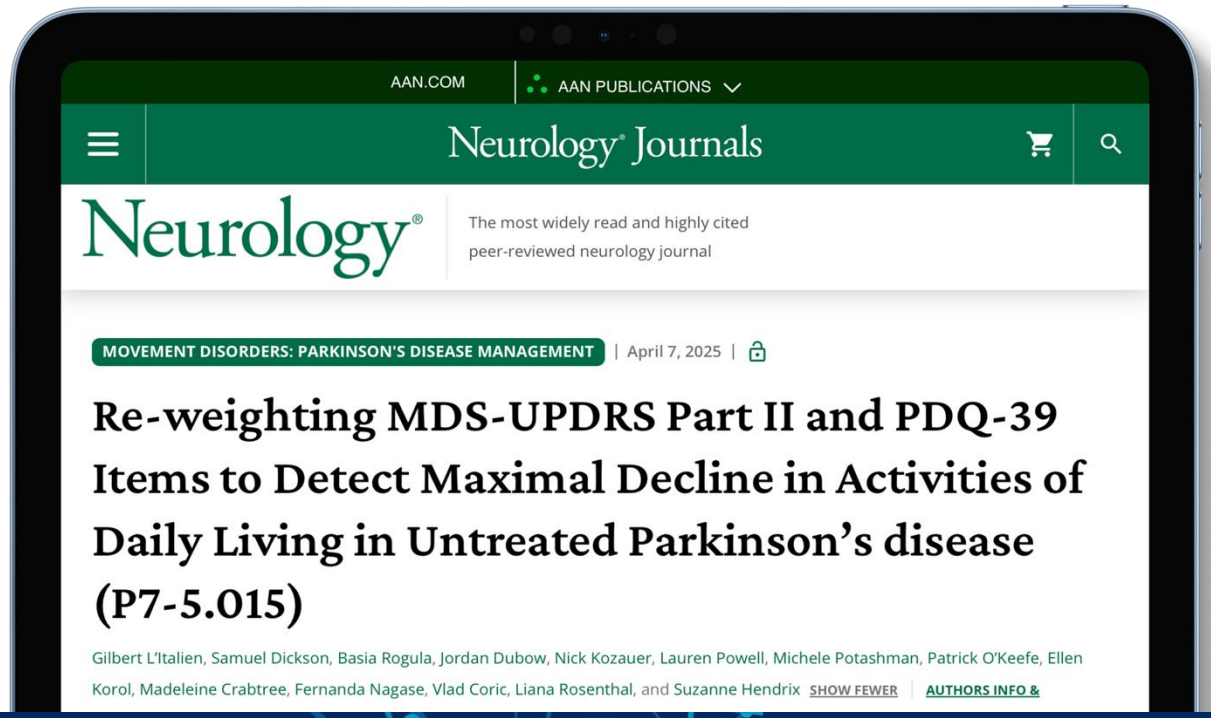
3. PARCOMS is a composite measure that may further enhance clinical trial efficiency in early PD

Composite Scoring Can Improve the Sensitivity of Detecting Patient-Reported Change in Early PD

TYK2/JAK1

Parkinson's Composite Scales (PARCOMS) were derived specifically for the early untreated PD patient (BHV8000-301 target population)

- These scales were designed using established methodologies (e.g., ADCOMS for early-AD)
- They represent a composite of the most sensitive measures across traditional motor/ADL scales
- At 1-year, PARCOMS significantly increases the ability to detect change compared to component scales alone



BHV800-301 PARCOMS-Function Scale

MDS-UPDRS	PDQ-39
Hygiene	Walking 1/2-mile
Speech	Muscle cramps
Handwriting	Buttons and shoelaces
Saliva and drooling	Cutting up food
Turning in bed	Looking after home
Getting out of bed/car/chair	Carrying shopping bags
Doing hobbies/activities	Writing clearly
	Aches and pains

PDQ-39: Parkinson's Disease Questionnaire-39, a health-related quality of life survey for people with PD

Panel

MODERATOR

Ash Verma

Equity Analyst

UBS

PANELISTS

David A. Hafler, MD

William S. and Lois Stiles Edgerly Professor of Neurology and Professor of Immunobiology
Yale School of Medicine

Peter Ackerman, MD

Senior Vice President, Clinical Development
Biohaven

Karl Kieburtz, MD, MPH

Professor of Neurology, University of Rochester
Managing Principal, Clintrex Research LLC, A BlueRidge Life Sciences company

BHVN LISTED NYSE

Ania Jastreboff, MD, PhD

Assoc. Prof. of Medicine (Endocrinology);
Director, Yale Obesity Research Center (Y-Weight);
Co-Director, Yale Center for Weight Management

Yale SCHOOL OF MEDICINE

Peter Ackerman, MD

Senior Vice President,
Clinical Development

biohaven®

Lindsey Lair, MD, MBA, FAAN

Vice President, Clinical Development

biohaven®

Leslie Hayes, MD

Attending Physician,
Department of Neurology

Boston Children's Hospital

Myostatin

biohaven®

Ania Jastreboff, MD, PhD
Assoc. Prof. of Medicine (Endocrinology);
Director, Yale Obesity Research Center (Y-Weight);
Co-Director, Yale Center for Weight Management

Yale SCHOOL OF MEDICINE

Anti-Obesity Medication for the Treatment of Obesity

biohaven®

Peter Ackerman, MD

Senior Vice President,
Clinical Development

biohaven®

Taldefgrobep:
For the Treatment of Obesity

biohaven®

Differentiated Pharmacology Key to Optimizing Benefit in Overweight and Obesity

- Taldefgrobep-myostatin complex competitively inhibits multiple key ligands from signaling through Activin II receptors (ActRII)
- Unique MOA leads to direct beneficial effects on both muscle and adipose tissues
- Safety profile established in diverse clinical populations (N >700) well-suited to overweight and obesity indication

Paradigm Shift to Improving Quality of Weight Loss

- Ability to lower total body weight by reducing fat mass while preserving lean muscle mass
- Use as monotherapy or in combination with Nutrient-Stimulated Hormone (NuSH)-based therapies, i.e., GLP-1 receptor agonists
- Weekly SC administration via off-the-shelf autoinjector, with potential for extended dosing intervals

KEY UPDATE

Phase 2 study in obesity planned for 2H 2025

Taldefgrobep Has Direct Effects on Muscle and Fat — Optimizing Quality of Weight Loss

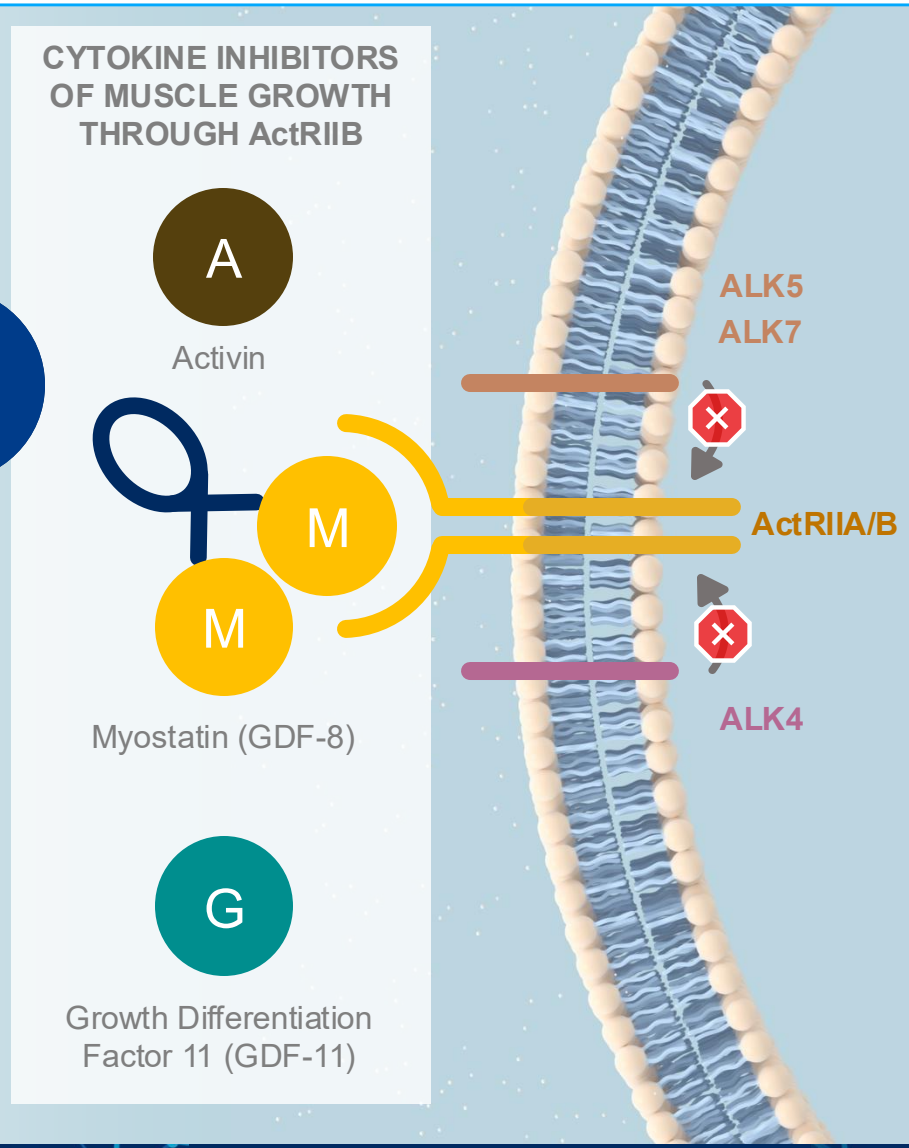
TALDEFGROBEP

Taldefgrobep alfa
Biohaven

BINDS
active myostatin
(GDF-8), GDF-11

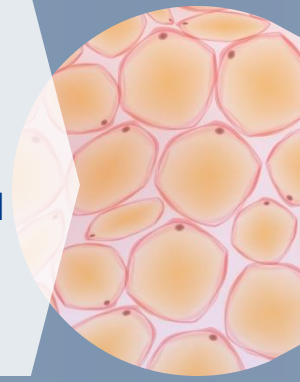
FORMS COMPLEX
that attaches to ActRIIA/B
prevents ActRII binding (ALK4,5,7)

INHIBITS
ActRIIA/B signaling
by key ligands including Activin A



Inhibition in adipocytes leads to **lipolysis**

Increased brown fat enhanced mitochondrial activity and increased thermogenesis



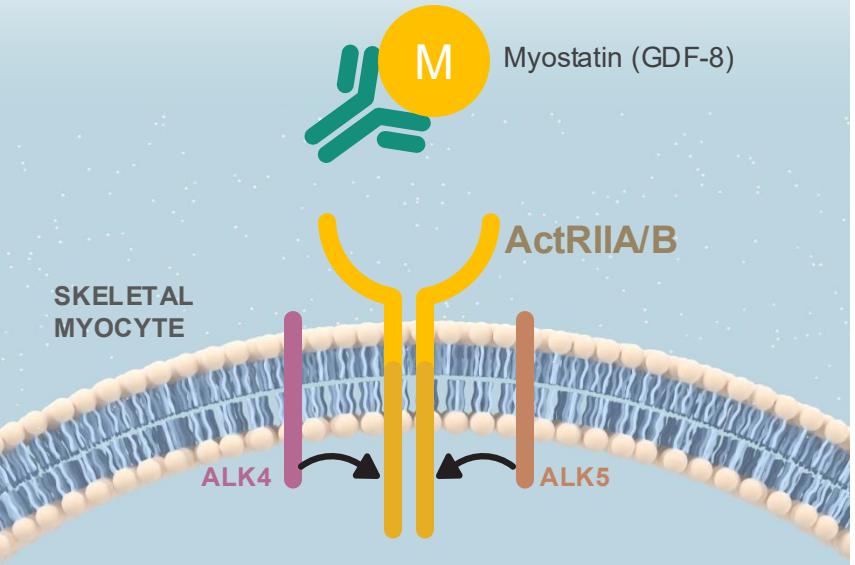
Inhibiting signal transduction in skeletal muscle leads to **hypertrophy**

Taldefgrobep's Differentiated Approach Balances Efficacy and Safety

TALDEFGROBEP

Apitegromab (SRK439)/GYM329
Scholar Rock/Roche

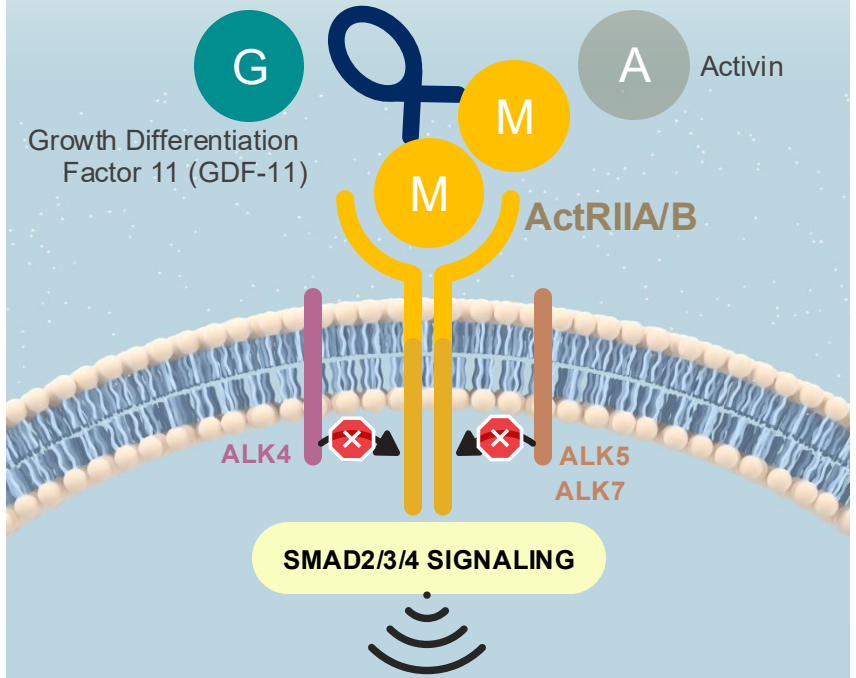
TARGETS pro- and latent myostatin



Targeting myostatin alone results in sub-optimal improvements in body composition and total body weight[1]

Taldefgrobep Alfa
Biohaven

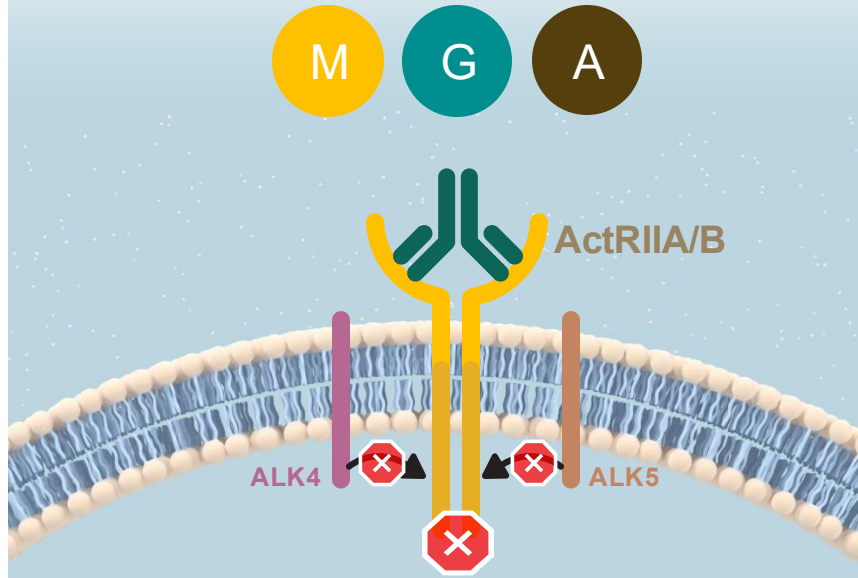
BINDS active myostatin (GDF-8), GDF-11
COMPLEX attaches to ActRII
INHIBITS ActRIIA/B signaling



ActRII signaling inhibits muscle growth and suppresses lipolysis

Bimagrumab
Versanis-Lilly

BLOCKS only ActRIIB signaling (all ligands) with very high affinity



Very tight and extended ActRII binding is associated with poor tolerability (high rates of muscle complaints and diarrhea)[2,3]

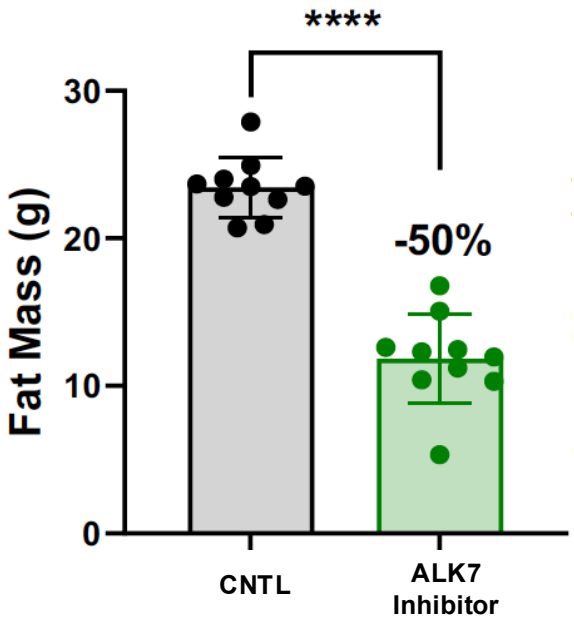
1. Fulham M, et al. ObesityWeek 2024. Poster 524.
2. Garito, *Diabetes Obes Metab.* 2018; 3. Heymsfield, JAMA Network Open. 2021.

Taldefgrobep Stimulates Lipolysis and Decreases Fat Mass

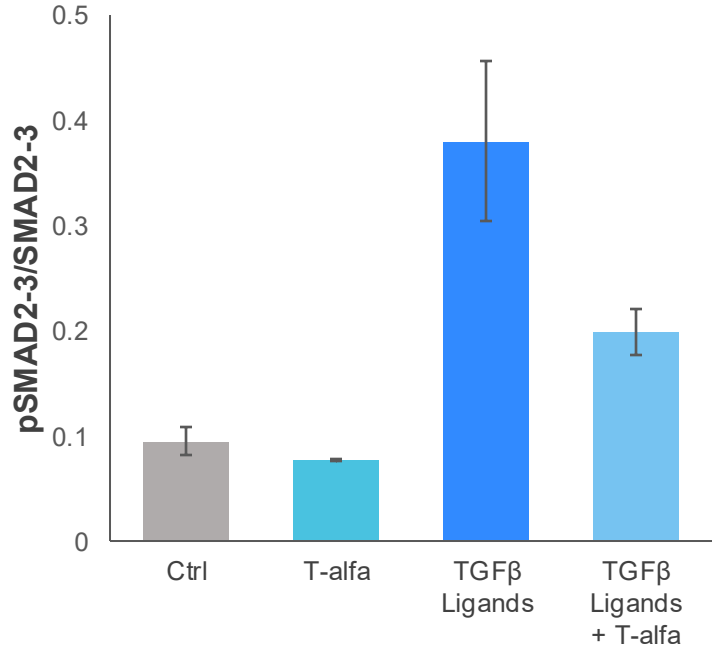
TALDEFGROBEP

- ALK7 activation blunts β-adrenoreceptor-mediated lipolysis and lipid oxidation in people with obesity[1]
- Reduction in ALK7 signaling can reduce fat mass in preclinical models[2]
- Taldefgrobep complex blocks ALK7-mediated SMAD2/3 signaling in adipocytes leading to increased lipolysis and a reduction in fat mass

ALK7 Inhibition Can Meaningfully Reduce Fat Mass in a DIO Mouse Model[1]



Taldefgrobep Blocks TGFβ-induced Signaling Through ALK7

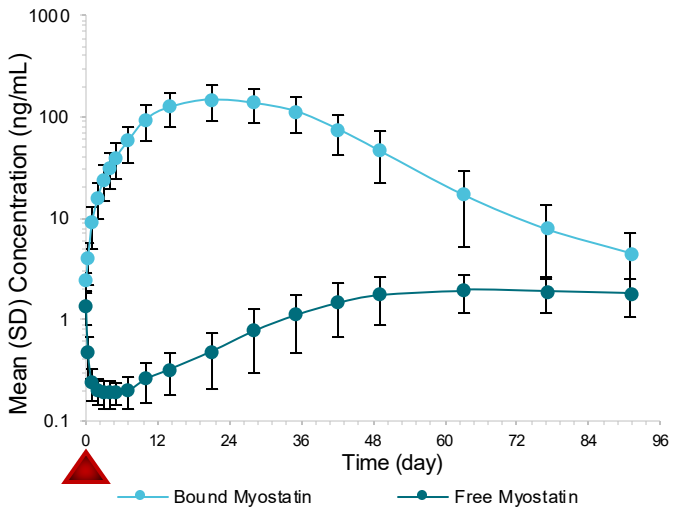


1. Guo. Elife 2014. 2. Ngai. Keystone Symposia on Obesity and Adipose Tissue, Poster. 2025

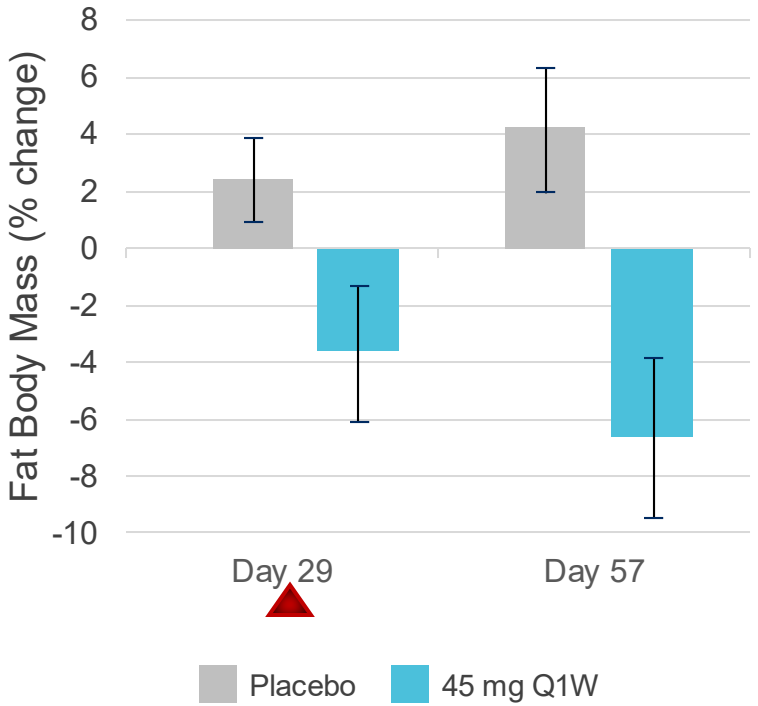
Taldefgrobep-Myostatin Complex Allows for Extended Pharmacodynamic Effects in the Clinic; Potential for Monthly Dosing in Obesity

TALDEFGROBEP

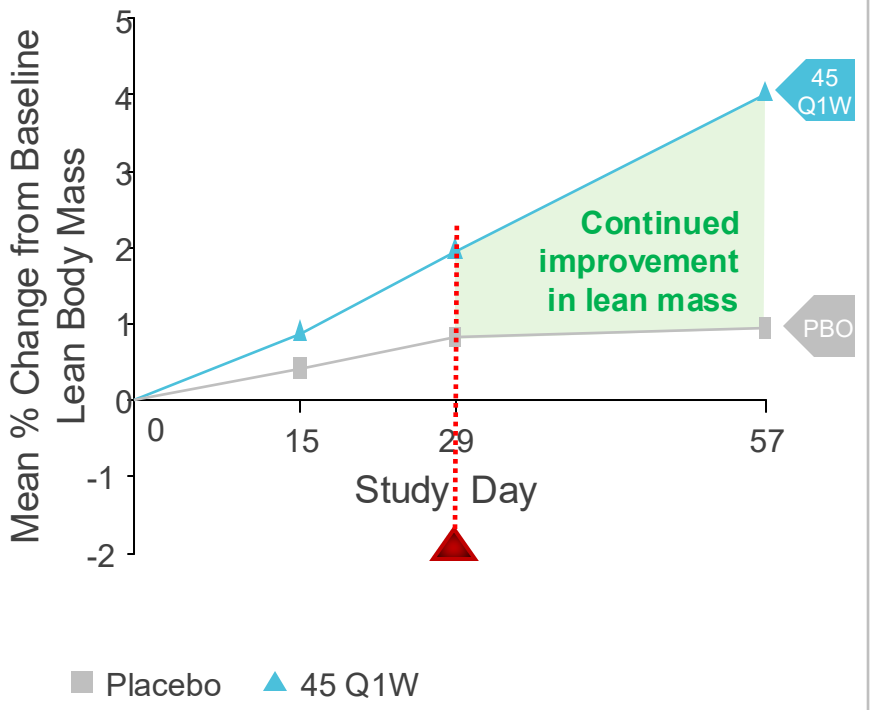
Peak Plasma Concentrations of Taldefgrobep-Myostatin Complex Occurs 20-30 Days Post Dose



Taldefgrobep Continued to Decrease **Total Fat Mass** Beyond the Dosing Period



Taldefgrobep Demonstrates Continued Improvement in **Lean Mass** in Healthy Adults at 30 Days Post Dosing



Last dose

Muntoni F. et al, *Neurol Ther*. 2024 Feb;13(1):183-219.

Taldefgrobep Monotherapy Offers Attractive Differentiation; but Also Potential for Combination With NuSH Therapies to Improve Quality of Weight Loss

TALDEFGROBEP

FURTHER REDUCE

- ✓ Total body weight
- ✓ Total body fat
- ✓ Visceral adipose tissue
- ✓ Subcutaneous adipose tissue
- ✓ Hepatic fat
- ✓ Intramuscular fat
- ✓ HbA1c
- ✓ BP

Augment beneficial effects of NuSH therapies

Address limitations of NuSH therapies

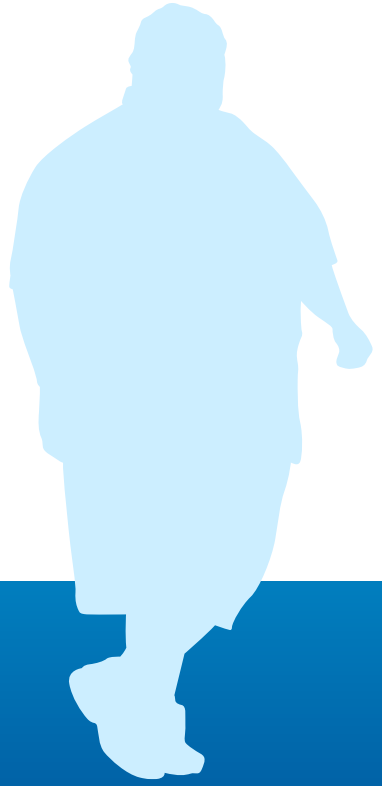
MITIGATE AGAINST

- ✓ Excess loss of lean mass
- ✓ Excess loss of bone mass
- ✓ Rapid weight rebound following interruption of dosing with NuSH therapies

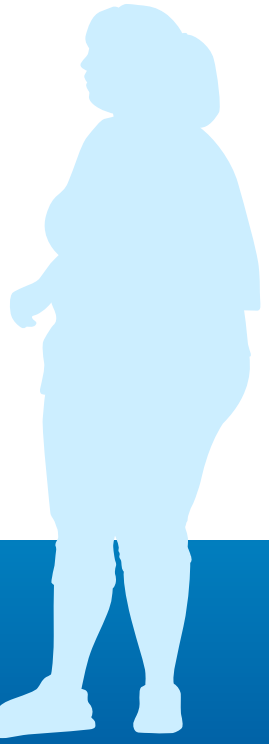
NuSH Therapies, Nutrient-stimulating hormone therapies.

Populations That Can Benefit From Taldefgrobep + NuSH Combination

TALDEFGROBEP



People living with extreme obesity — BMI ≥40



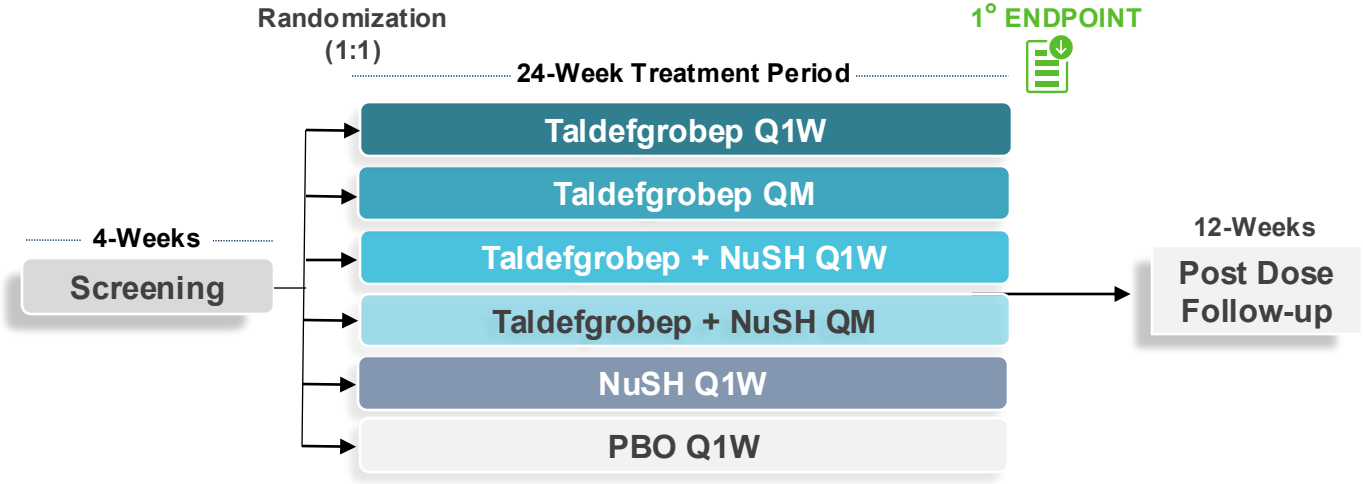
People living with overweight and obesity + comorbid T2DM

Males living with overweight and obesity +/- T2DM

Older individuals

Taldefgrobep Phase 2 Combination Therapy Study in Overweight and Obesity

TALDEFGROBEP



DESIGN	Randomized, double-blind, placebo-controlled dose-ranging trial
POPULATION	Male and female adults (18 – 75yo) living with overweight and obesity (BMI ≥27)
SAMPLE SIZE	Eligible participants randomized 1:1 (Sex [M/F] and BMI [<36, ≥36])
TREATMENT	Taldefgrobep SC once-weekly or once-monthly +/- NuSH-based therapeutic vs PBO
TREATMENT DURATION	24-week double-blind treatment period followed by 12-week post dose follow-up
ENDPOINTS	**Primary Endpoint**: Change in Total Body Weight (TBW) **Secondary Endpoints**: Lean Mass, Fat Mass, anthropometric measures, bone density, lipids, glycemic control, BP, PROs; PK/PD; safety/tolerability

Design provides insight into key questions

- Impact of taldefgrobep monotherapy on body composition, TBW, metabolic endpoints in representative population
- Ability of taldefgrobep to provide additional benefits on top of NuSH therapies alone
- Ability of taldefgrobep to mitigate against reductions in lean mass associated with NuSH therapies

Preliminary design

Lindsey Lair, MD, MBA, FAAN

VP, Clinical Development

biohaven®

Taldefgrobep Alfa for the Treatment of Spinal Muscular Atrophy (SMA)

biohaven®

Differentiated Pharmacology Balancing Efficacy and Safety in SMA

- Taldefgrobep-myostatin complex competitively inhibits multiple key ligands from signaling through Activin II receptors (ActRII)
- Unique MOA leads to direct beneficial effects on both muscle and adipose tissues
- Safety profile established in diverse clinical populations (n >700)

Phase 3 Data in Spinal Muscular Atrophy

- Clinically meaningful improvements in motor function at all timepoints
- Robust target engagement (myostatin reduction)
- Beneficial impacts on body composition parameters (fat mass, lean muscle mass and bone density)
- Well-tolerated with 97% of participants continuing into optional OLE

KEY UPDATE

FDA interaction planned to discuss SMA registrational path in 1H 2025

Taldefgrobep Alfa: Well-Characterized Clinical Profile

CLINICAL DEVELOPMENT

>700 trial participants treated (adults and children) across 6 studies

- Completed: 3 Phase 1 trials (SAD/MAD, SC BA, autoinjector BE); 1 Phase 1b/2 trial in DMD and 1 Phase 2/3 trial in DMD
- Ongoing: Phase 3 trial in SMA

PHARMACOLOGY

Demonstrated target engagement and increased muscle mass

- Explored broad range of doses (4 mg to 180 mg SC QW) for up to 120 weeks of repeat dosing
- Demonstrated target engagement with dose-related free myostatin suppression
- Noted accumulation of drug-myostatin complex with sustained pharmacological activity beyond dosing period in healthy adults
- Demonstrated increased muscle in healthy adults, DMD and SMA

SAFETY

Safe and well-tolerated to date with differentiated profile

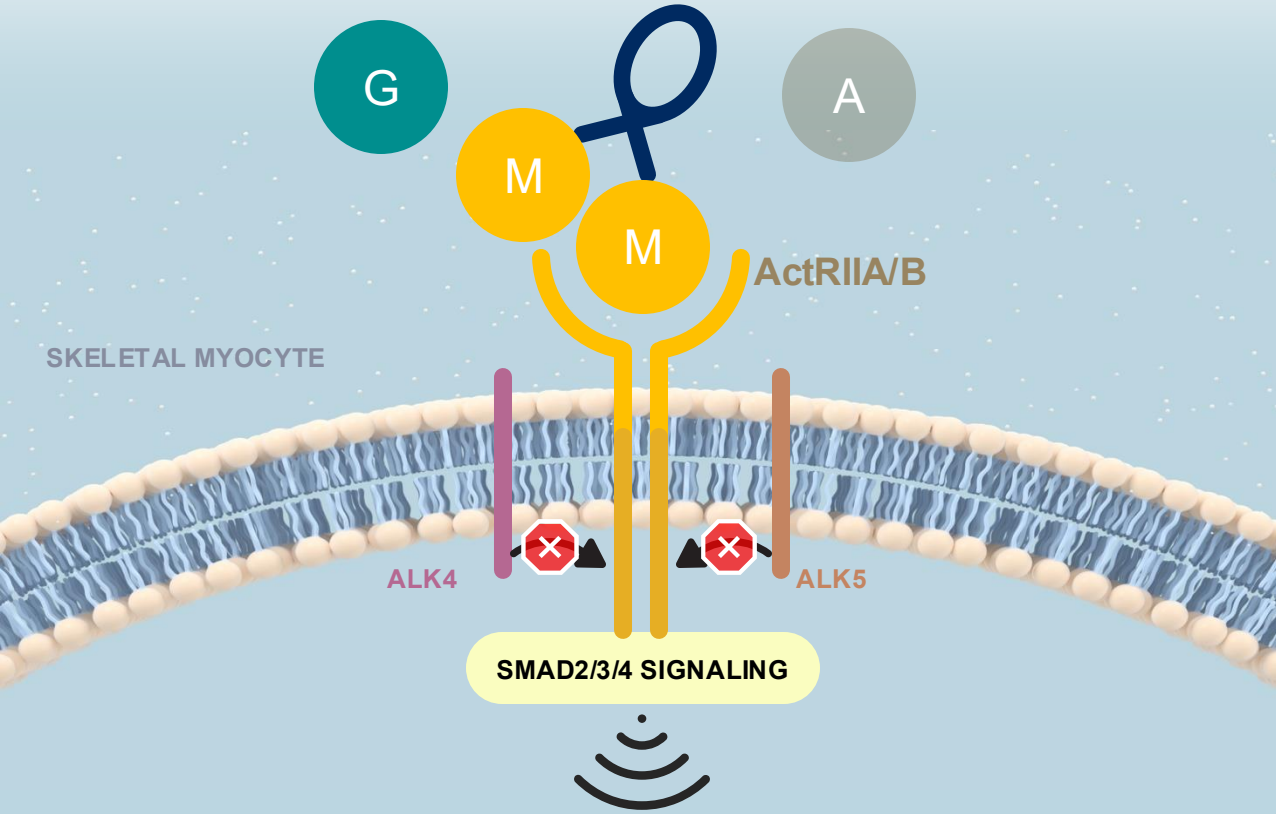
- Low rates of SAEs, and few AEs leading to discontinuation
- Does not have AEs commonly reported in other drugs in the class (e.g., GI-related and muscle-related side effects)

Taldefgrobep Alfa: Differentiated Approach Balances Efficacy and Safety

TALDEFGROBEP

Taldefgrobep Alfa
Biohaven

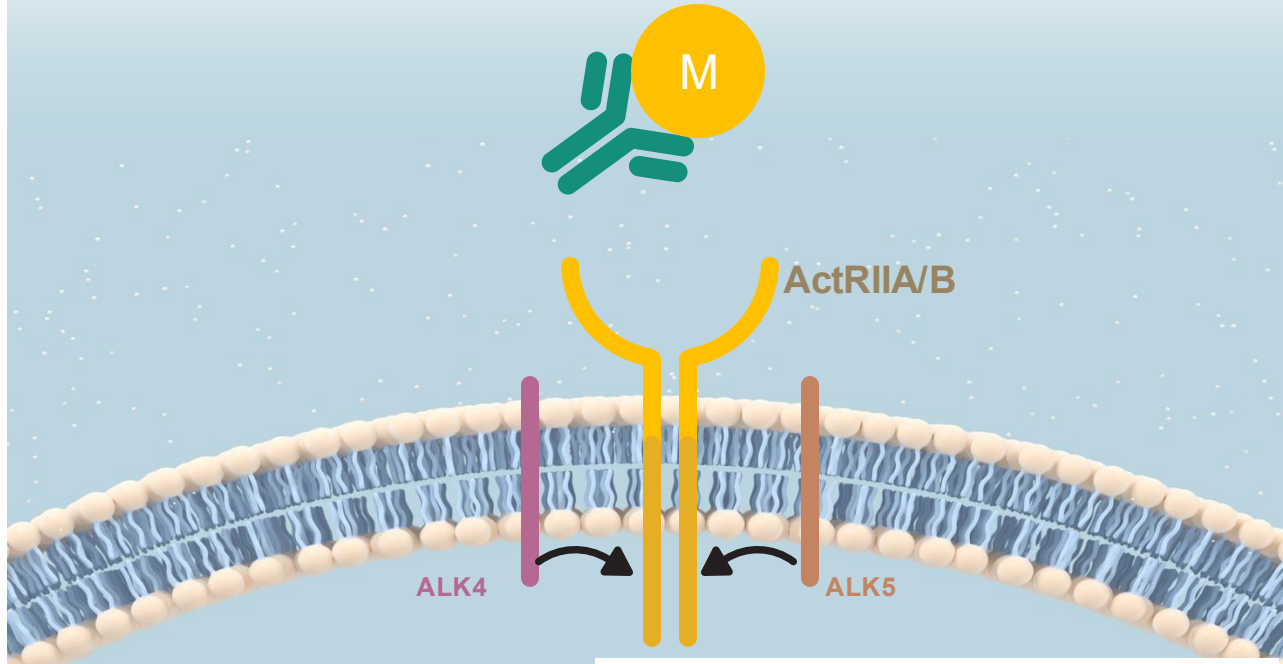
BLOCKS active myostatin (GDF-8), GDF-11 and
INHIBITS ActRIIA/B signaling through key ligands



ActRII signaling inhibits muscle growth

Apitegromab/GYM329
Scholar Rock/Roche

TARGET pro- and latent myostatin



CYTOKINE INHIBITORS OF MUSCLE GROWTH THROUGH ActRIIB

- M Myostatin (GDF-8)
- G Growth Differentiation Factor 11 (GDF-11)
- A Activin

Leslie Hayes, MD

Attending Physician,
Department of Neurology

Boston Children's Hospital

Taldefgrobep Alfa: Unmet Need in SMA and RESILIENT Phase 3 Data

biohaven®

High Unmet Need Still Remains For SMA

TALDEFGROBEP

SOC treatments
target motor neurons
not muscle

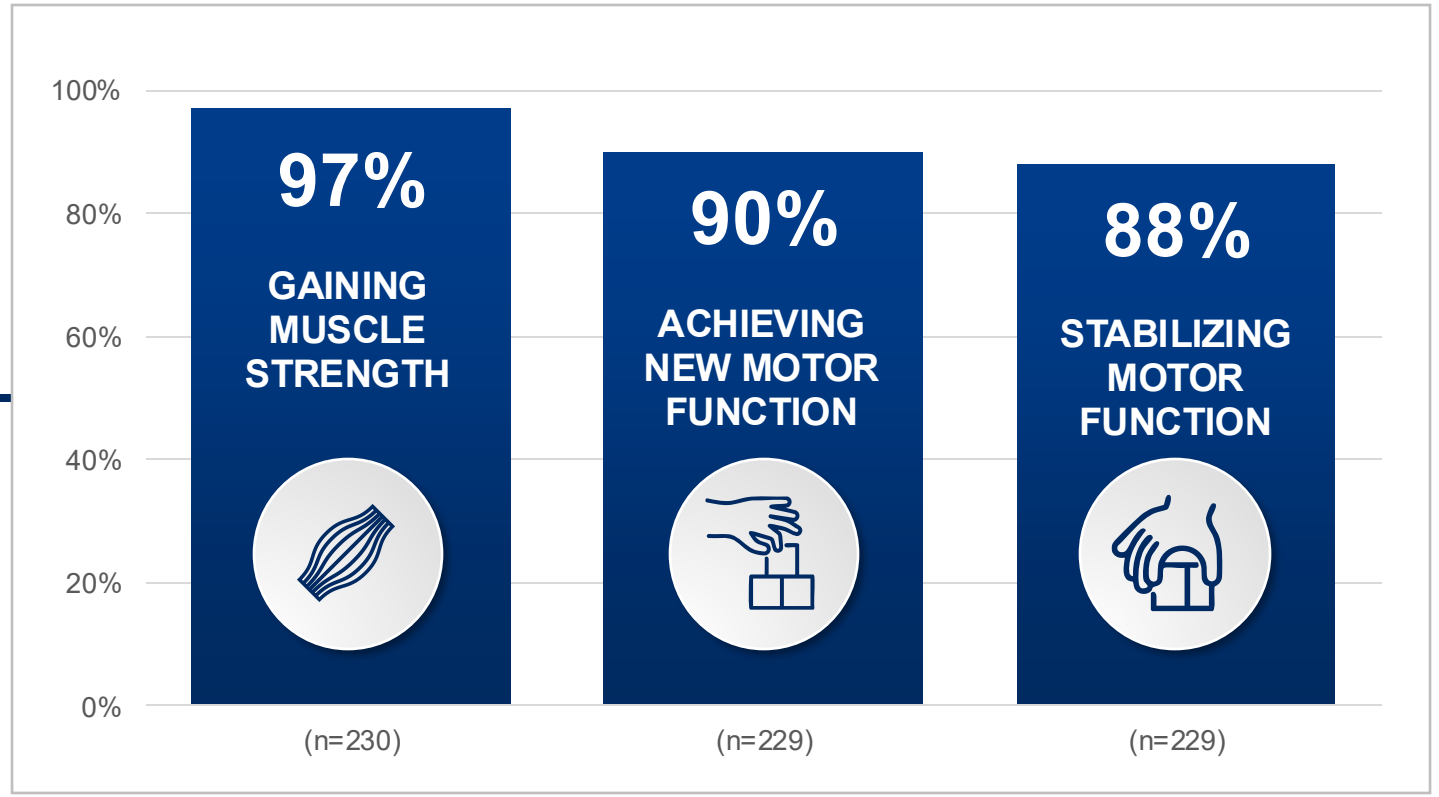
Patients on SOC treatment continue to experience
significant muscle weakness, reduced functioning and decreased quality of life[1–7]

1. Mercuri E, et al. *Nat Rev Dis Primers*. 2022 Aug 4;8(1):52 . 2. Day JW, et al. *BMC Pediatr*. 2022;22(1):632. 3. Darras BT, et al. *N Engl J Med*. 2021;385(5):427-435. 4. Finkel RS, et al. *N Engl J Med*. 2017;377(18):1723-1732 5. Cure SMA. Accessed November 2024. https://www.curesma.org/wp-content/uploads/2018/01/SMA-VoP-for-publication-1-22-2018.pdf. 6. Darras BT, et al. *N Engl J Med*. 2021;385(5):427-435. 7. Finkel RS, et al. *N Engl J Med*. 2017;377(18):1723-1732.

97% of Adults With SMA Hope New Therapies Will Help Them Gain Muscle Strength

TALDEFGROBEP

"What are your most significant current unmet needs that you hope new therapies would address?"[1]



1. Cure SMA. Accessed November 2024. https://www.curesma.org/wp-content/uploads/2024/06/9042024_State-of-SMA_vWeb.pdf.

KEY POINT

Muscle-targeting therapy is needed on top of SOC treatment (SMN upregulation)

RESILIENT
STUDY

RESILIENT Phase 3 Data

Taldefgrobep Alfa

biohaven®

Taldefgrobep Alfa Demonstrated Benefits in SMA in RESILIENT

LUNGS

Respiratory issues cause morbidity and mortality[1]

Benefits respiratory muscle function

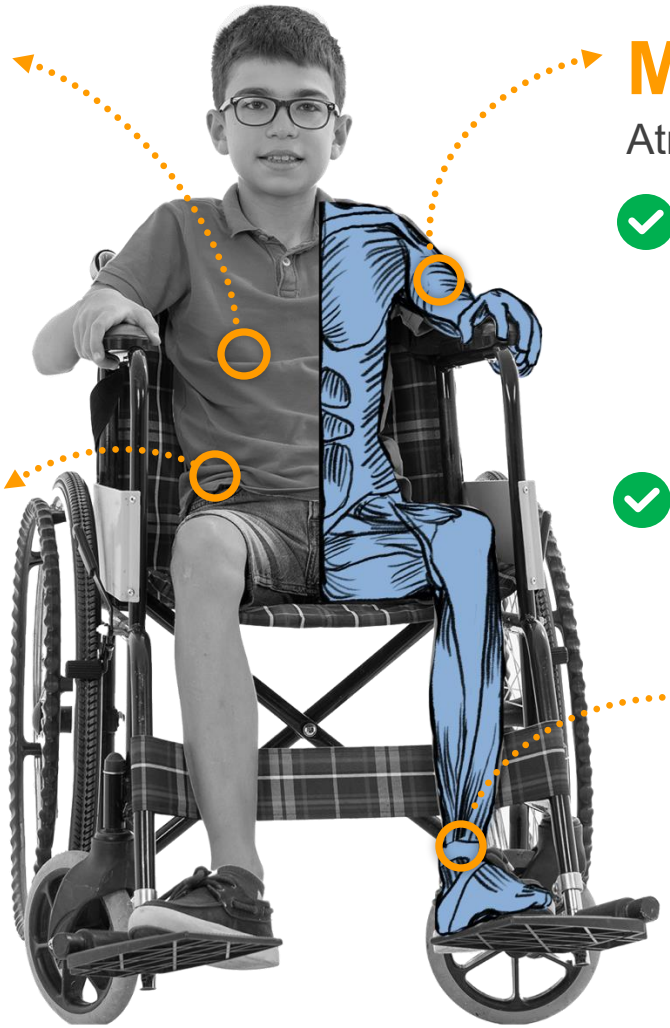
- Increases in MIP and MEP vs placebo

FAT

Obesity causes morbidity[2]

Decreases fat mass accumulation

- 6.1% (p=0.01) reduction in total body fat mass vs placebo



MUSCLES

Atrophy and weakness

Improves motor function

- Clinically meaningful on primary outcome
- Significant effect in largest prespecified population (1.1-point placebo-adjusted improvement (p=0.04))
  - Further enhanced when myostatin-positive

Benefits lean muscle mass

- 1.3% increases vs placebo

BONE

Low bone density is common; fractures cause morbidity[3]

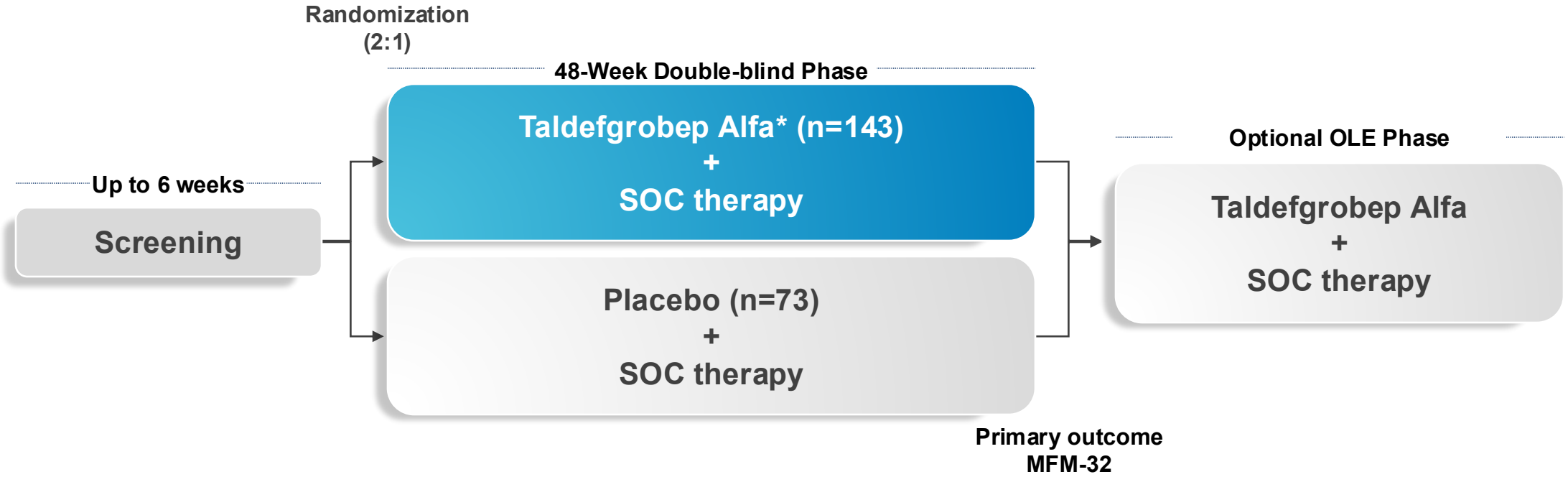
Benefits bone density

- 0.8% increases vs placebo

MIP, Maximum inspiratory pressure; **MEP,** Maximum expiratory pressure.

1. Lagae L, et al. *Front Pediatr* 2024;12:1366943. DOI: 10.3389/fped.2024.1366943. 2. Vetlesen HS, et al. CNOS 2024;53:57-67; 3. Mercuri E, et al. Neuromuscl Disord. 28 (2018) 103-115.

Taldefgrobep Alfa SMA Phase 3 Trial (RESILIENT)



KEY ENTRY CRITERIA & STRATIFICATION**

Age**: 4–12 or 13–21 years old

Ambulatory status**: Ambulatory or non-ambulatory (sit independently)

Stable SOC therapy**: Nusinersen, Risdiplam, previous Onasemnogene or combination

MFM-32 score: < 90%

MFM-32, 32 item Motor Function Measure; **SOC, s**tandard of care; **SMN,** survival motor neuron. *Weight-based 35 mg or 50 mg weekly; SC. **Stratification factors (age, ambulatory stays, stable SOC therapy).

KEY POINT

Given high unmet need across SMA, RESILIENT enrolled diverse racial populations, a wide age range, and all standard of care medications, regardless of SMA type, SMN2 copy number, or ambulatory status

Taldefgrobep Alfa SMA Phase 3 Trial Design Rationale

TALDEFGROBEP

DOSE SELECTION Targets ≥90% suppression of free myostatin

- 35/50 mg Q1W weight-based dosing
- Sub-mL subcutaneous injection volumes
- Patient friendly autoinjector

POPULATION Broad SMA population with unmet need and potential for clinical benefit

- Focus on functional status rather than SMA Type
- Includes range of age, ambulatory status and SOC therapy
- Considers evolving landscape for diagnosis and treatment (newborn screening, timing of SOC treatment, shifting and combining SOC treatments)

PRIMARY ENDPOINT MFM-32 is sensitive measure of motor function, validated in SMA

- Validated across full spectrum of age and disease severity
- Not subject to floor and ceiling effects
- FDA-accepted outcome in SUNFISH registrational trial

MFM-32, 32-Item Motor Function Measure; **Q1W** weekly.

KEY POINT

Optimized to demonstrate clinically meaningful benefit in broad SMA population

Biohaven SMA Phase 3 Trial Design Enrolled Broader SMA Population Than Other Myostatin Inhibitor Trials

TALDEFGROBEP

	Broad Ages	Broad Functional Capabilities	Broad SMA Types	Broad Background Therapy
Biohaven RESILIENT[1]	✓ 4–21yo	✓ Ambulatory and non-ambulatory	✓ No restriction on SMA type	✓ Stable regimen of Nusinersen, Risdiplam, and/or Onasemnogene
Scholar Rock SAPPHIRE[2]	X 2–12yo primary population	X Non-ambulatory	X SMA Type 2 or 3 No Type 1	X Nusinersen or Risdiplam No history of Onasemnogene No SMN upregulator combination therapy
Roche MANATEE[3]	✓ 2–25yo	X Ambulatory (part 2)	X Not specified	X Risdiplam (+/- history of Onasemnogene) No use of current Nusinersen

60% of SMA patients have SMA Type 1[4,5]

1. ClinicalTrials.gov: NCT05337553 2. ClinicalTrials.gov: NCT05156320. 3. ClinicalTrials.gov: NCT05115110. 4. Lally C, et al. *Orphanet J Rare Dis.* 2017 Nov 28;12(1):175.5. Verhaart I, et al, *Orphanet J Rare Dis.* 2017 Jul 4;12(1):124.

Taldefgrobep Alfa SMA Phase 3 Baseline Characteristics

	Placebo (n=73)	Taldefgrobep Alfa (n=143)
Female Sex, n (%) / Male, n (%)	35 (47.9%) / 38 (52.1%)	65 (45.5%) / 78 (54.5%)
Race		
Caucasian	65 (89%)	124 (86.7%)
Non-Caucasian	8 (11%)	19 (13.3%)
Age at Screening – years, mean (SD)	9.2 (4.4)	9.0 (4.3)
4–12, n (%) / 13–21, n (%)	57 (78.1%) / 16 (21.9%)	116 (81.1%) / 27 (18.9%)
Ambulatory Status: Non-ambulatory/Ambulatory	51 (69.9%) / 22 (30.1%)	100 (69.9%) / 43 (30.1%)
Age x Ambulatory Status		
Younger Ambulatory	16 (21.9%)	32 (22.4%)
Younger Non-ambulatory	41 (56.2%)	84 (58.7%)
Older Ambulatory	6 (8.2%)	11 (7.7%)
Older Non-ambulatory	10 (13.7)	16 (11.2%)

KEY POINTS

- Many studies in SMA lack racial and ethnic diversity
- Response rates in other studies by race and ethnicity have not been well characterized

Taldefgrobep Alfa SMA Phase 3 Baseline Characteristics (Cont.)

	Placebo (n=73)	Taldefgrobep Alfa (n=143)
SOC Therapy, n (%)		
Risdiplam	17 (23.3%)	35 (24.5%)
Nusinersen	43 (58.9%)	79 (55.2%)
Onasemnogene or any combination	13 (17.8%)	29 (20.3%)
SMN Therapy Initiation Age, <6 years (%)	53 (72.6%)	99 (69.2%)
SMN2 Copy Number, 2 / 3 / 4 (%)	13 (17.8%) 50 (68.5%) 10 (13.7%)	37 (25.9%) 91 (63.6%) 15 (10.5%)
Baseline MFM-32 Score, mean (SD)	58.3 (15.8)	54.9 (17.4)

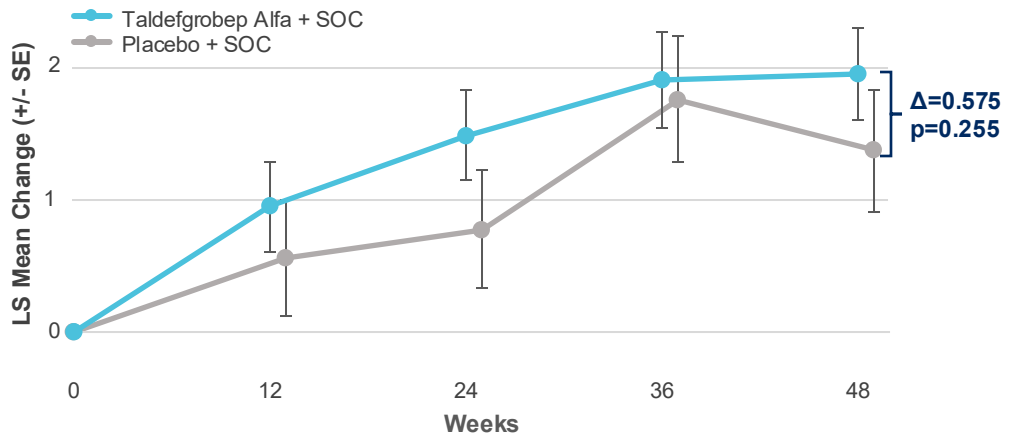
SOC, standard of care; **SMN**, survival motor neuron; **MFM-32**, 32-Item Motor Function Measure; **SD**, standard deviation; **NfL**, neurofilament light chain.

KEY POINTS

- Enrolled target population (not too weak or strong based on MFM-32)
- Imbalances in race/ethnicity, SMN2 copy number, and baseline NfL levels

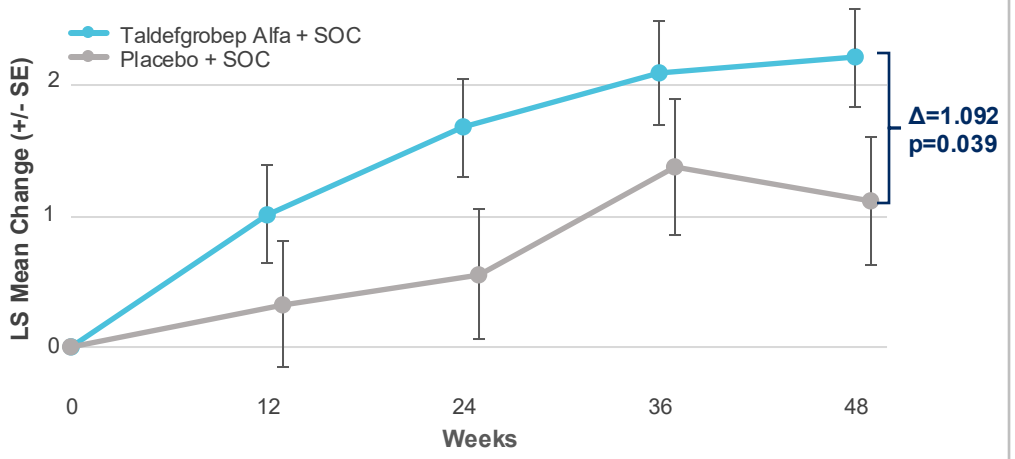
Taldefgrobep Alfa Showed Treatment Effect at all Timepoints on Motor Function Measured by MFM-32 Primary Outcome Measure

Overall Population
MFM-32 Total Score Change From Baseline



Taldefgrobep	142	135	136	137	135
Placebo	73	72	70	71	71

Caucasian Population
MFM-32 Total Score Change From Baseline



Taldefgrobep	123	116	117	119	117
Placebo	65	64	62	63	63

LS, least squares; **MFM-32**, 32-Item Motor Function Measure; **SE**, standard error; **SOC**, standard of care.

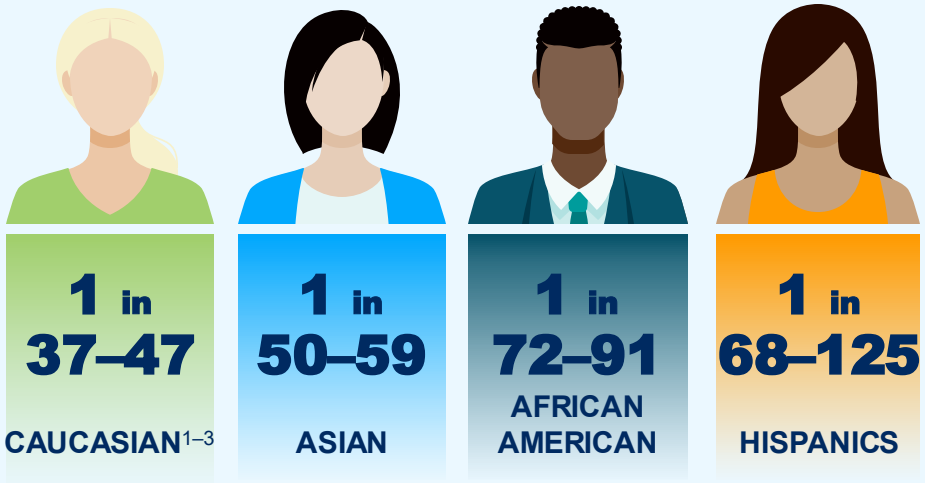
KEY POINT

Largest prespecified study population (87% Caucasian, n=180) showed 2.2-point (taldefgrobep) vs 1.1-point (placebo) p=0.039 improvement on MFM-32 at Week 48

Genetics May Underpin Lack of Treatment Response in Non-Caucasians

TALDEFGROBEP

Genetic differences have been described among diverse populations



Carrier rate differences: More frequent in Caucasians

SMN1 and SMN2 copy number differences:

- African ancestry confers high frequency of multi-copy SMN1 alleles; fewer SMN2 copies[4,5]
- Genetic variability may adversely affect disease severity and response to treatment

Myostatin and other gene differences:

- Polymorphisms in non-Caucasian participants may confer myostatin-inhibitory independence for myostatin therapies[6]
  - A2379 (myostatin) and A-5003 (follistatin) mutations influence muscle growth, function
  - 77% of African ancestry carry one or both mutations in ligands of ActRIIB receptor, which are uncommon in other subgroups (5%)

→ **Placebo participants with myostatin/follistatin mutations might demonstrate sustained improvements**

- Taldefgrobep alfa might have limited ability to improve function further in these patients

SMN, survival motor neuron; **ActRIIB**, activin receptor type IIB.

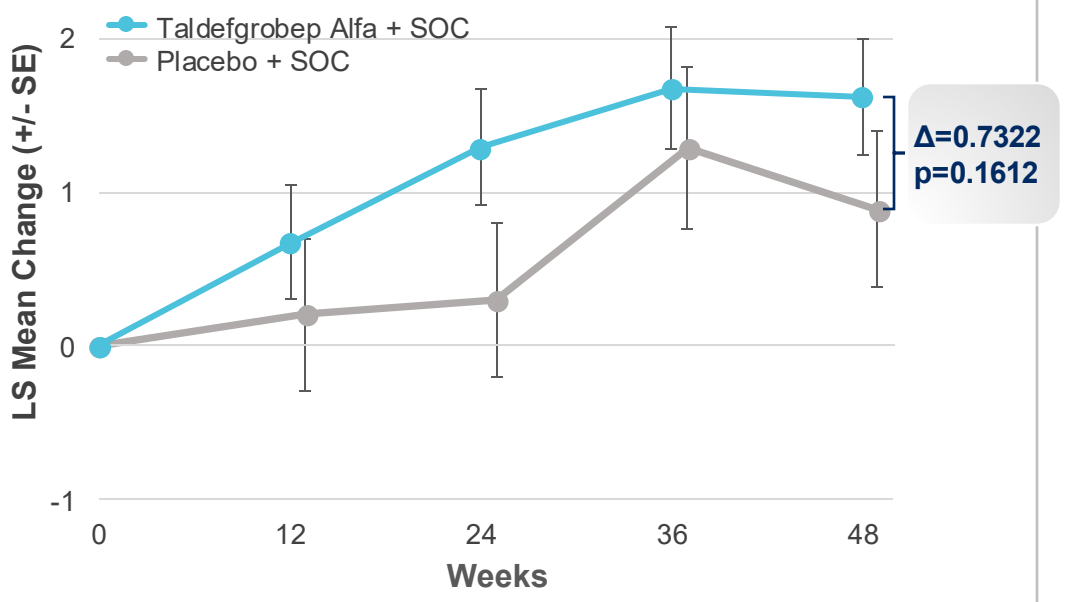
1. Verhaart IEC, et al. *Orphanet J Rare Dis* 2017;12(1):124. 2. Hendrickson BC, et al. *J Med Genet* 2009. 3. Sugarman EA, et al. *Eur J Hum Genet* 2012;20(1):27-32. 4. Sangare M, et al. *Ann Neurol* 2014;75(4):525-32. 5. Vorster E, et al. *Front Genet* 2020; 6. Kostek et al, *Med Sci Sports Exerc.* 2009 May;41(5):1063–1071.

KEY POINT

Myostatin and other gene mutations in non-Caucasian participants may explain lack of treatment response

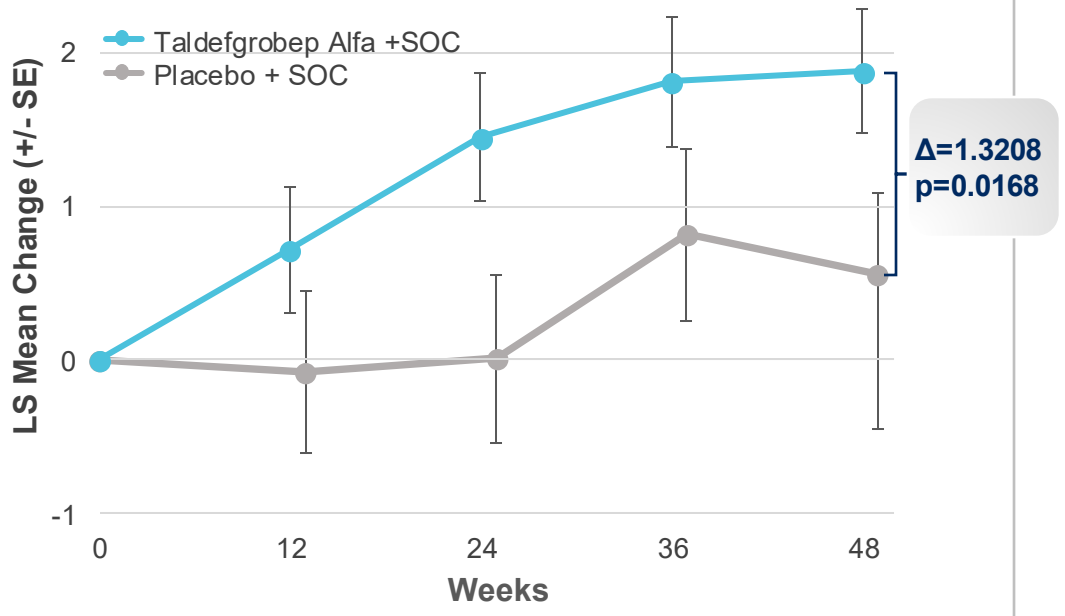
Taldefgrobep Alfa Treatment Effect Enhanced in Sensitivity Analyses Accounting for Imbalance in SMN2 Copy Number and Myostatin Level

Overall Population
MFM-32 Total Score Change From Baseline



Taldefgrobep	142	135	136	137	135
Placebo	73	72	70	71	71

Caucasian Population
MFM-32 Total Score Change From Baseline



Taldefgrobep	123	116	117	119	117
Placebo	65	64	62	63	63

LS, least squares; **MFM-32**, 32-Item Motor Function Measure; **SE**, standard error; **SOC** standard of care.

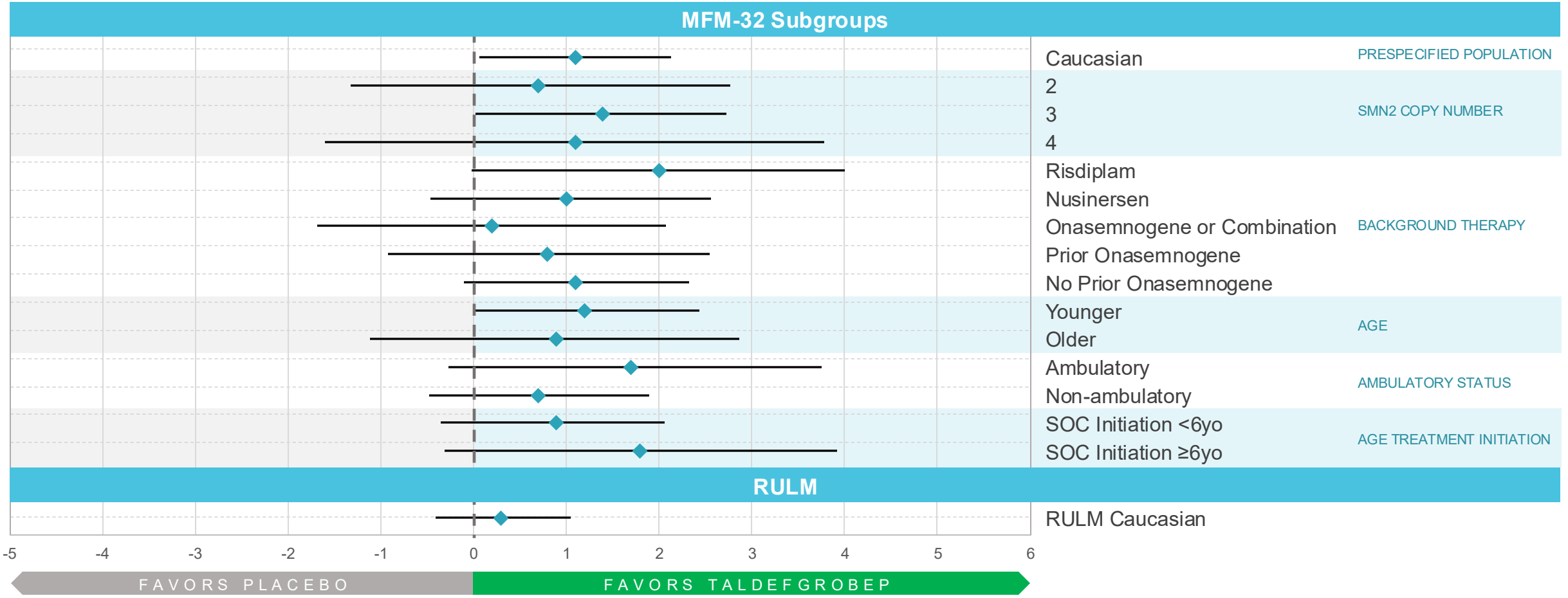
SMN2 copy number and baseline myostatin added as covariates in analysis model

KEY POINT

In the Caucasian population, the taldefgrobep alfa treatment effect was further enhanced

Treatment Difference Favors Taldefgrobep Alfa in Caucasian Population: MFM-32 Subgroups and RULM at Week 48

TALDEFGROBEP



MFM-32 maximum attainable score: 100; RULM maximum attainable score: 37; All subgroups were prespecified in the overall population; **MFM-32**, 32-Item Motor Function Measure; **RULM**, revised upper limb module; **SMN**, survival motor neuron; **SOC**, standard of care.

KEY POINT

Results favored taldefgrobep alfa on the primary outcome in participant groups not enrolled in other studies

Taldefgrobep Alfa Achieved Robust Target Engagement

Free Myostatin Mean ng/mL, (SD)			
	Baseline	**Week 12**	**Week 48**
Taldefgrobep alfa	0.233 (0.118)	undetectable	undetectable
Placebo	0.259 (0.147)	0.267 (0.133)	0.255 (0.112)

Myostatin measured by commercial ELISA kit with BLQ < 0.125 ng/mL

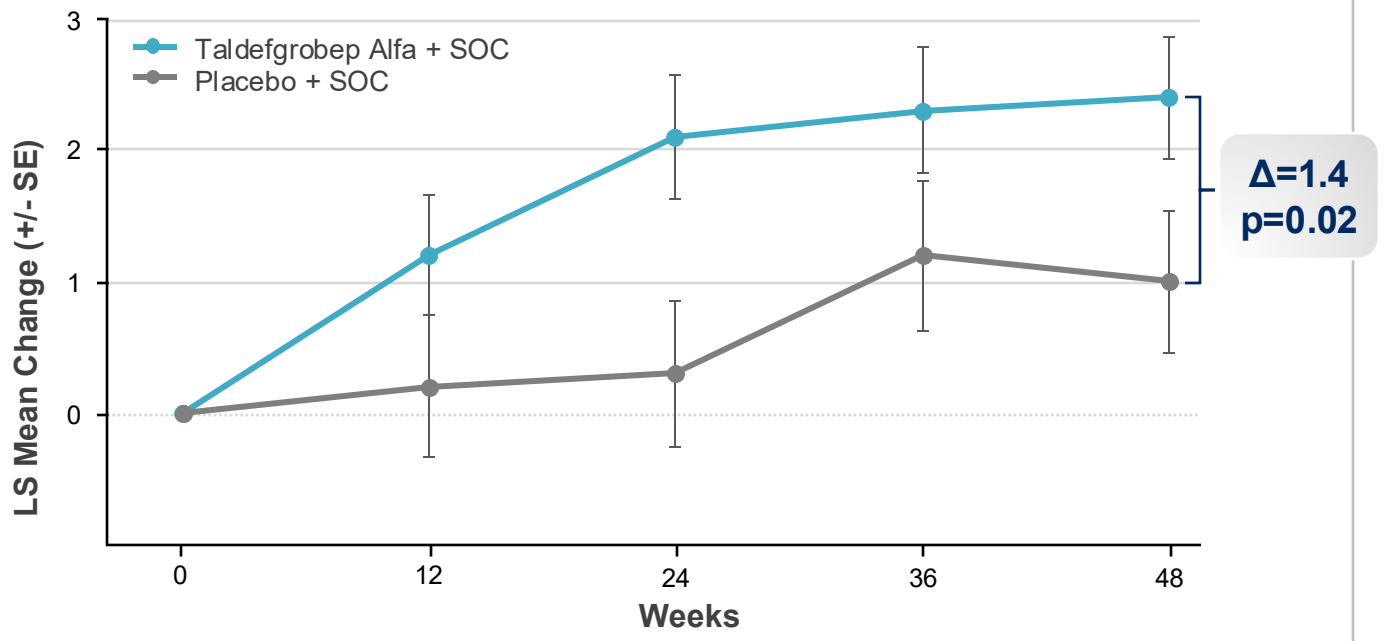
One third of taldefgrobep alfa participants had undetectable myostatin at baseline (pre-treatment)

KEY POINT

Taldefgrobep alfa reduced free myostatin levels below detection in myostatin-positive participants

Taldefgrobep Alfa Clinically Meaningful Treatment Effect Enhanced in Quantifiable Myostatin Caucasian Population

MFM-32 Total Score Change from Baseline



Taldefgrobep	72	68	68	70	68
Placebo	51	51	49	50	50

* response defined as ≥ 3-point change from baseline improvement on MFM-32 at Week 48

LS, least squares; **MFM-32**, 32-Item Motor Function Measure; **SE**, standard error; **SOC**, standard of care.

Responder Analysis*

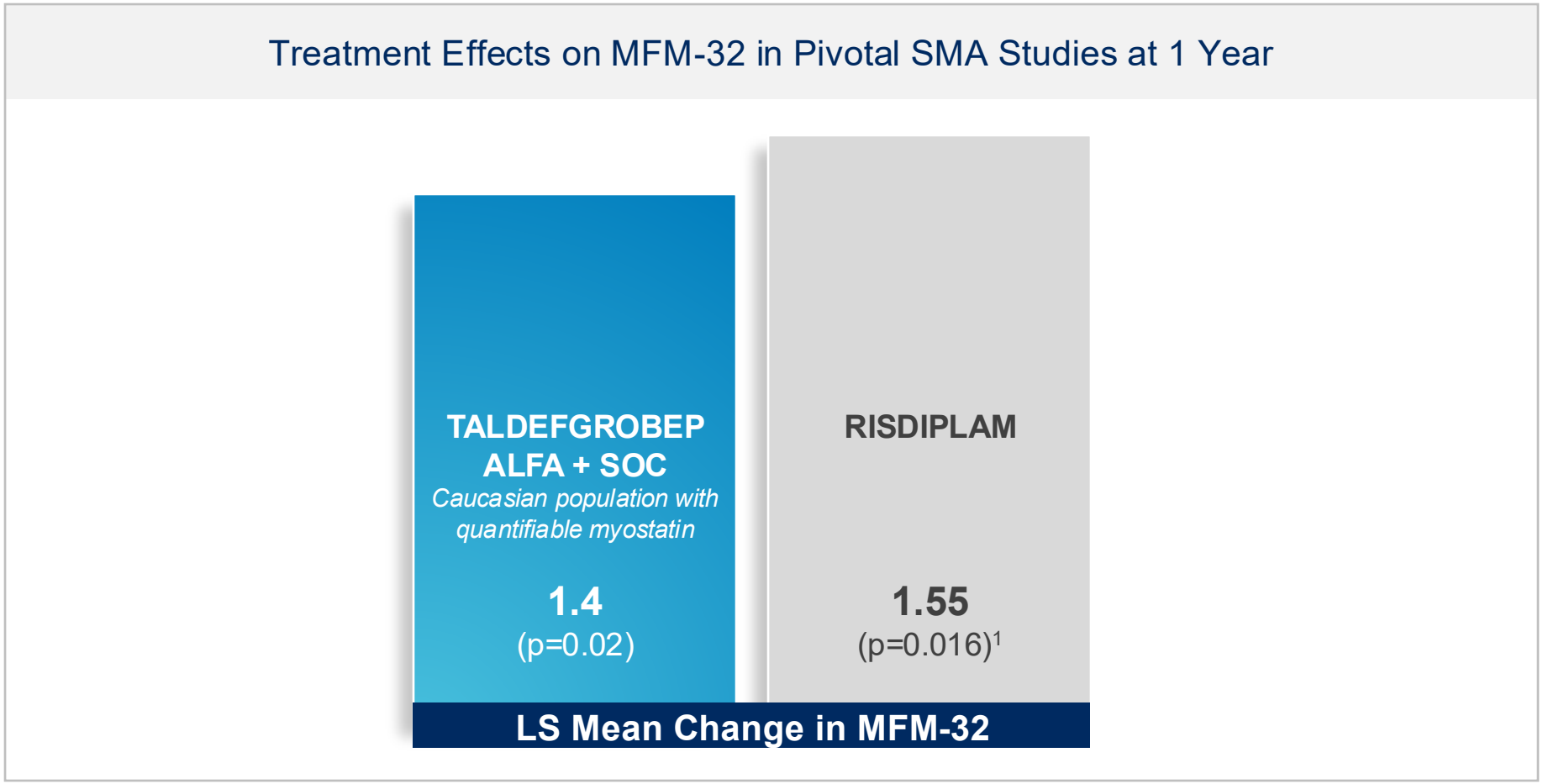
≥ 3-point improvement on MFM-32

50% on taldefgrobep alfa vs
30% on placebo

KEY POINTS

- Magnitude of placebo-adjusted difference is similar to Risdiplam in registrational SUNFISH trial
- Taldefgrobep alfa effect is additive to SOC effect

Magnitude of Taldefgrobep Alfa Placebo-Adjusted Treatment Effect on MFM-32 Is Similar to That of Risdiplam in Registrational SUNFISH Trial



MFM-32, 32 item Motor Function Measure; **LS**, least squares; **SOC**, standard of care.

1. Mercuri E, et al. *Lancet Neurol.* 2022 Jan 21(1) 42-52 2

Taldefgrobep Alfa Treatment Effect on MFM-32 Is Additive to SOC

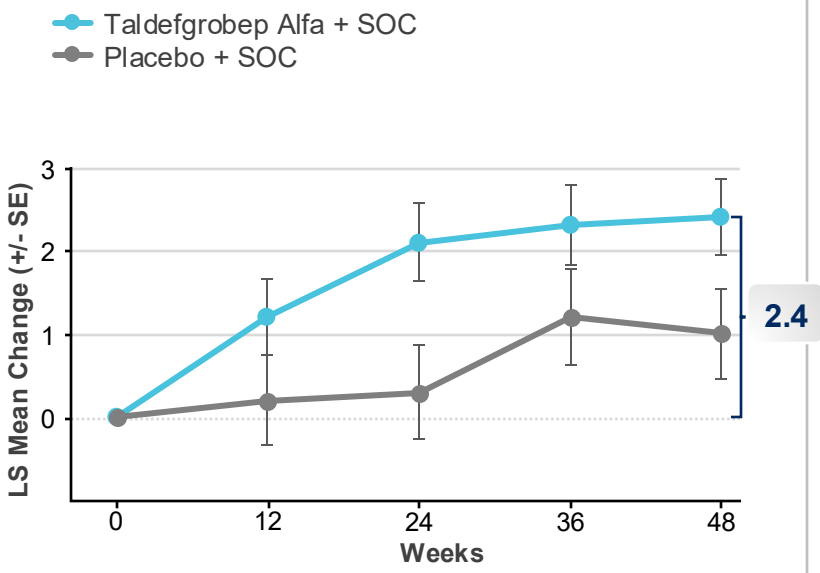
Change From Baseline on MFM-32

TALDEFGROBEP ALFA + SOC
Caucasian population with quantifiable myostatin
2.4

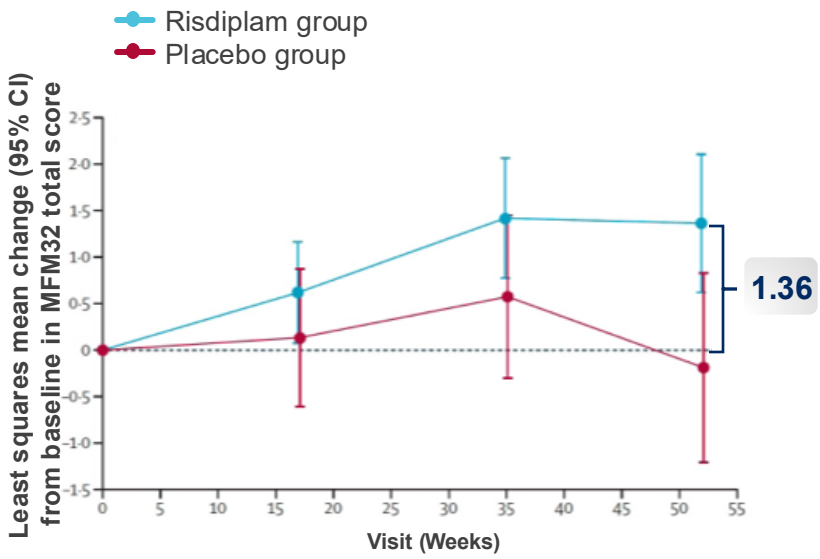
RISDIPLAM
1.36[1]

MFM-32

Taldefgrobep Alfa



Risdiplam[1]

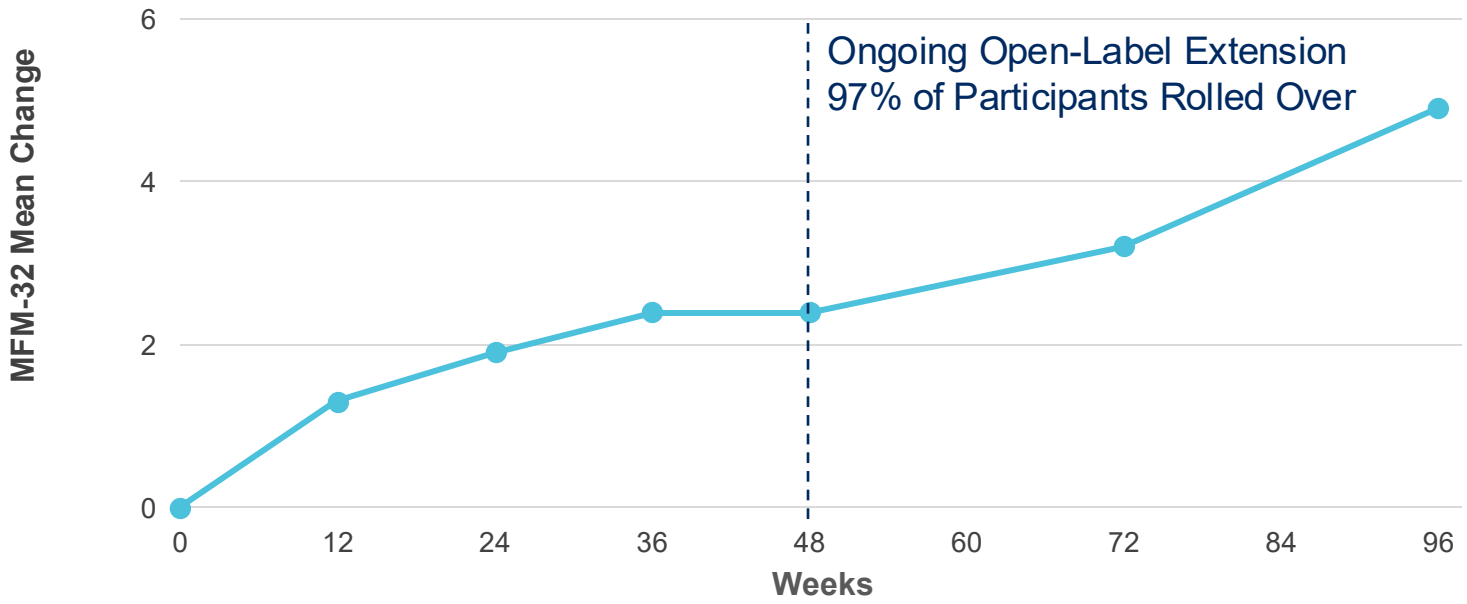


LS, least squares; **MFM-32**, 32-Item Motor Function Measure; **SE**, standard error; **SOC**, standard of care.

1. Mercuri E, et al. *Lancet Neurol*. 2022 Jan 21(1) 42-52 2

Taldefgrobep Alfa Clinically Meaningful Treatment Effect Continues to Increase After 1 Year of Treatment in Overall Population

MFM-32 Total Score Change from Baseline
48-Week Double-Blind Phase and Open-Label Extension



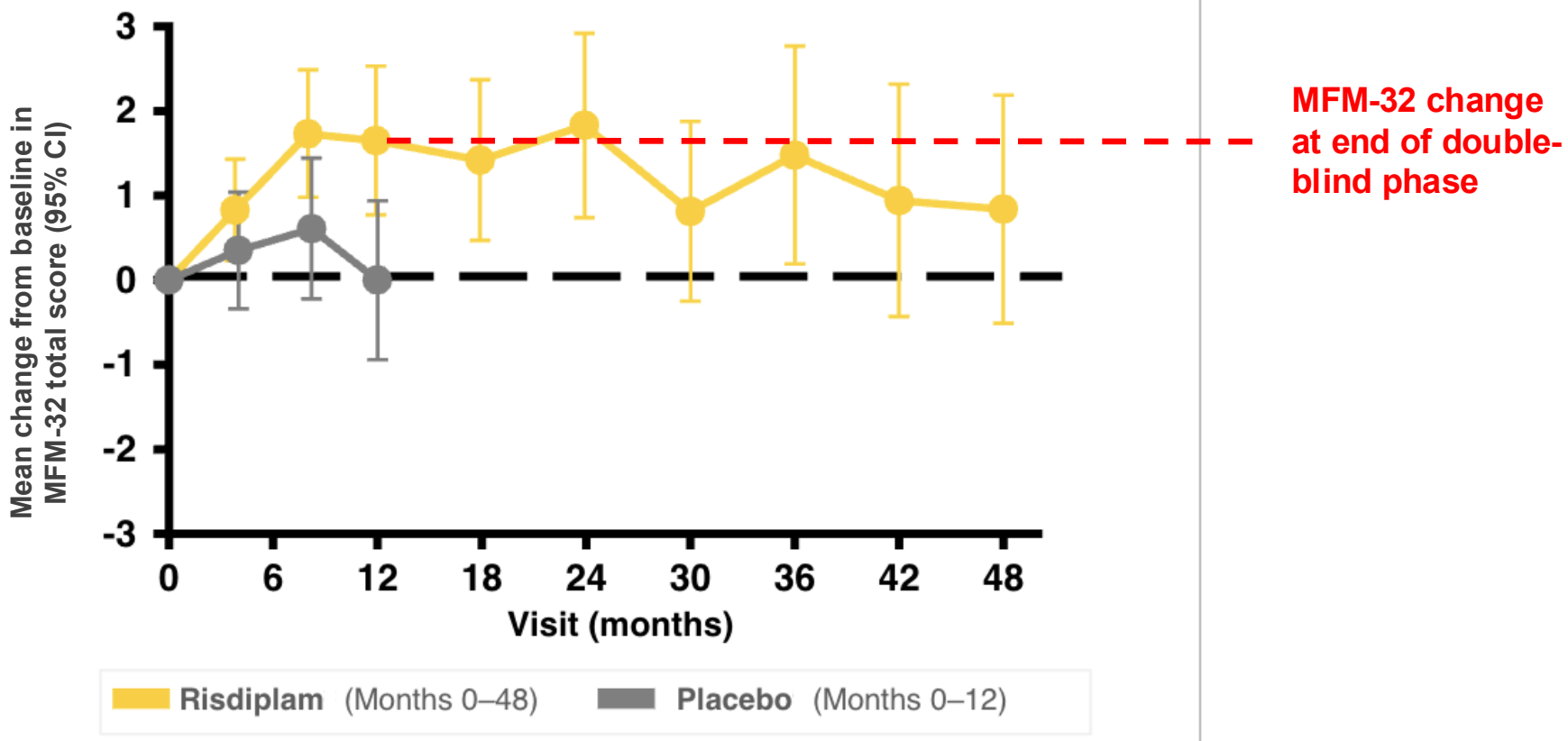
KEY POINT

Supports treatment benefit in taldefgrobep alfa-treated participants vs expected MFM-32 trajectory

MFM-32 Trajectory Expected to Decline on Stable SOC Treatment

TALDEFGROBEP

MFM-32 Total Score Change from Baseline
Risdiplam SUNFISH Registrational Trial with OLE[1]



MFM-32, 32-Item Motor Function Measure; **CI**, confidence interval; **SOC**, standard of care; **OLE**, open-label extension.

1. L Servais, et al. Presented at: AAN; April 22-27, 2023; Boston, MA.

Taldefgrobep Alfa Safe and Well-Tolerated in Phase 3 SMA Study: TEAEs Reported in ≥ 10% of Participants Overall During DB Phase

	Placebo (n=73)	Taldefgrobep Alfa (n=143)	Overall (n=216)
	Participants with Event: n (%)	Participants with Event: n (%)	Participants with Event: n (%)
Upper respiratory tract infection	21 (28.8)	37 (25.9)	58 (26.9)
Pyrexia	21 (28.8)	27 (18.9)	48 (22.2)
Nasopharyngitis	19 (26.0)	23 (16.1)	42 (19.4)
Cough	9 (12.3)	23 (16.1)	32 (14.8)
Vomiting	9 (12.3)	22 (15.4)	31 (14.4)
Injection site erythema	4 (5.5)	26 (18.2)	30 (13.9)
Headache	9 (12.3)	20 (14.0)	29 (13.4)

DB, double-blind; **SAE**, serious adverse event; **TEAE**, treatment emergent adverse event.

KEY POINTS

- All SAEs judged not related to study drug
- Low rate of TEAEs leading to discontinuation: 4 participants on taldefgrobep (2.8%); 1 on placebo (1.4%)

Taldefgrobep Alfa: Consistent Meaningful Improvements, Well-Tolerated

Clinically Meaningful Improvements in Motor Function on MFM-32 Primary Outcome with Magnitude Similar to Risdiplam

- Treatment effect at all timepoints in overall population
- Significant treatment effect in largest prespecified population (Caucasian participants)
- Significant treatment effect in myostatin-positive Caucasian participants
- Treatment effect continues to increase beyond 1-year in open-label extension in overall population

Robust Target Engagement

Favorable Changes in Body Composition

Benefits on Respiratory Muscle Function

Established Safety and Tolerability Profile

- >700 pediatric and adult participants in multiple clinical trials (n=6)
- Taldefgrobep alfa was well-tolerated in SMA; favorable safety profile consistent with other clinical studies

Path Forward/Regulatory Strategy

- Focus on totality of data across multiple analyses in well-defined population
- Engagement with global health authorities

MFM-32, 32-Item Motor Function Measure.

KEY POINTS

- FDA interaction planned to discuss SMA registrational path in 1H 2025
- New Phase 3 study in 2 month to <4 years old with SMA to start 2H 2025

Panel

MODERATOR

Brian Skorney

Equity Analyst

BAIRD

PANELISTS

Peter Ackerman, MD

Senior Vice President, Clinical Development
Biohaven

Ania Jastreboff, MD, PhD

Associate Professor of Medicine (Endocrinology); Director, Yale Obesity Research Center (Y-Weight); Co-Director, Yale Center for Weight Management
Yale University School of Medicine

Lindsey Lair, MD, MBA, FAAN

VP, Clinical Development
Biohaven

Leslie Hayes, MD

Attending Physician, Department of Neurology
Boston Children's Hospital

BHVN
LISTED
NYSE

Brian Lestini, MD, PhD
President, Oncology

biohaven®

Nushmia Khokhar, MD
CMO, Oncology

biohaven®

Scott T. Tagawa, MD, MS, FACP, FASCO
Professor of Medicine

Weill Cornell Medicine

Oncology

biohaven®

Brian Lestini, MD, PhD
President, Oncology

biohaven®

Nushmia Khokhar, MD
CMO, Oncology

biohaven®

Next-Gen Antibody Drug Conjugates (ADCs)

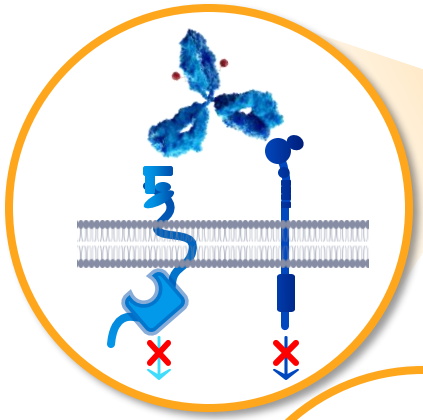
biohaven®

Biohaven's Innovative Technologies Modernizing Next-Gen ADCs

ONCOLOGY

NOVEL AND BISPECIFIC mAbs

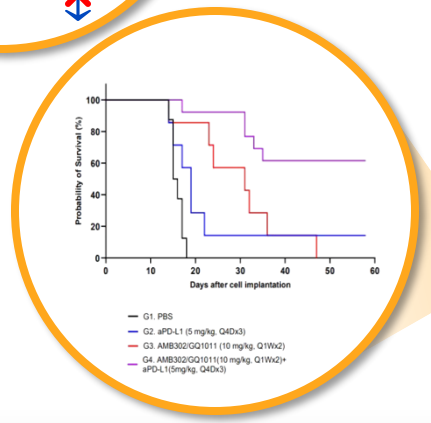
Validated and emerging targets

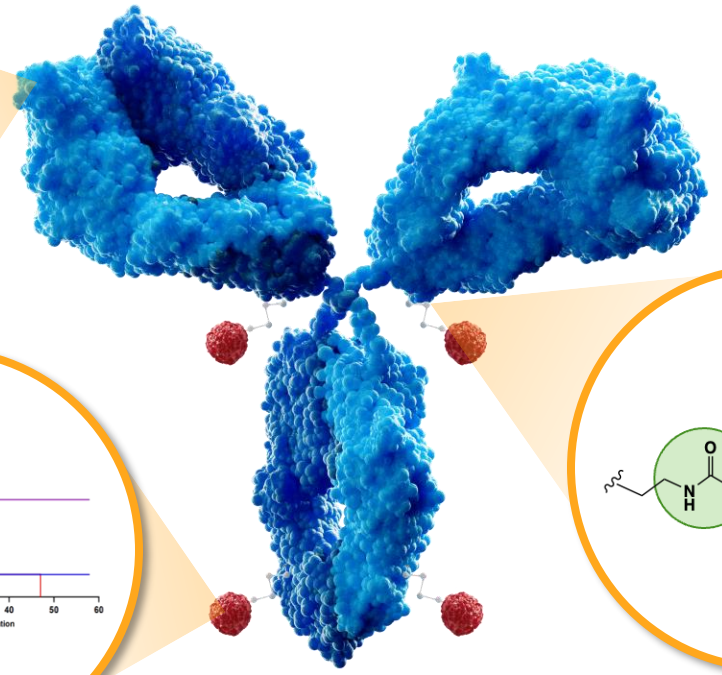


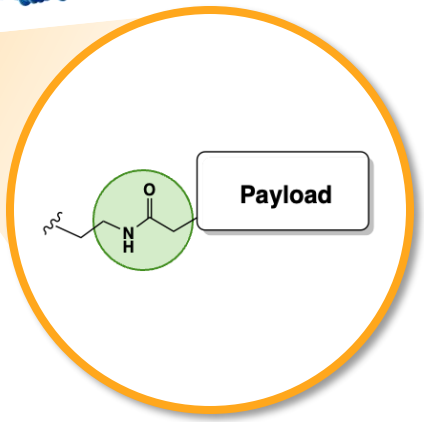
TOPOIX PROPRIETARY PAYLOAD

PD-1/PD-L1 synergy

Broad target exclusivity







MODERN ADC TECHNOLOGY, FLEXIBLE PLATFORM

- ✓ Site-specific
- ✓ Irreversible
- ✓ Single-Step
- ✓ Native mAbs
- ✓ Multiple payload class

STRATEGIC COLLABORATIONS

Merus | REGENERON | Yale | GeneQuantum Healthcare 启德医药

EXPANDING CLINICAL STAGE ASSETS

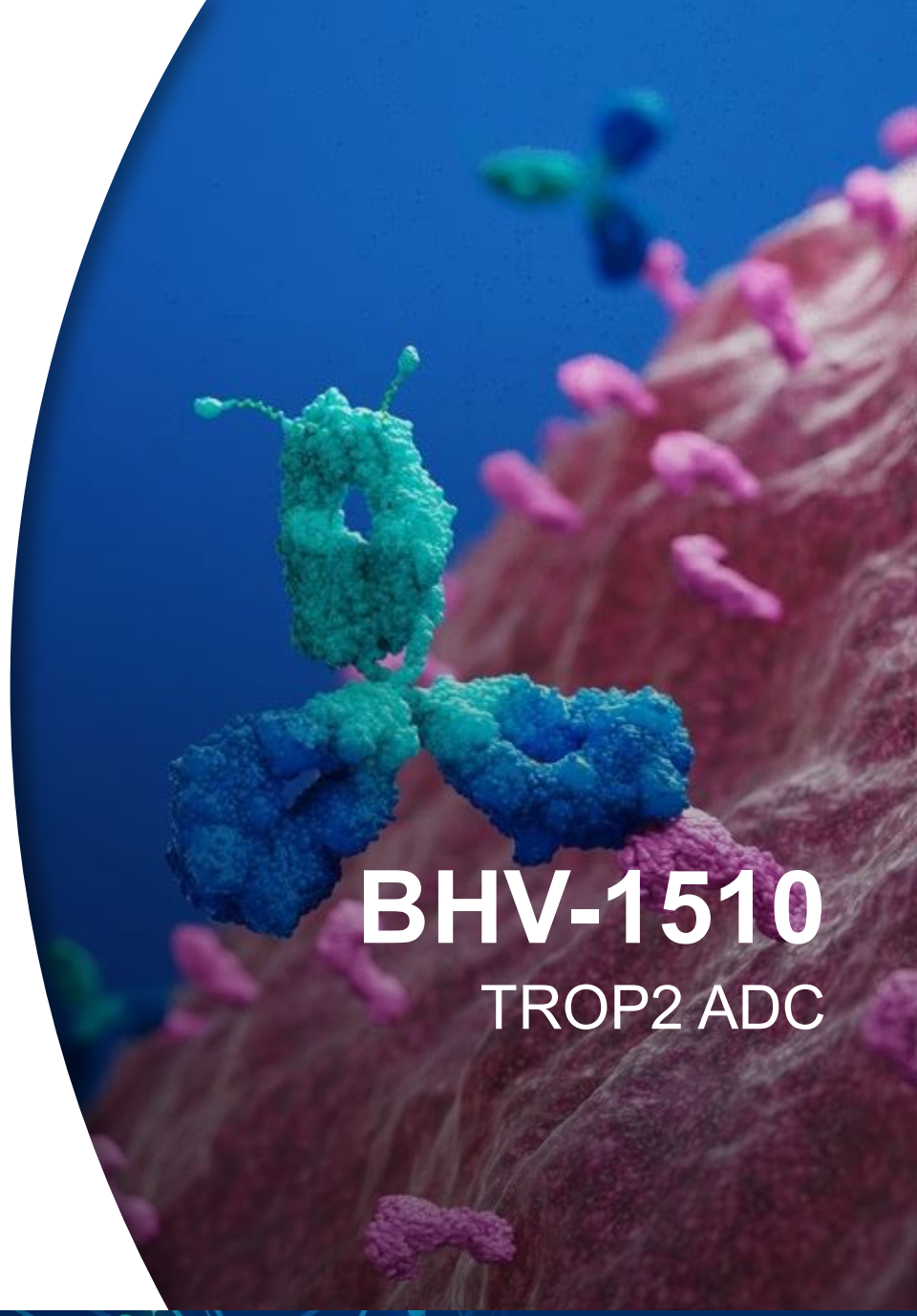
BHV-1510 (Trop2 Topolx) Phase 1 mono and anti-PD-1 combo	**BHV-1530** (FGFR3 Topolx) Phase 1	**BHV-1500** (CD30 MMAE) IND planned 2H 2026	**Merus** (undisclosed)

BHV-1510 Is a Highly Differentiated Trop2 ADC

- Site-specific, highly stable conjugation-linker
- TopoIx payload ideally positions for fast-to-market strategy with anti-PD-1 combo
- Remains competitive as fast-follower

Emerging Clinical Data Shows Predicted Profile and Potential of Proprietary TopoIx Payload

- Clinical activity demonstrated as monotherapy and in combination with anti-PD-1 cemiplimab
- No interstitial lung disease (ILD) with TopoIx observed in early cohorts
- Target exclusivity of TopoIx payload for up to 18 ADCs

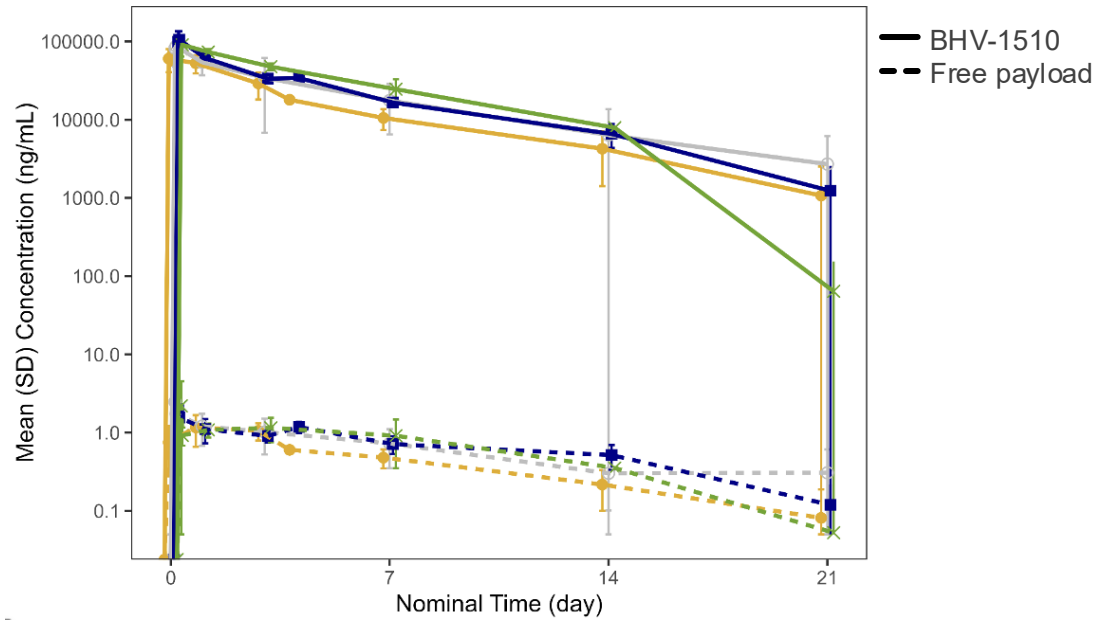


BHV-1510: Favorable PK and Safety Profile With Very Low Free Payload

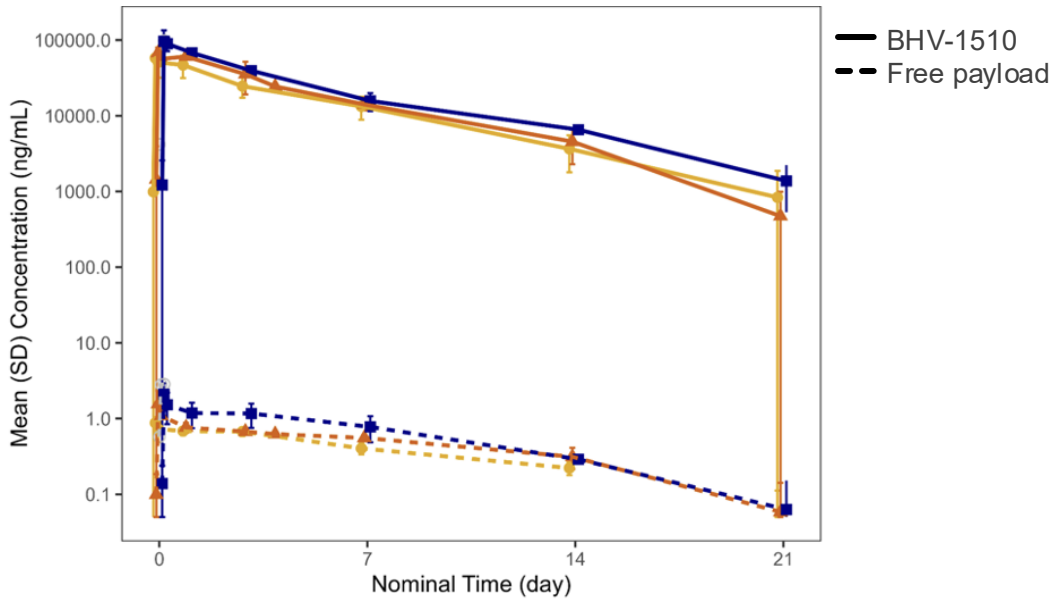
ONCOLOGY

- Mean serum exposure of BHV-1510 increased with increasing doses
- Very low levels of serum free payload, demonstrating high ADC stability

ADC and Payload, Semi-Log Scale: Cycle 1



ADC and Payload, Semi-Log Scale: Cycle 3



KEY POINT

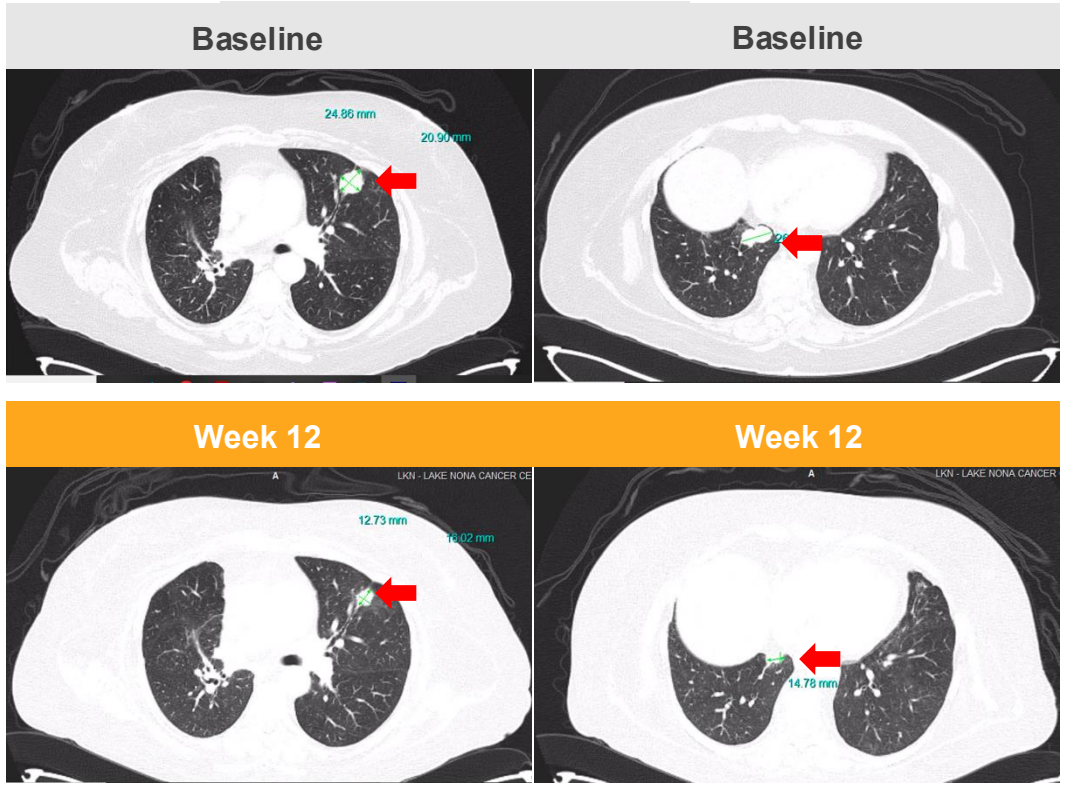
High ADC stability with payload to ADC ratio <1%

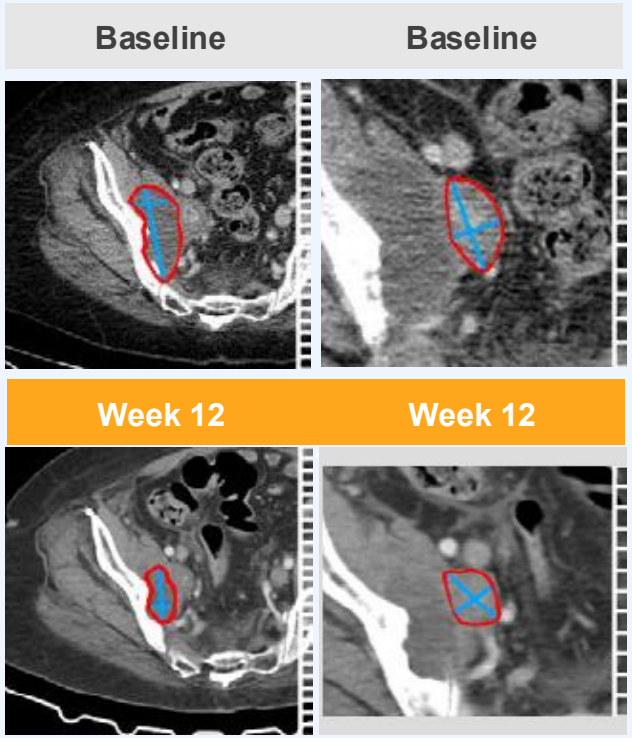
Monotherapy Shows PRs in Patients Failing Standard Therapies

ONCOLOGY

Case: 72 y/o with EGFRwt NSCLC

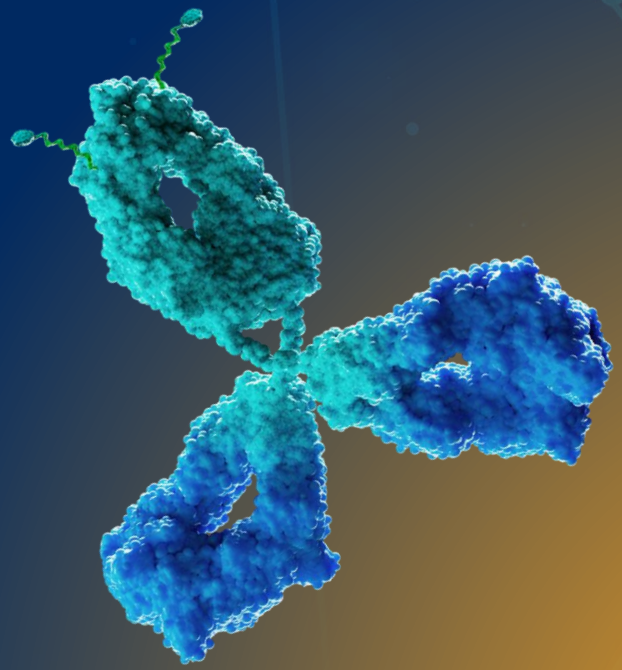
Prior therapies include carboplatin and paclitaxel, pembrolizumab then pemetrexed and carboplatin





Case: 60 y/o female with endometrial cancer

Prior therapies included dostarlimab, carboplatin and paclitaxel



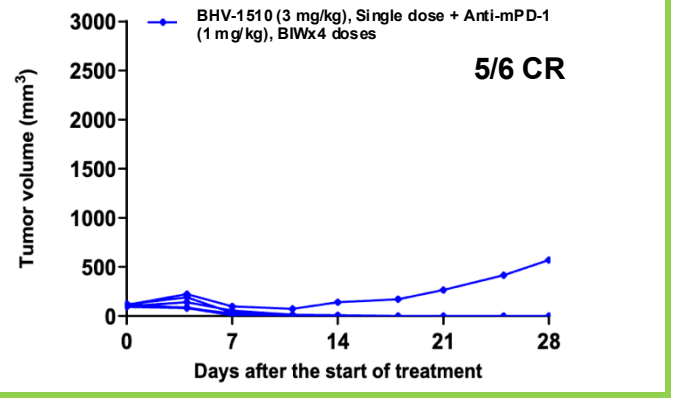
BHV-1510 Combination With Anti-PD-1

biohaven®

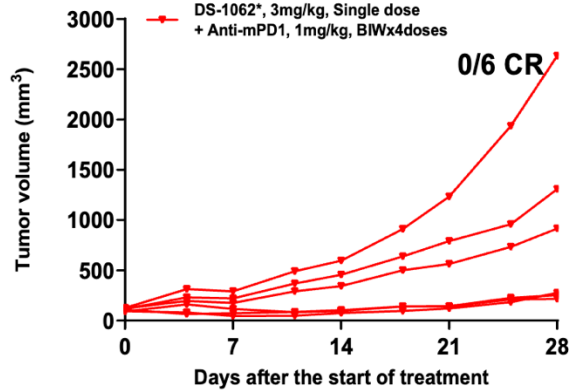
BHV-1510+Anti-PD-1: Syngeneic Models Suggest Superior to DS-1062

ONCOLOGY

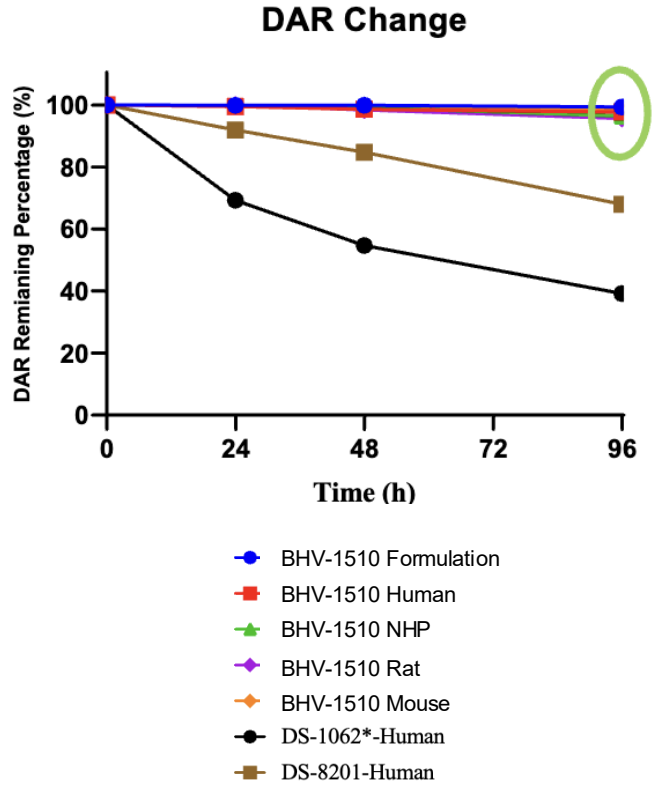
BHV-1510 + Anti-PD-1



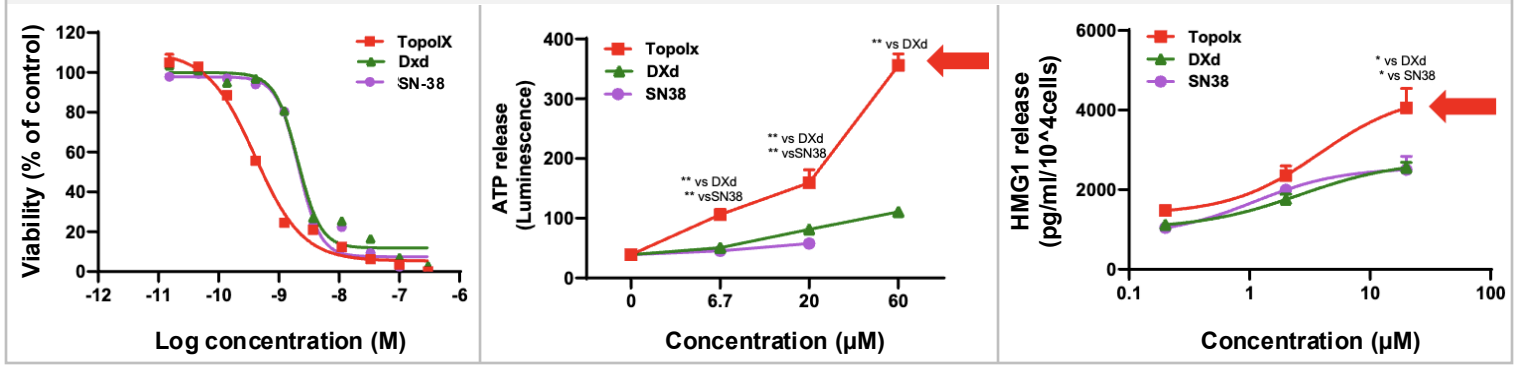
DS-1062 + Anti-PD-1



Highly Stable Linker vs DS-1062



Superior Immunogenic Cell Death with TopoIx Compared to Other Payloads (DXd and SN-38)



DS-1062, datopotamab deruxtecan; AACR 2023 Annual Meeting, abstract 1549.

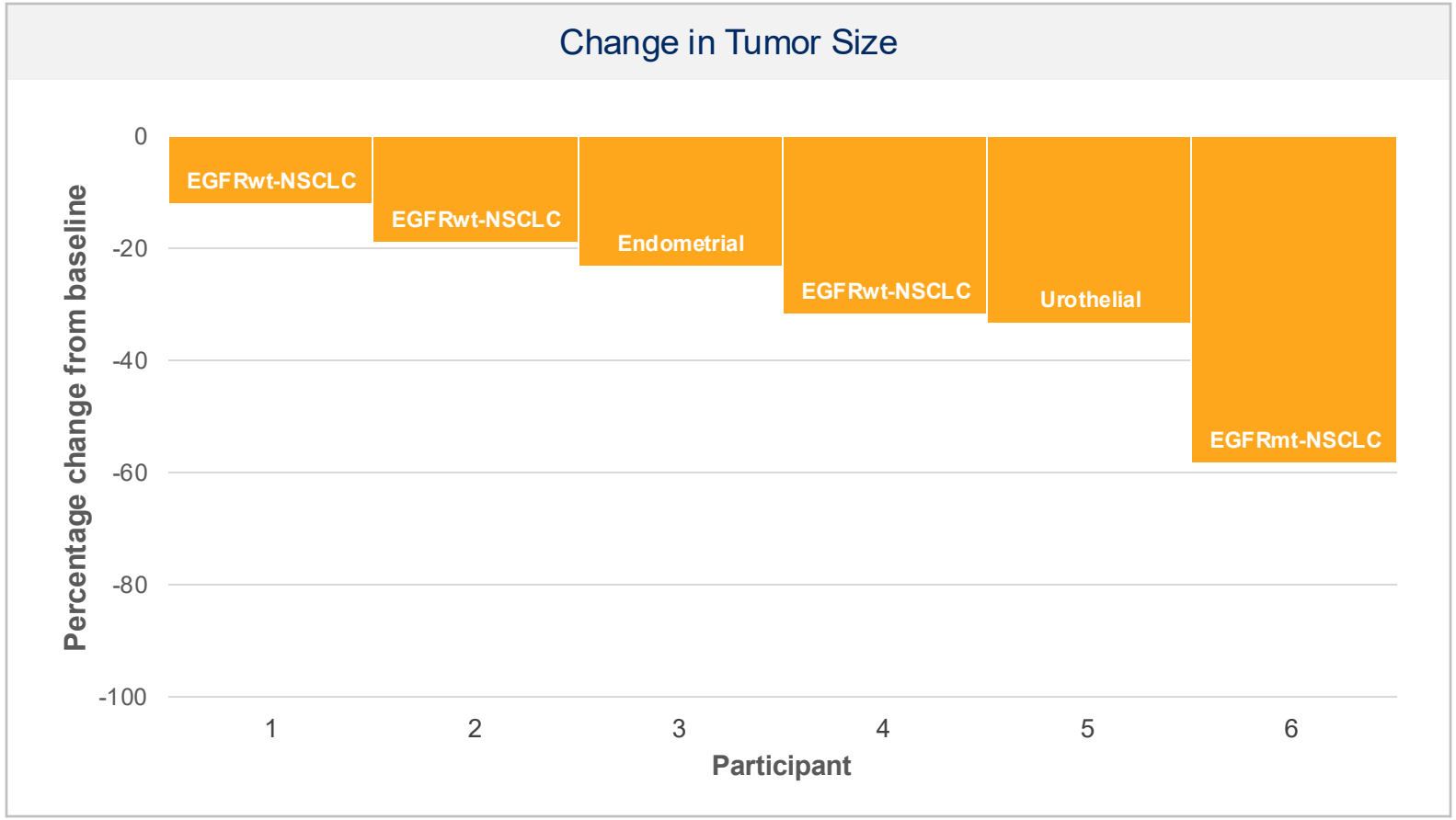
KEY POINTS

- Preclinical profile of BHV-1510 positions it for superiority in ADC therapy with anti-PD-1
- Landscape open for Trop2 combinations with safer more efficacious ADC

BHV-1510 + Cemiplimab: Preliminary Activity Observed With Tumor Reduction Seen in First 6 Patients Treated

ONCOLOGY

- Encouraging preliminary efficacy with tumor reductions seen on first scan for all patients
- Partial responses starting at lowest dose tested
- Clinical activity demonstrated in patients failing standard of care therapies. Majority with prior anti PD1/PL1 agents
- Responses seen in patients with brain metastasis
- Combination well tolerated; no DLTs or ILD in initial cohorts



EGFR: Epidermal Growth Factor Receptor, **WT**: Wild type, **MT**: Mutant, **NSCLC**: Non-Small Cell Lung Cancer

KEY POINTS

- Early data suggests synergy with an anti-PD1, with a favorable safety profile
- Potential to move to early lines of therapy in tumors like urothelial, NSCLC and endometrial carcinoma

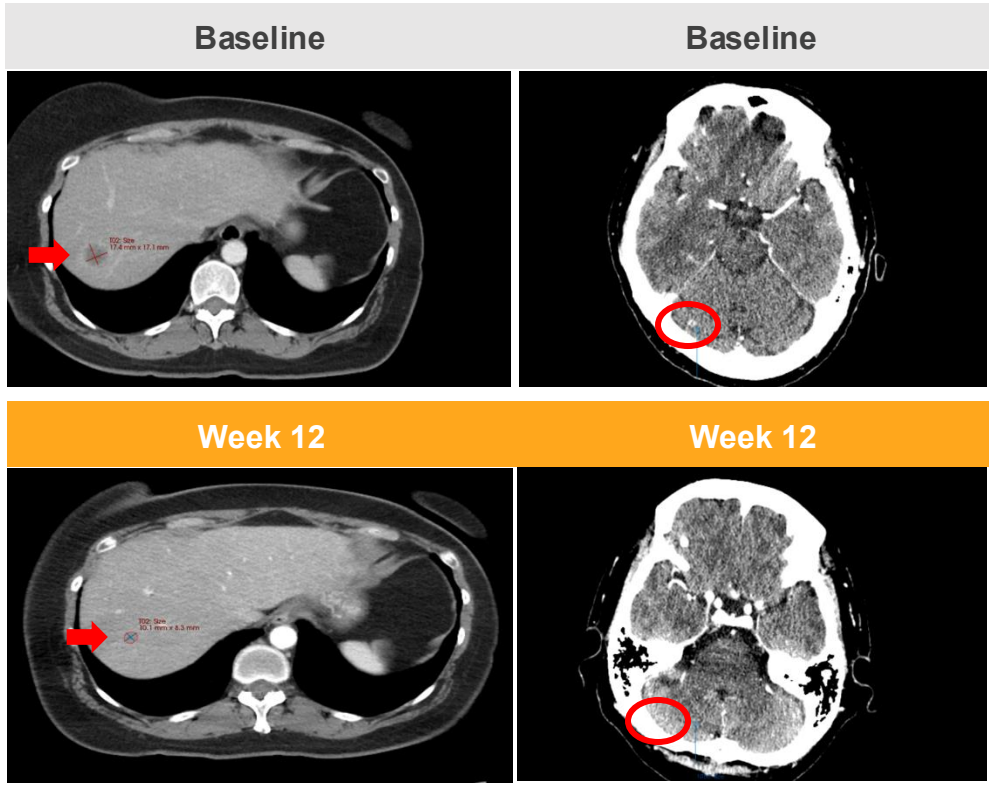
Partial Response in Patients Failing SOC Therapy Including Targeted Therapy and Immunotherapy

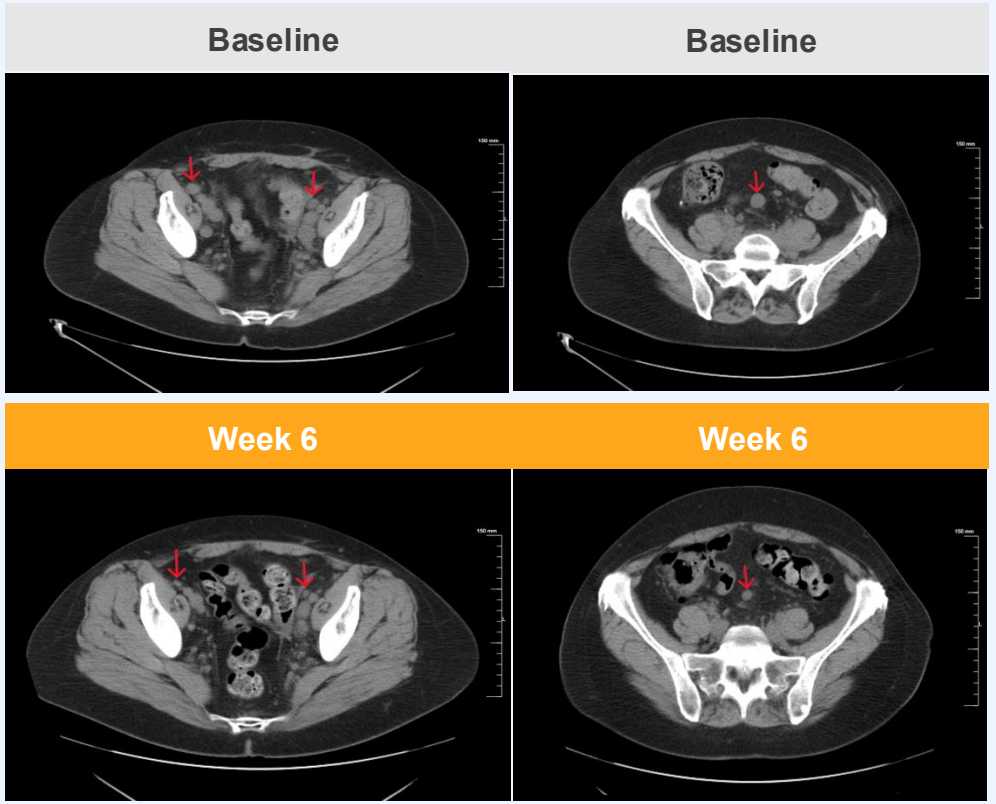
ONCOLOGY

Case: 57 y/o female with EGFRmt NSCLC and Brain Metastasis

Confirmed PR (58% reduction) at 12 weeks after 1510+cemiplimab combo

- Prior therapies included cisplatin and pemetrexed chemotherapy
- Failed two EGFR targeting therapies including EGFR-MET bispecific amivantamab-vmjw and investigational EGFR-HER2 inhibitor





Red arrows: tumor metastasis

Case: 53 y/o with urothelial cancer

PR (33% reduction) at 6 weeks after 1510+cemiplimab combo

- Prior therapies included cisplatin and gemcitabine chemotherapy
- Enfortumab Vedotin and pembrolizumab for metastatic disease.

BHV-1510: Tumor Reduction Seen in Difficult to Treat Tumors, in Patients Progressing on Standard and Approved Therapies

ONCOLOGY

- Clinical activity seen across doses starting at the lowest dose
- As monotherapy partial response seen in tumor types (SCLC, Endometrial, NSCLC) in patients that are heavily pretreated and have progressed on standard of care therapies
- Patients on treatment with durable clinical benefit, several at 6 months and beyond
- Tumor reductions seen in first 6/6 evaluable patients treated with cemiplimab combination; PRs in urothelial and NSCLC patients
- Favorable preliminary safety profile
  - No payload-associated ILD, low GI toxicity like diarrhea, and low hematological toxicity
  - Main toxicity observed is on-target Trop2 ADC class mucositis; an expected and manageable effect
  - Combination with cemiplimab well tolerated with no DLTs to date in initial cohorts

Prelim data from ongoing study. Data cut off May 2, 2025

KEY POINTS

Preliminary efficacy and tolerability of BHV-1510, incorporating the novel TopoIx payload and highly stable linker, indicate potential for use in earlier treatment settings across various cancers

Novel FGFR3 mAb With Proprietary TopoIx Payload

- Only FGFR3 directed ADC in clinic
- Site-specific conjugation with favorable nonclinical tox profile

FGFR3 Is a Validated Target With Limited Competition

- No current FGFR3 ADCs approved or in advanced development Core opportunity in FGFR3-altered metastatic urothelial cancer
  - Only 1 Tyrosine Kinase Inhibitor approved
  - TKI toxicity due to Pan FGFR inhibition
- Potential extension into other FGFR3-driven solid tumors

Synergistic Efficacy With Checkpoint Inhibitors *In Vivo*

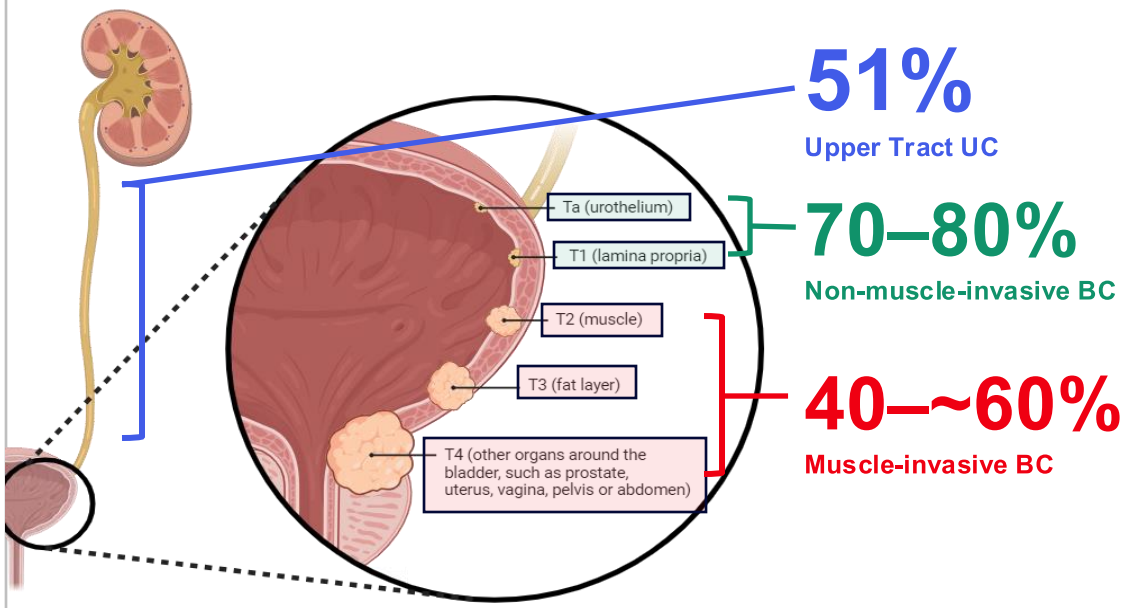
Anti-PD-L1 combination showed synergy similar to BHV-1510

FGFR3 Is a Promising Therapeutic Target in Several Tumors

ONCOLOGY

FGFR3 Overexpression and Alteration in Urothelial Carcinoma

FGFR3 Overexpression and Alteration (%)



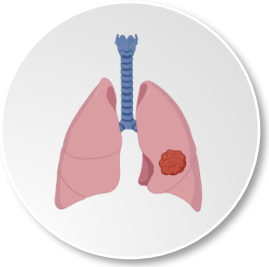
51%
Upper Tract UC

70–80%
Non-muscle-invasive BC

40–~60%
Muscle-invasive BC

~15% of HNSCC have FGFR3 mutations with overexpression noted in nearly half of oral and oropharyngeal cancers

FGFR3 expression in **38% of lung cancers** suggests substantial overexpression within these types



5% of endometrial cancers have FGFR3 alterations, potentially indicating more widespread overexpression

4% of cervical cancer cases exhibit the FGFR3-TACC3 fusion, which is associated with higher FGFR3 expression

~ 8% of glioblastomas show a FGFR3-TACC3 fusion, commonly linked to increased levels of FGFR3 protein

HSCC, Head and Neck Squamous Cell Carcinoma.

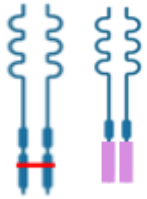
KEY POINT

ADC and CPI combinations are emerging as a powerful strategy in urothelial cancer—offering the potential to drive deeper, more durable responses and shift the standard of care

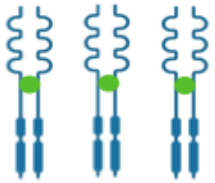
BHV-1530: Potential to Address Unmet Need in Metastatic Urothelial Cancer (mUC) and other FGFR3-Driven Tumors

ONCOLOGY

FGFR3 overexpression, mutation,
or **fusion** leads to excessive pathway activation
and increased **tumorigenicity**



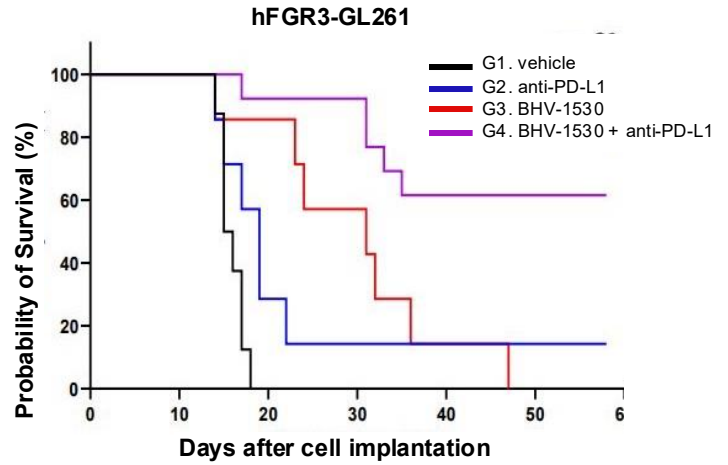
FGFR3 mutation/fusion ~20% mUC



FGFR3 overexpression ~35% mUC

- 62K new mUC cases, 14K deaths/year in US (2023)
- Multiple opportunities for BHV-1530 across therapy lines
  - Synergistic CPI combinations in FGFR3+ biomarker-selected 1L
  - Limited efficacy of current 2L options
- Several tumor types beyond mUC also driven by FGFR3

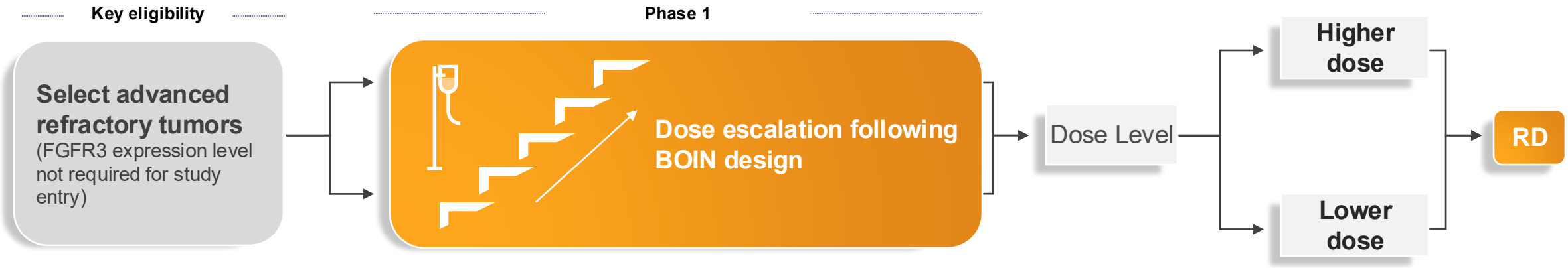
BHV-1530 shows **synergistic activity**
in vivo with anti-PD-L1 combination



Group	% Increased Life Span (ILS)	Median Survival (days)
G1	-	15
G2	27%	19
G3	107%	31
G4	>300%	>63

BHV-1530: Phase 1 Study in Advanced Tumors

ONCOLOGY



DESIGN	Open label, dose escalation (Ph1)
POPULATION	Advanced tumors having failed SOC therapy
SAMPLE SIZE	95 patients
TREATMENT	BHV-1530
TREATMENT DURATION	Until disease progression or toxicity
KEY ENDPOINTS	Safety and tolerability, ORR, PFS, PK and ADA

ORR, Overall Response Rate; **PFS,** Progression Free Survival; **ADA,** Antidrug Antibody; **BOIN**, Bayesian Optimal Interval; **RD**, Recommended Dose.

BREAKING NEWS

First patient dosed in April 2025

Nushmia Khokhar, M.D.
CMO, Oncology

biohaven®

Scott T. Tagawa, MD, MS, FACP, FASCO
Professor of Medicine

Weill Cornell Medicine

Oncology Fireside Chat Q&A

biohaven®

Tova Gardin, MD, MPP
Chief Translational Officer
BIOHAVEN

Terry F. Davies, MD
Florence and Theodore Baumritter Professor of Medicine
ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI

Volkan Granit, MD, MSc
Senior Medical Director, Head of Neuromuscular Disease
BIOHAVEN

Brian McGuire, MD
Medical Director
BIOHAVEN

Kayle Shapero, MD, PhD
BROWN UNIVERSITY HEALTH
CARDIOVASCULAR INSTITUTE
Clinical Assistant Professor of Medicine
ALPERT MEDICAL SCHOOL OF BROWN UNIVERSITY

Professor Jonathan Barratt, PhD, FRCP
The Mayer Professor of Renal Medicine,
Department of Cardiovascular Sciences
UNIVERSITY OF LEICESTER

MoDE™ and TRAP™ Degraders

biohaven®

Tova Gardin, MD, MPP

Chief Translational Officer

biohaven®

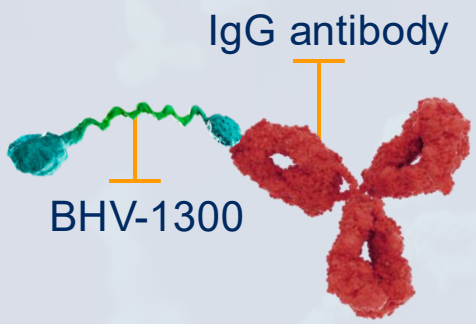
MoDE™ and TRAP™ Degraders: Clinical Updates

biohaven®


biohaven®

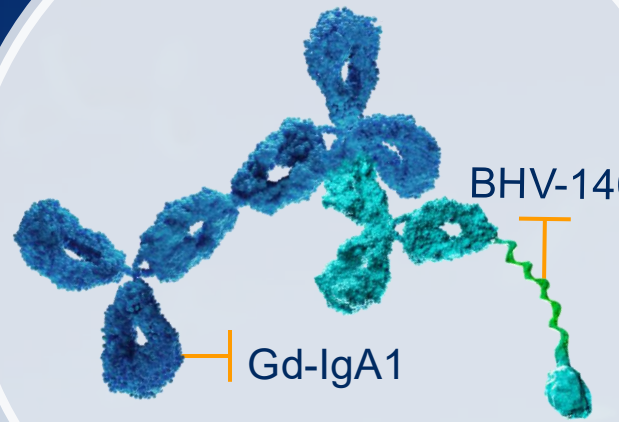
biohaven®
OUR NOVEL DEGRADER PLATFORM

MoDE™



Target a **class of proteins** implicated in pathogenesis of disease

TRAP™



Remove **specific disease-causing proteins and** leave rest of immune system intact

KEY POINT

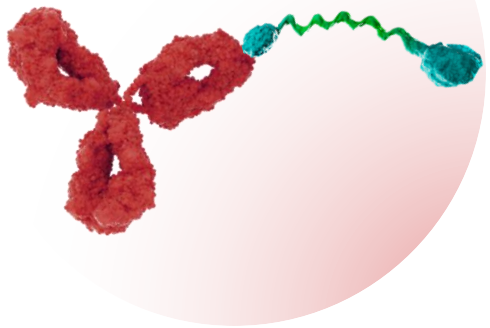
Revolutionary Yale-licensed technology to remove disease-causing proteins from the body

Catalyzing Innovation for Patients and Early Demonstration of Removal of Disease-Causing Protein

DEGRADERS

Follow the Science

PRECISION IMMUNOLOGY
TARGET THE DISEASE, NOT THE PATIENT



Understand the Need

KEEP THE PATIENT AT THE CENTER

Establish Early Target Efficacy

PHASE 1 PD ENDPOINT

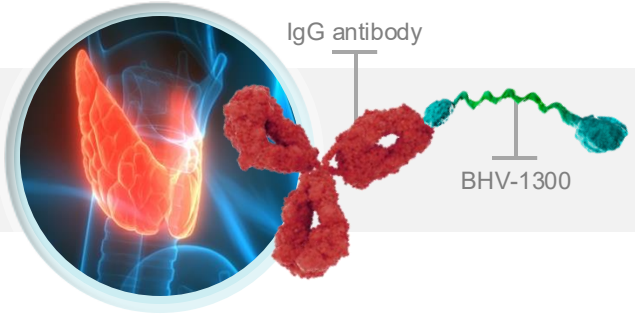
Create Value

NEAR- AND LONG-TERM

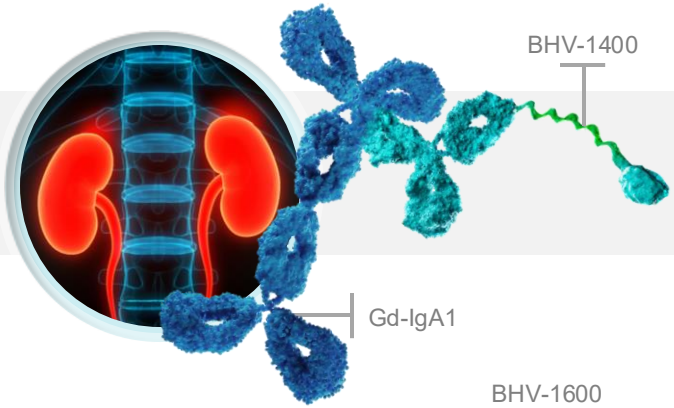
INNOVATING | EXECUTING | CREATING VALUE

Biohaven's Novel Degraders Validated in the Clinic: 166 Individuals Dosed With MoDE™ and TRAP™ Degraders

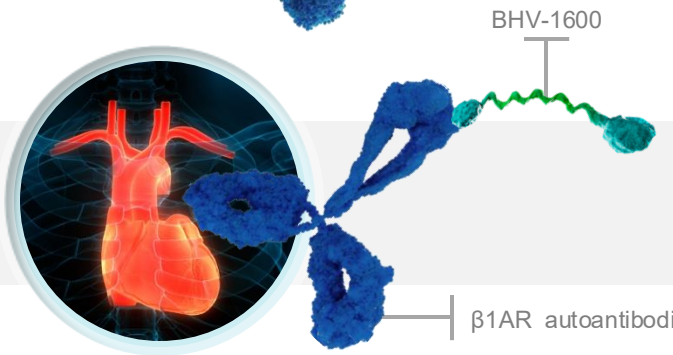
BHV-1300
GRAVES' DISEASE



BHV-1400
IgA NEPHROPATHY



BHV-1600
PERIPARTUM CARDIOMYOPATHY



PHASE 1 DATA DEMONSTRATES BIOHAVEN'S MoDE AND TRAP DEGRADERS:

- ✓ Safe
- ✓ Well-tolerated
- ✓ Highly selective
- ✓ Deep and rapid lowering of targeted IgG and Gd-IgA1

In ongoing clinical trials

1H 2025

BHV-1400
Phase 1

BHV-1300
Phase 1

BHV-1600
Phase 1

2025 MoDE™ and TRAP™ platform validation catalyzes 2026 pivotal development in key therapeutic indications

2H 2025–2026

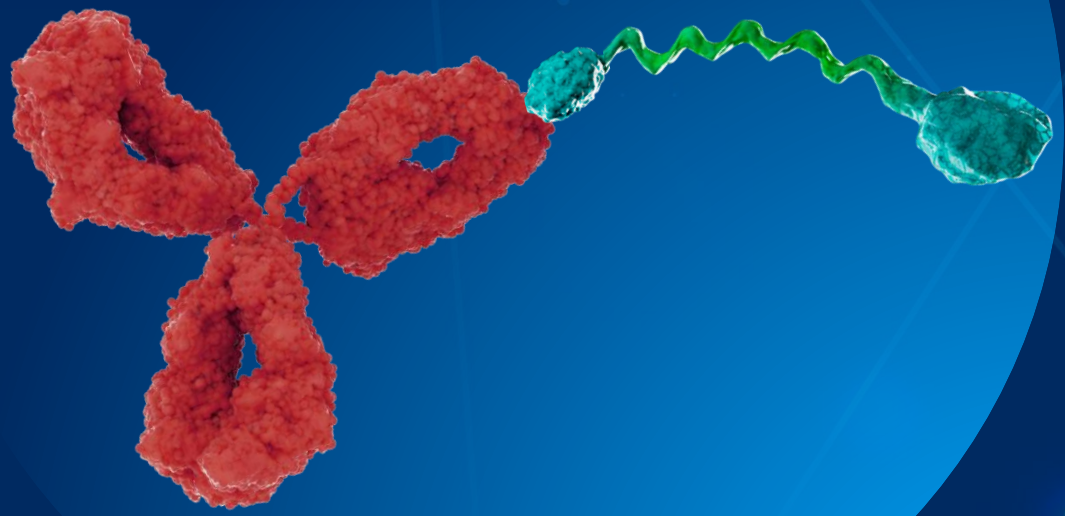
BHV-1400
IgA Nephropathy Study

BHV-1310
Myasthenia Gravis Study

BHV-1300
Graves' Disease 2025 Study
2026 Topline Data

BHV-1600
Cardiomyopathy Study

New MoDE and TRAP Degraders
Enter Phase 1
IgG4 degrader, PLA2R autoantibody degrader, TSHR autoantibody degrader

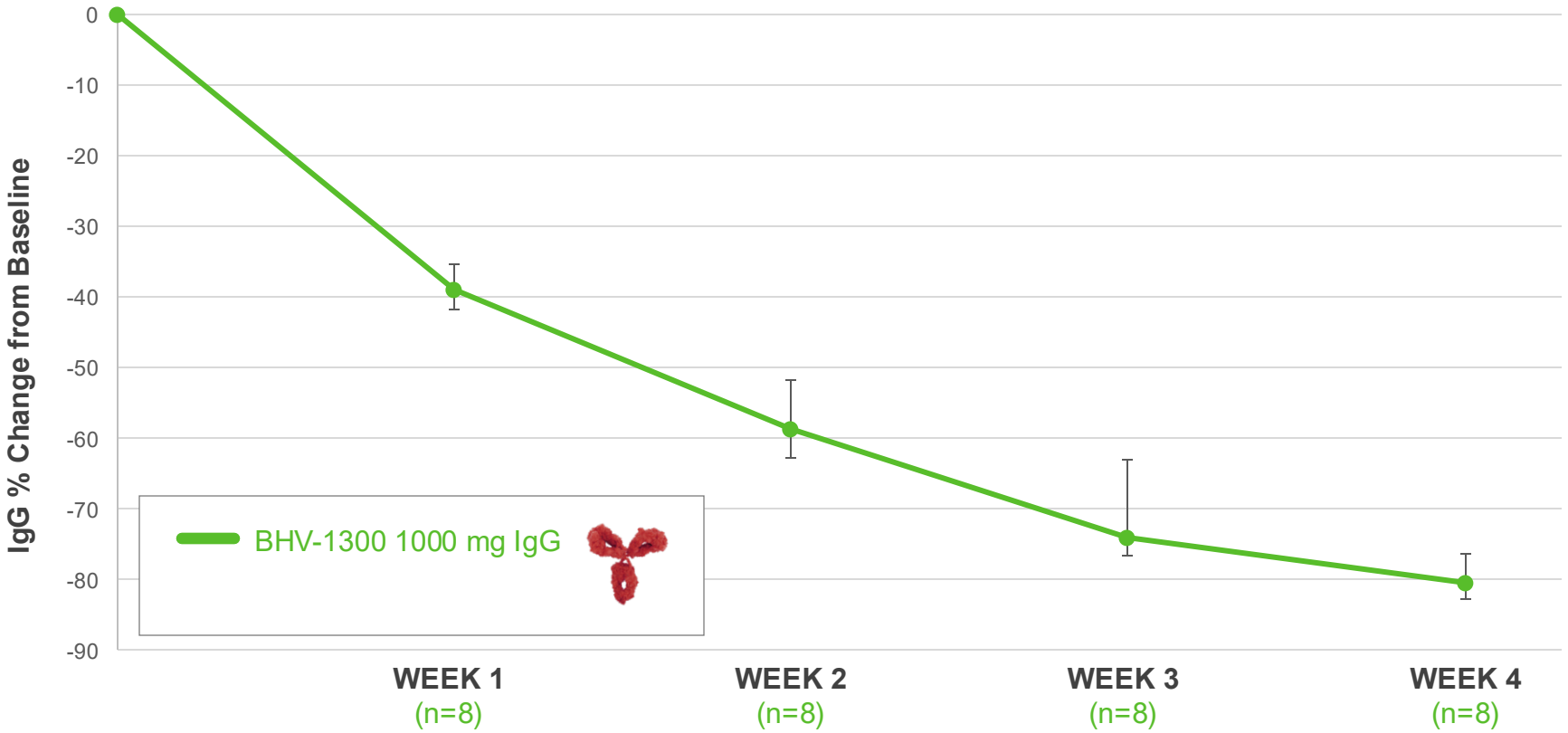


IgG MoDE™ Degrader

biohaven®

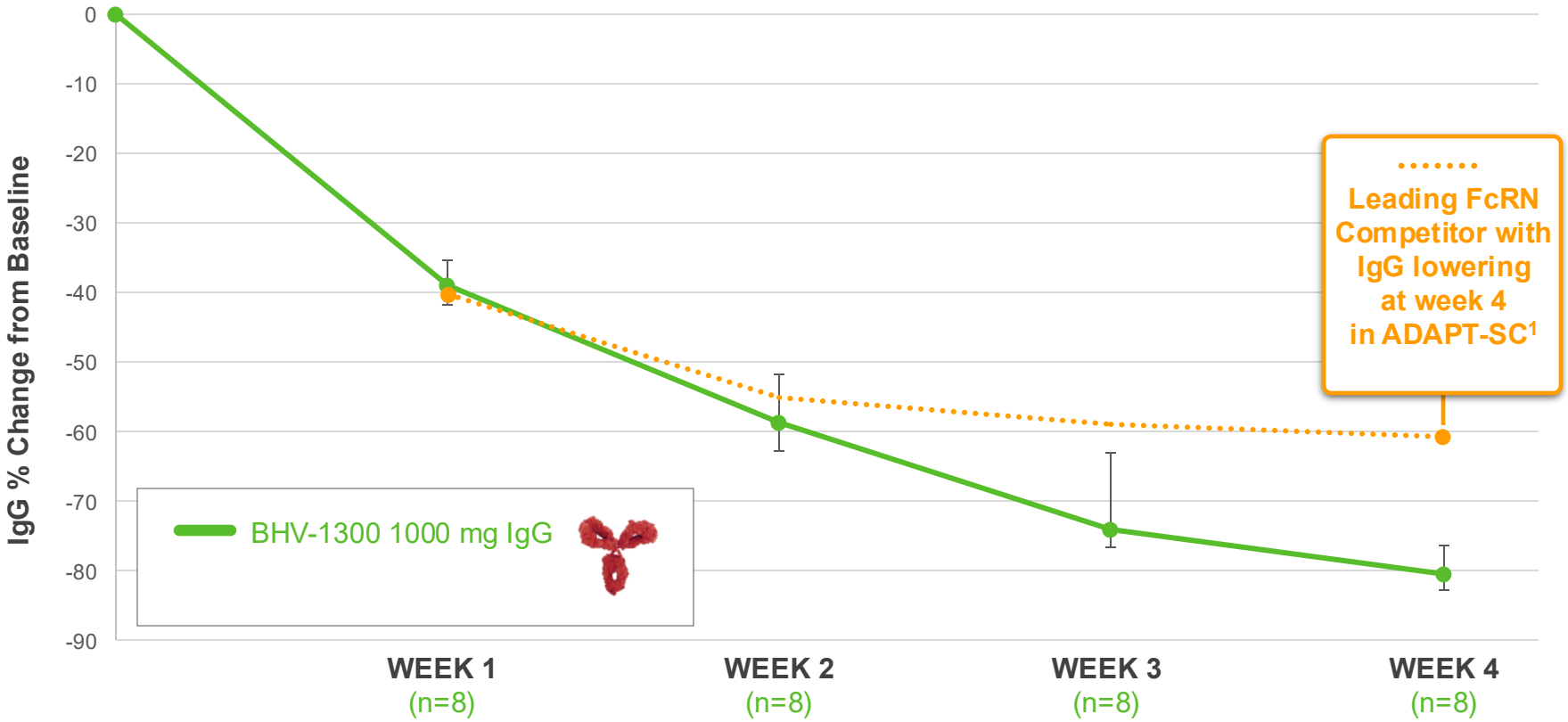
BHV-1300: Differentiated Small Molecule Degrader Achieves *Deep, Rapid and Tunable* IgG Reductions Customized to the Needs of Specific Diseases

DEGRADERS



Preliminary data, study ongoing, baseline is the Average of Day -1 and Day 1 pre-dose
Solid dots represent the median of the maximal total IgG % change from baseline for the Week and bars represent the 25th and 75th percentiles

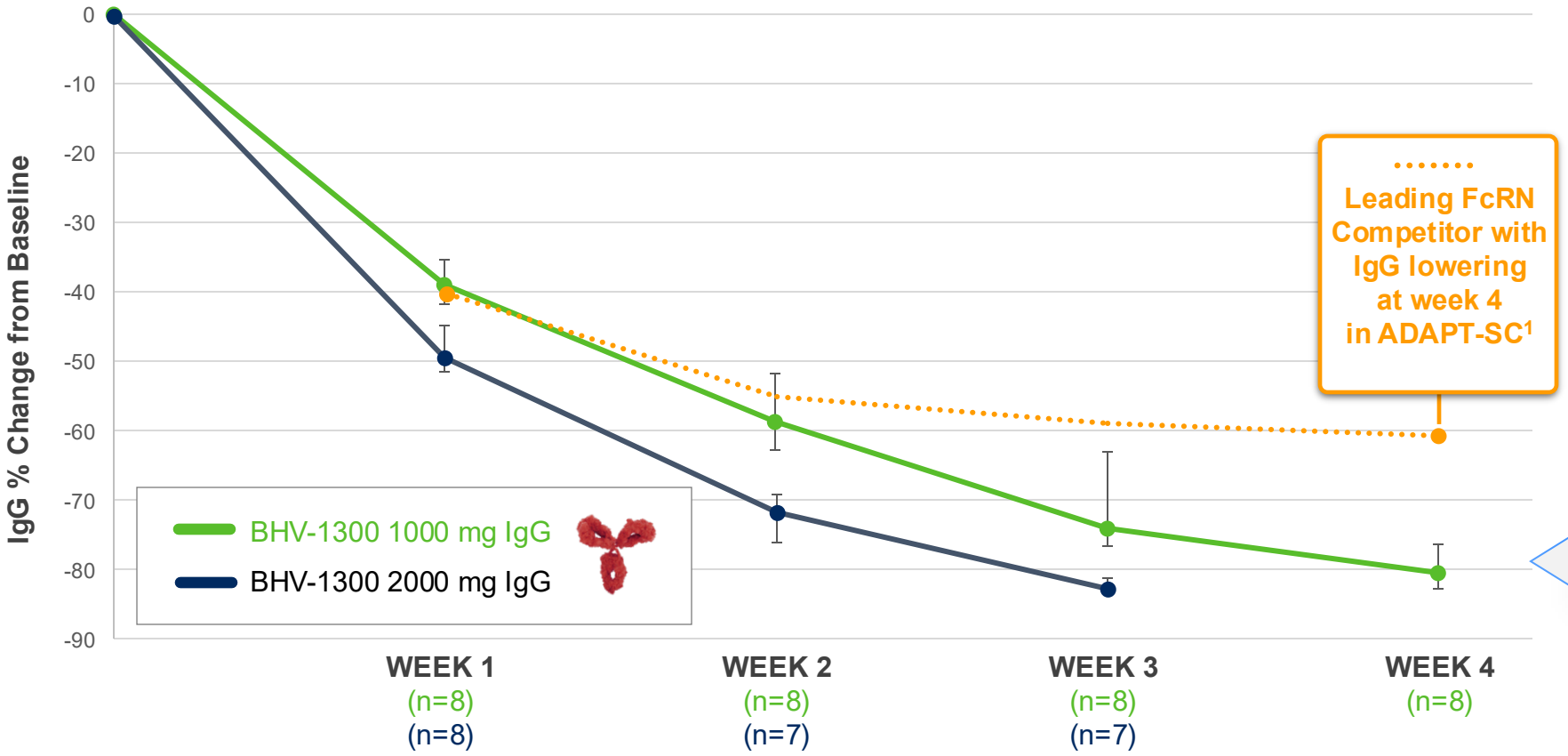
BHV-1300: Differentiated Small Molecule Degrader Achieves *Deep, Rapid and Tunable* IgG Reductions Customized to the Needs of Specific Diseases



1. Adapted from Howard, et al. *Neurotherapeutics*, 2024
Preliminary data, study ongoing, baseline is the Average of Day -1 and Day 1 pre-dose
Solid dots represent the median of the maximal total IgG % change from baseline for the Week and bars represent the 25th and 75th percentiles

BHV-1300: Differentiated Small Molecule Degrader Achieves *Deep, Rapid and Tunable* IgG Reductions Customized to the Needs of Specific Diseases

DEGRADERS



Subcutaneous BHV-1300 achieved median maximal reductions in total IgG of

83%

by day 18

1. Adapted from Howard, et al. *Neurotherapeutics*, 2024

Preliminary data, study ongoing, baseline is the Average of Day -1 and Day 1 pre-dose

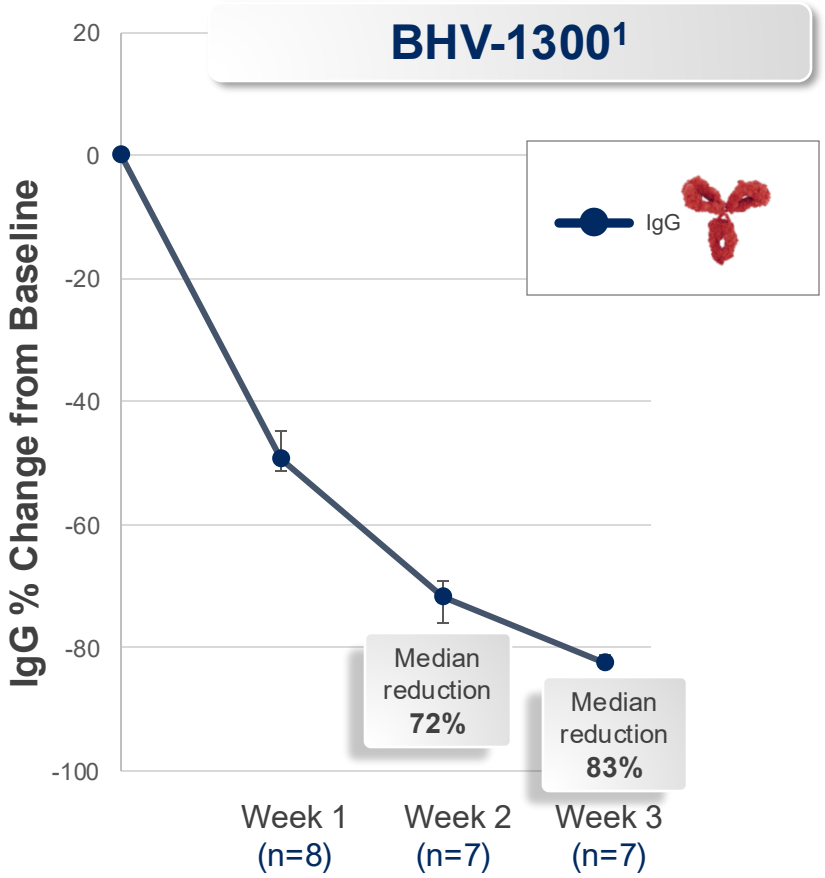
Solid dots represent the median of the maximal total IgG % change from baseline for the Week and bars represent the 25th and 75th percentiles

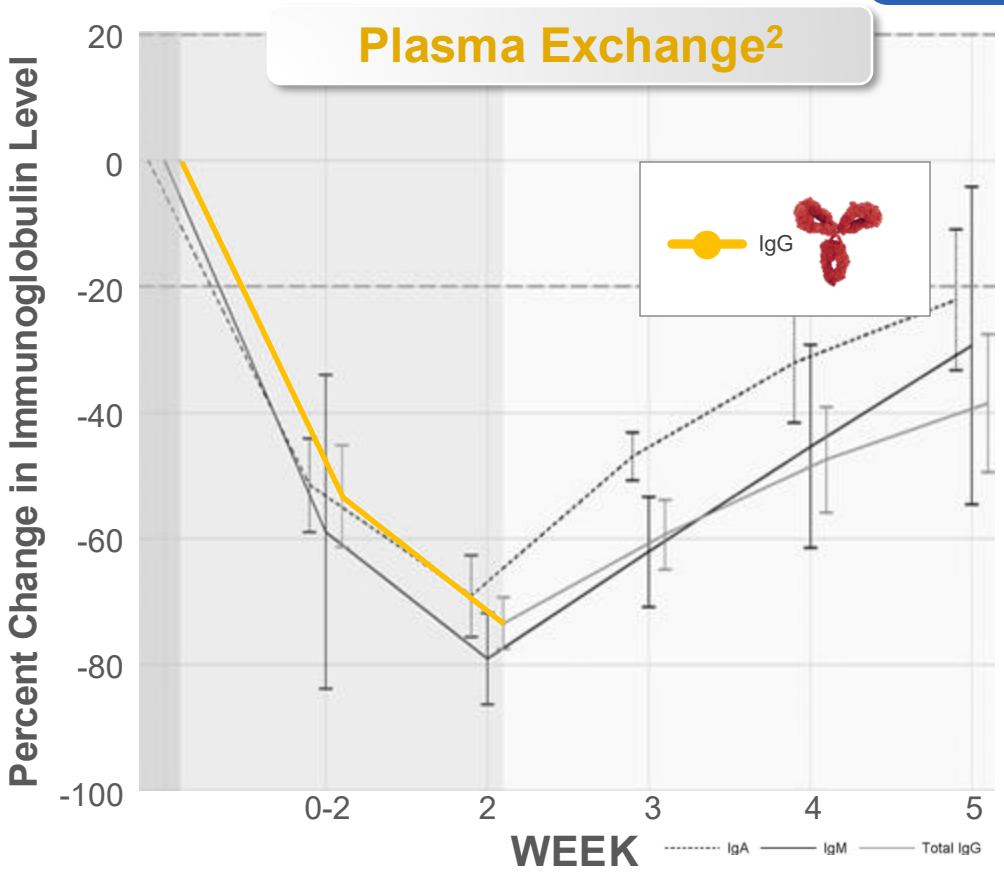
BREAKING NEWS

BHV-1300 achieved rapid and deep IgG reductions of 83%, highlighting tunability of dosing paradigms depending on disease indication

BHV-1300: Offers a New Potential Paradigm for Management of Acute Disease, Lowering IgG as Rapidly and Deeply as Plasma Exchange

DEGRADERS





1. 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. 2. Guptill JT, et al. *Autoimmunity.* 2016;49(2016):472-9.

KEY POINT

Two doses of BHV-1300 lower IgG as deeply and quickly as these invasive methods including plasma exchange

BHV-1300 Could Represent Replacement Plasma Exchange (PLEX) in an Auto-Injector

BHV-1300

VS

Plasma Exchange

DEGRADER
PLATFORM TECHNOLOGY

FAST AND DEEP
Removes disease-causing proteins within hours

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

PATIENT CENTRIC

LIFE ALTERING

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

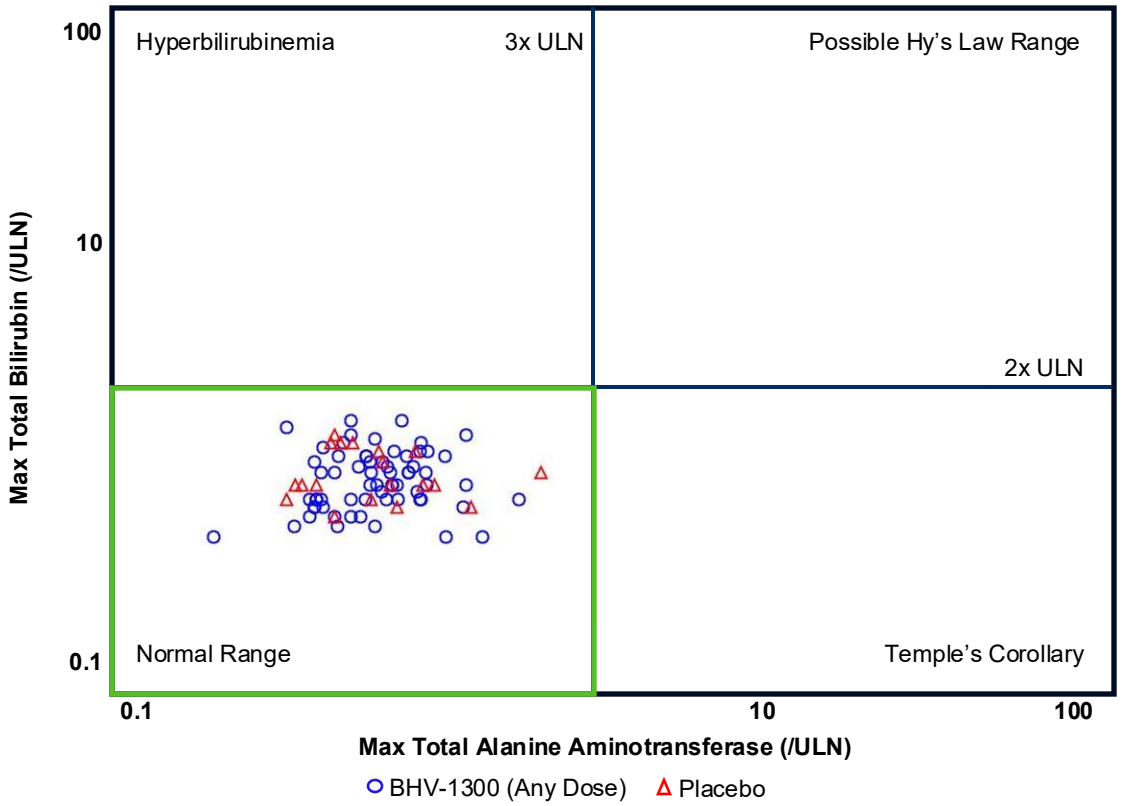
TUNABLE
- Level of degradation carefully modulated by dose level and frequency
- Employs body's natural mechanism for removal of senescent proteins

biohaven®

BHV-1300: Preliminary MAD and SAD Safety Data

- Single IV doses (50 mg to 500 mg via IV infusion) and single and multiple SC doses (up to 2000 mg) have been well-tolerated to date
- No SAEs or severe AEs reported, most AEs were mild (Grade 1). Expected administration-site-related AEs including injection site reactions observed both with BHV-1300 and placebo and have mostly been mild and resolved after dosing
- No clinically meaningful trends related to liver DILI safety labs (ALT/AST/total bilirubin), decreases in albumin elevations in cholesterol, vital signs, or ECGs
- No reductions in other antibodies including IgA, IgE and IgM

eDISH Plot: Maximum Total Bilirubin versus Maximum Alanine Aminotransferase On-Treatment – Safety Population*



eDISH, evaluation of drug-induced serious hepatotoxicity; **ULN,** upper limit of normal.
*Preliminary data April 24, 2025. Study ongoing
Ratios to ULN <0.1 are set to 0.1

Not Just Another FcRn Inhibitor: Biohaven IgG MoDE™ Degrader Differentiates as a Novel MOA, First-in-Class Molecule

DEGRADERS

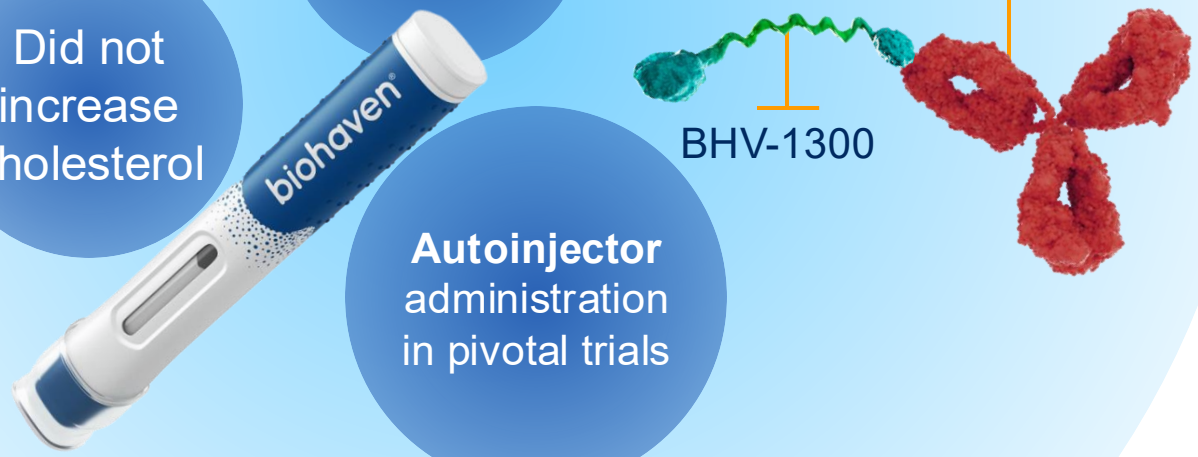
83%
IgG lowering by day 18

Small Molecule

Did not increase headaches

Did not increase cholesterol

biohaven®



Autoinjector administration in pivotal trials

IMAAVY™ J&J

- 74.6% IgG lowering after load, 68.8% in maintenance in Vivacity MG-3[1,2]
- **IV infusion**
- Increased cholesterol (24%), muscle spasms (12%), edema (12%)

Vyvgart® argenx

- Approximately 61% IgG lowering @ week 4 (VYVGART Hytrulo® in MG trial)[3] (Average 75% in MAD)[4]
- Prefilled Syringe
- Cyclical dosing can lead to symptom rebound

Rystiggo® ucb

- Approximately 76% IgG lowering in the MycarinG study [5]
- Healthcare administered SC infusion
- **44% headaches**
- Cyclical dosing can lead to symptom rebound

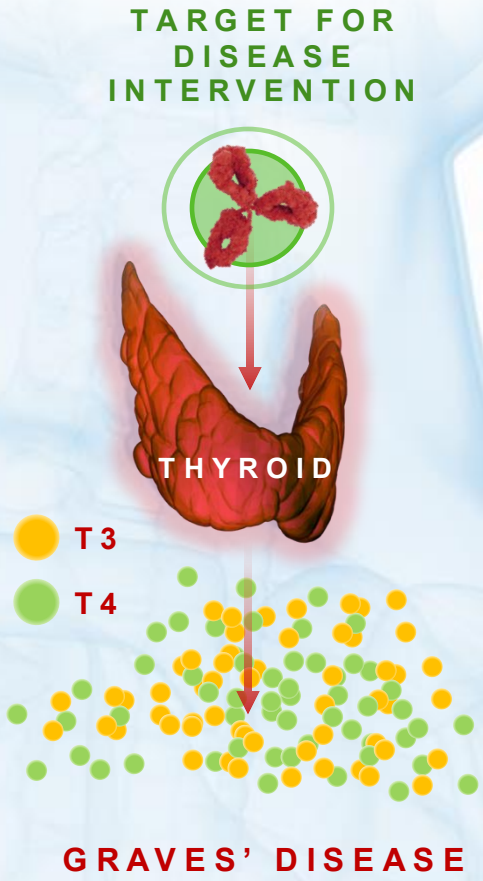
1. Antozzi et al, Lancet Neurology, 2025. **2.** 84% mean maximum IgG lowering (twice the labeled frequency) in Phase 1: Ling LE, et al. *Clin Pharmacol Ther.* 2019; **3.** Howard JF, Jr., et al. ADAPT (SC) Data – 2024 (Max reduction range 58.1%-63.5%) ; **4**. Ulrichts P, et al. *J. Clin. Invest.* 2018 **5**.Bril et al. *Lancet Neurology*, 2023 – (median maximum IgG reduction 73% with 7mg/kg and 79% with 10mg/kg dose – mean reductions were lower). Rystiggo MAD data not available

Graves' Disease: Precision Target Selection Enables Speed and Facilitates Confidence of Success

DEGRADERS

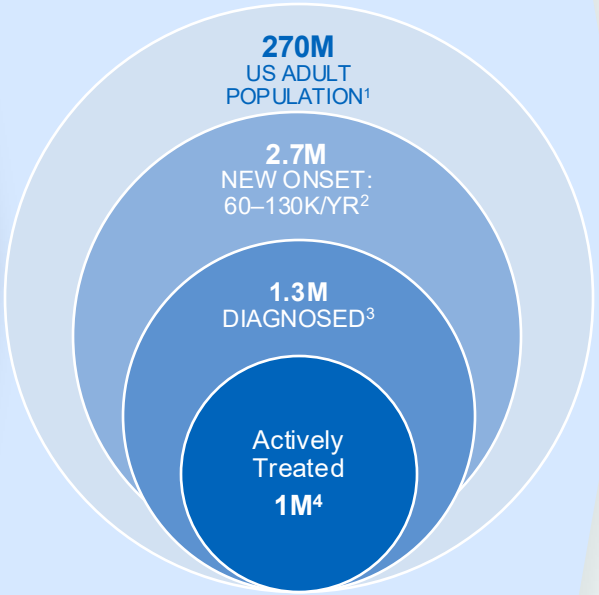
Follow the Science

PRECISION TARGETING OF DISEASE BIOLOGY



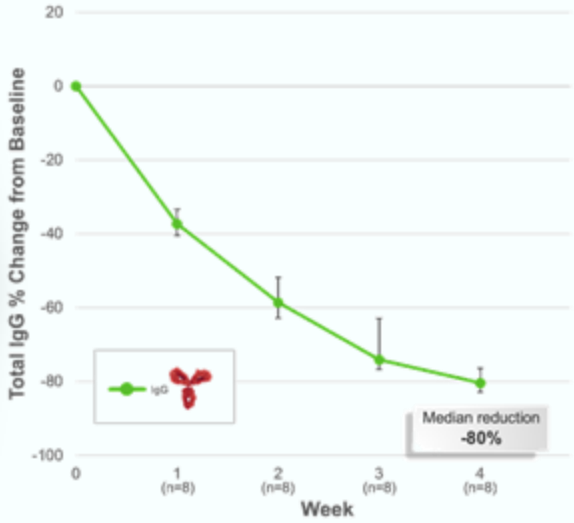
Understand the Need

UNMET NEED & LARGE COMMERCIAL OPPORTUNITY



Demonstrate Early Target Efficacy

PHASE 1 PD ENDPOINT



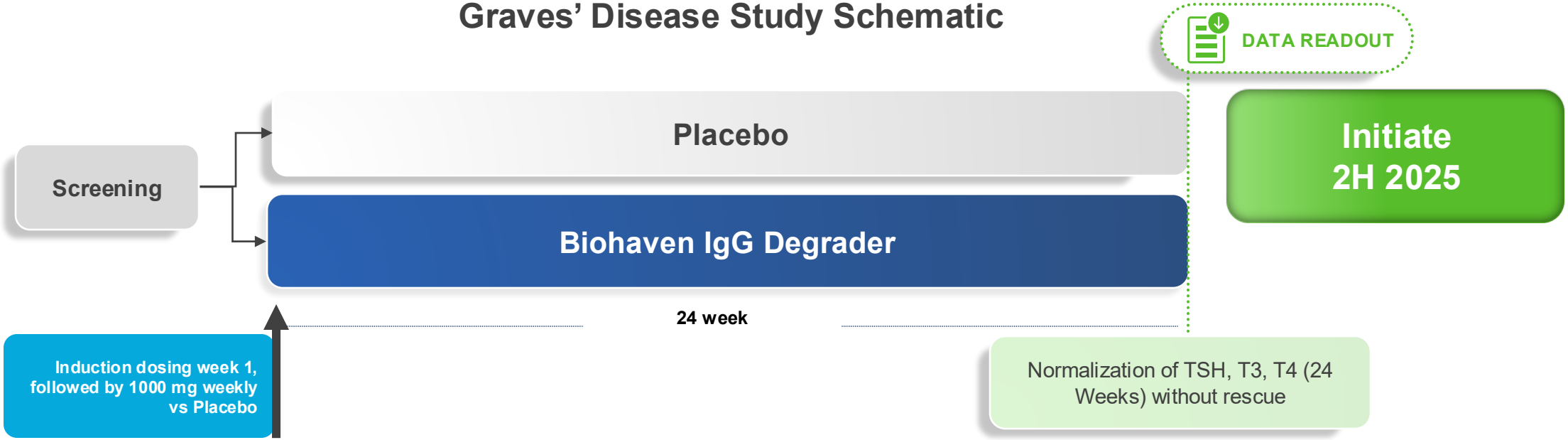
Phase 1 Pharmacodynamic endpoint **predicts success** and **enables speed** in Pivotal Studies

Create Value

PIVOTAL TRIAL TO INITIATE 2H 2025

2H 2025 Graves' Disease Pivotal Trial

Graves' Disease Study Schematic



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Male and female adults with Graves' disease
TREATMENT DURATION	24-week treatment period
KEY ENDPOINTS	Normalization of T3, T4 and TSH without rescue at week 24

KEY POINT

Biomarker driven study enables speed to near-term value inflection

Terry F. Davies, MD
Florence and Theodore Baumritter
Professor of Medicine

Icahn School of Medicine at Mount Sinai

IgG MoDE™ Degrader: Graves' Disease

biohaven®

Volkan Granit, MD, MSc
Senior Medical Director,
Head of Neuromuscular Disease

biohaven®

IgG MoDE™ Degrader: Myasthenia Gravis

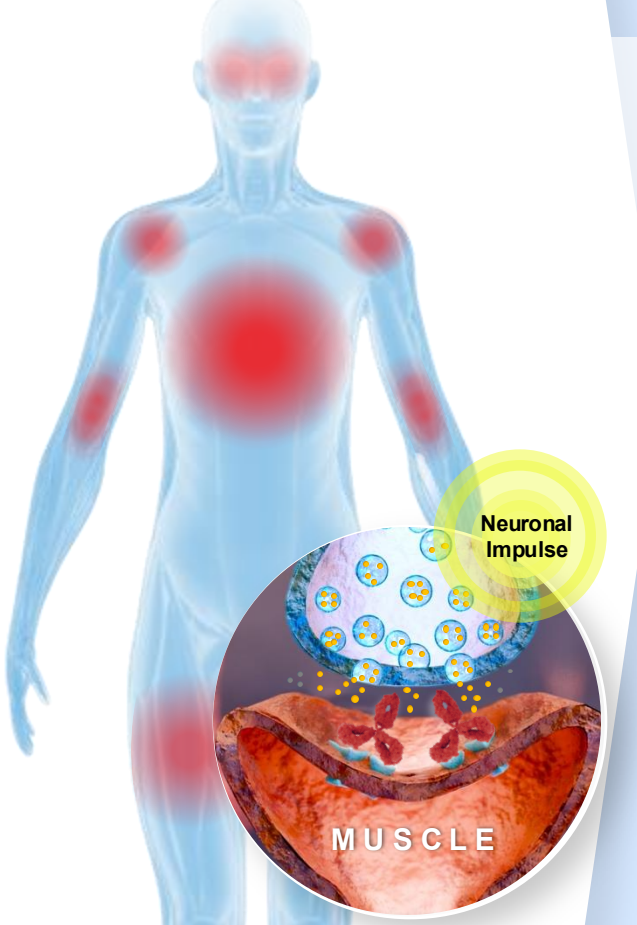
biohaven®

Myasthenia Gravis: Biohaven's IgG Degraders are Tunable Therapy for Acute and Chronic Phases of Disease

DEGRADERS

Follow the Science

PRECISION TARGETING OF DISEASE BIOLOGY



Understand the Need

UNMET NEED & LARGE COMMERCIAL OPPORTUNITY

~100K[1]
US PATIENTS

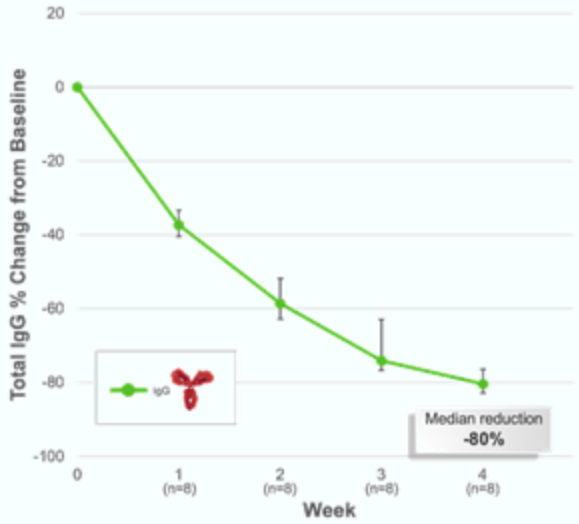
$3.2B
2024 TOTAL
- Soliris®
- Vyvgart®
- Ultomiris®
- Rystiggo®
- Zilbrysq®

$2.2B
2023 TOTAL
- Soliris®
- Vyvgart®
- Ultomiris®
- Rystiggo®

Multi-billion dollar nationally and internationally **growing market opportunity**[2]

Demonstrate Early Target Efficacy

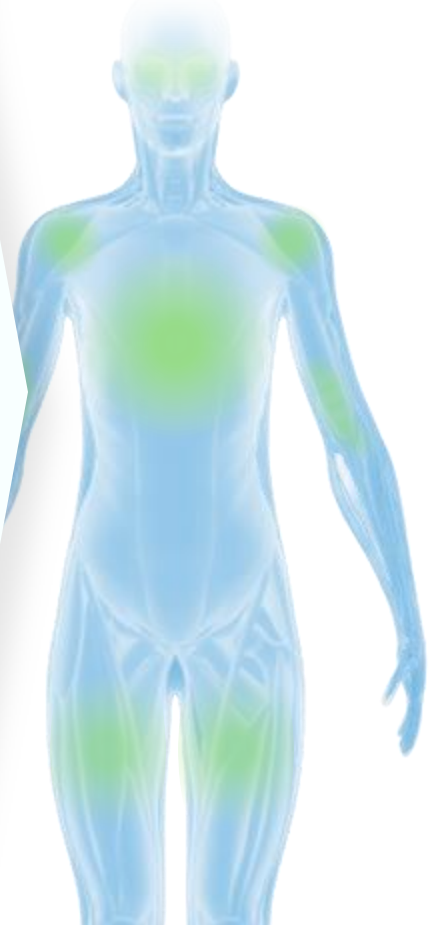
PHASE 1 PD ENDPOINT



Phase 1 Pharmacodynamic endpoint **predicts success** and **enables speed** in Pivotal Studies

Create Value

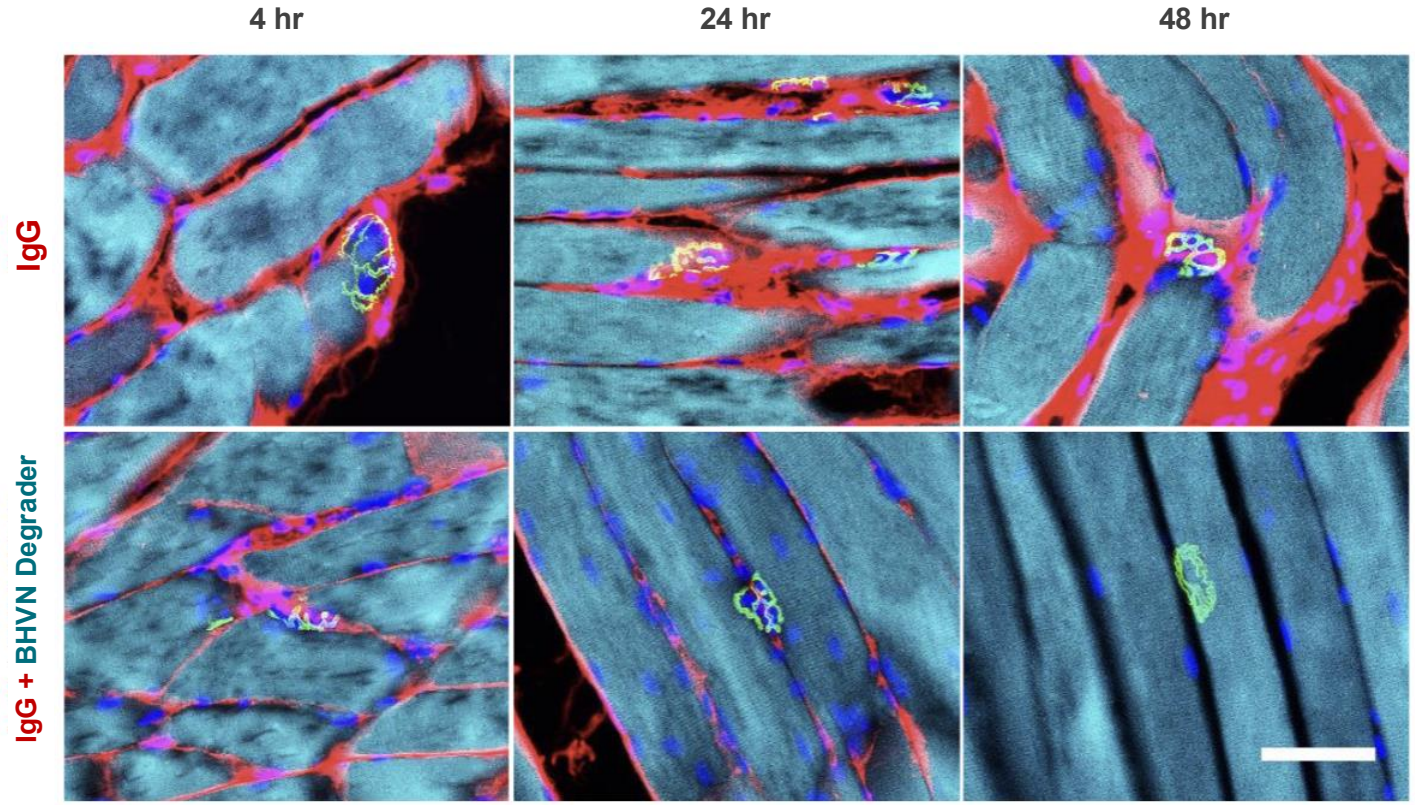
PIVOTAL TRIAL TO INITIATE 2026



1. Rodrigues E et al. doi: 10.1002/mus.28006. Epub 2023 Dec 1. PMID: 38040629.
2. Estimated revenue contribution for gMG based on Biohaven internal analysis.

In Vivo Pre-Clinical Validation of the IgG Degrader Mechanism of Action

IgG Reduction in Neuromuscular Junction with Degrader Treatment



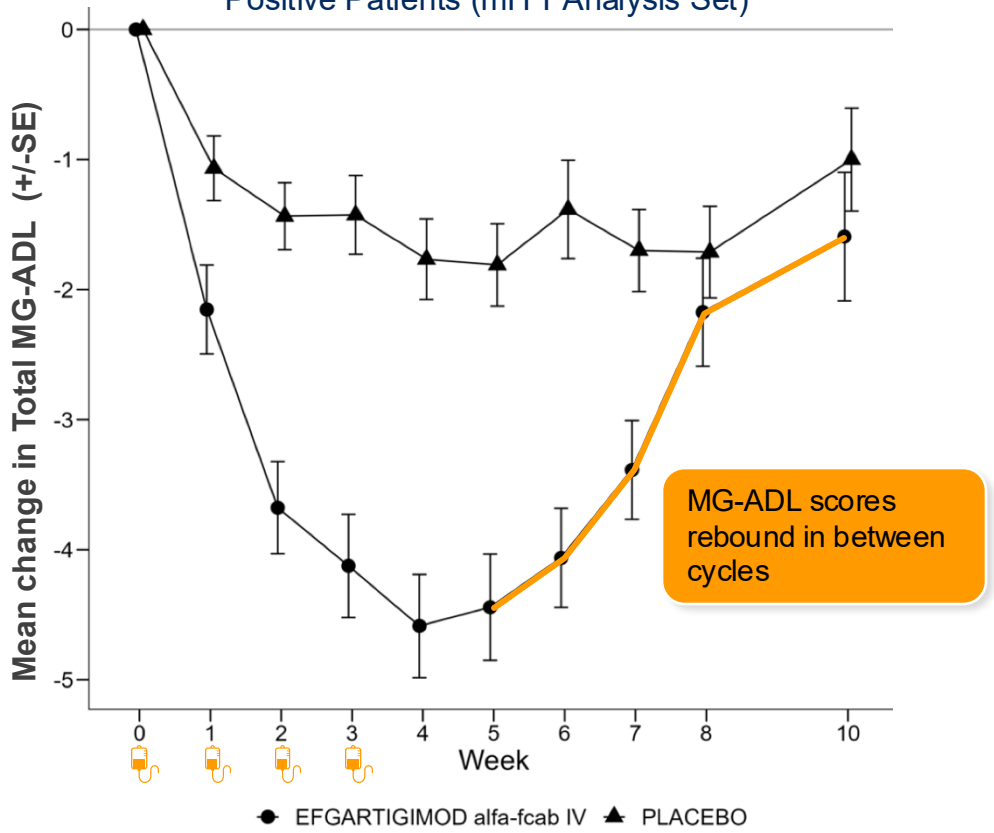
KEY POINT

Biohaven IgG degraders can rapidly clear IgG from the interstitial space and neuromuscular junction

Cycles of Dosing with FcRns Lead to Cycles of Recovery Punctuated by Periods of Symptom Rebound

Mean Change in Total MG-ADL From Cycle 1 Baseline Over Time in AChR-Ab

Positive Patients (mITT Analysis Set)



- Chronic diseases like MG require sustained therapy to prevent symptom fluctuations and worsening
- Drug holidays or cyclic dosing can lead to MG-ADL score rebound, disrupting patient quality of life[1,2]

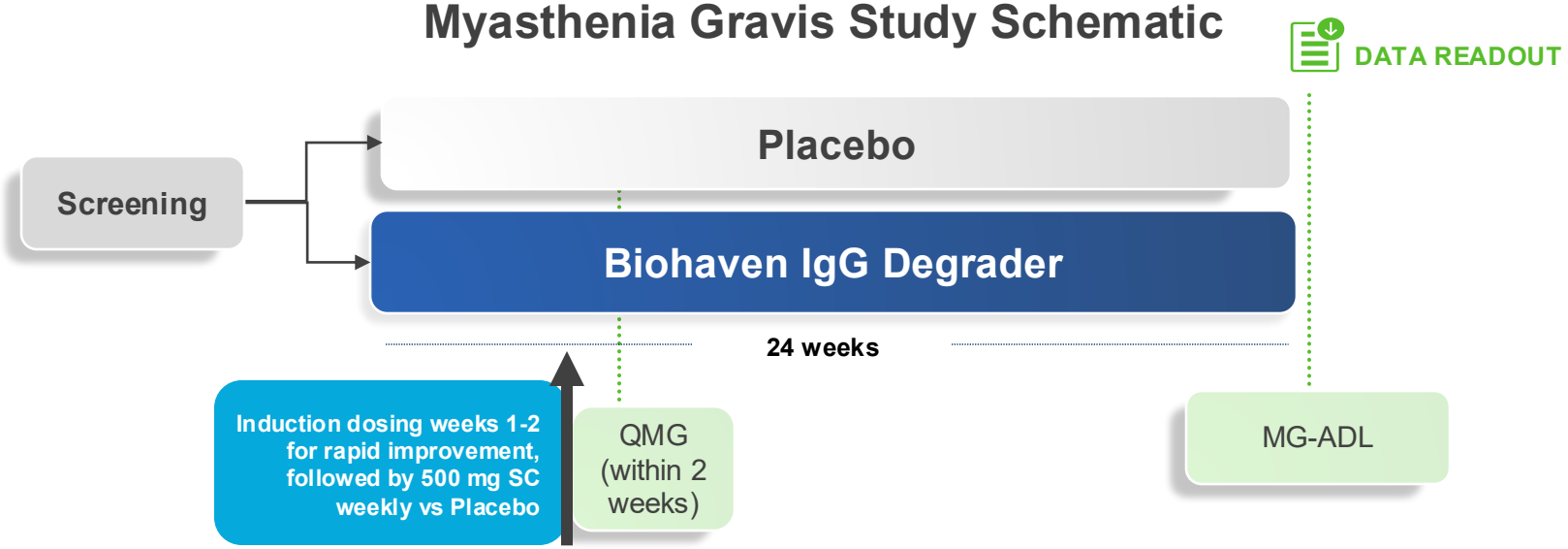
MG-ADL, Myasthenia Gravis Activities of Daily Living scale 1. Vyvgart Hytrulo® Prescribing Information – argenx 2.Rystiggo® Prescribing Information – UCB

KEY POINT

PATIENT-CENTERED CARE: Continuous and sustained dosing (e.g., BHVN degraders) can improve adherence and potentially reduce disease burden

Biohaven IgG Degrader: Clinical Trial Design Highlights Potential Efficacy in Acute and Maintenance MG Therapy

Myasthenia Gravis Study Schematic



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Male and female adults with gMG
TREATMENT DURATION	24-week treatment period
KEY ENDPOINTS	QMG (within 2 weeks), MG-ADL (week 24)

QMG, Quantitative Myasthenia Gravis score; **MG-ADL**, Myasthenia Gravis Activities of Daily Living scale

KEY POINT

BHV-1300 candidate to treat acute MG exacerbation and maintenance therapy with a single drug

Brian McGuire, MD
Medical Director

biohaven®

IgG TRAP™ Degrader: Peripartum Cardiomyopathy (PPCM)

biohaven®

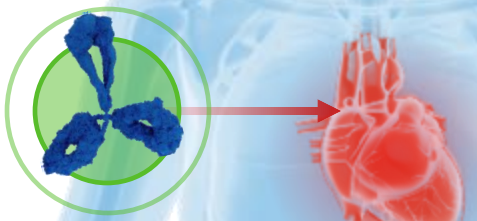
PPCM: BHV-1600 Targets β1AR Autoantibodies for First Potential Disease-Specific Therapy

DEGRADERS

Follow the Science

PRECISION TARGETING OF DISEASE BIOLOGY

TARGET FOR DISEASE INTERVENTION



β1AR autoantibodies

Cardiac beta-adrenergic receptors (β1AR)

Sustained β1AR stimulation ▶ Increased Contractility ▶ Ventricular Strain ▶ Dilated Cardiomyopathy

Peripartum Cardiomyopathy

Understand the Need

PPCM is rare disease with poor outcomes in new mothers and no currently FDA-approved treatment

Maternal mortality highest since 1965 and primary contributor is PPCM with mortality rates reported up to 20%

10% go on to require mechanical support (LVAD or heart transplant)

Phase 1 PD Predicts Success in Phase 3

✓ **PHASE 1 SAD/MAD**
Completed dosing, β1AR PD biomarker results pending

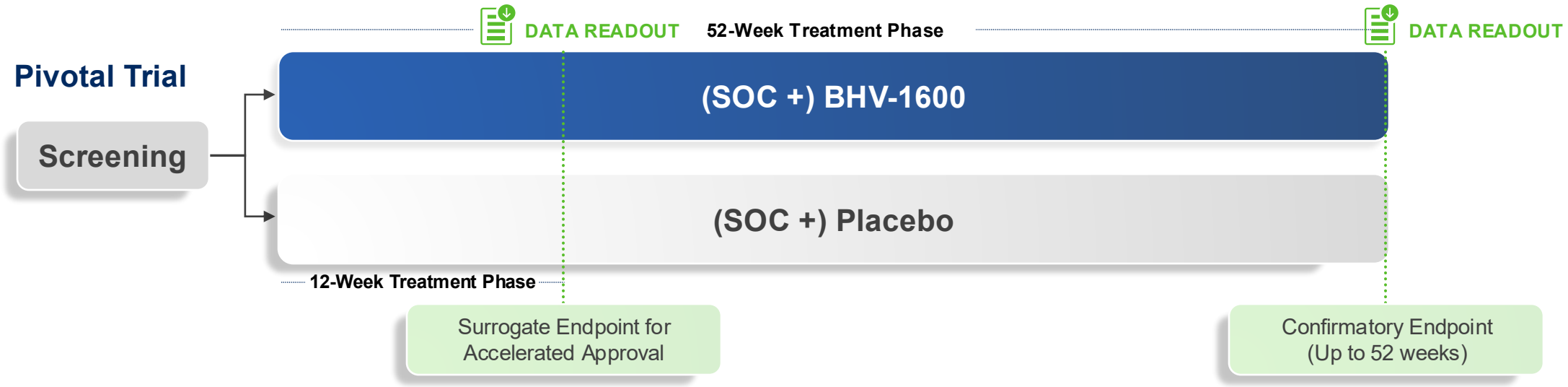
Create Value

PHASE 1 SAD/MAD completed dosing: IV and SC dosing up to 500mg IV

2026 STUDY in PPCM patients

BHV-1600: Phase 2/3 Pivotal Study Design Based Upon FDA INTERACT

PPCM Study Schematic



KEY POINT

Pivotal trial plans to leverage accelerated approval pathway to bring a much-needed therapeutic to women with PPCM efficiently

Kayle Shapero, MD, PhD
BROWN UNIVERSITY HEALTH
CARDIOVASCULAR INSTITUTE
Clinical Assistant Professor of Medicine

THE WARREN ALPERT Medical School
BROWN UNIVERSITY

BHV-1600, a Novel Targeted β1AR Autoantibody Degrader, in Development for Treatment of Non-Ischemic Cardiomyopathies

biohaven®

Peripartum Cardiomyopathy (PPCM)

- PPCM is a pregnancy-associated idiopathic cardiomyopathy presenting with heart failure and the following criteria:
  - An ejection fraction less than 45%
  - Occurring towards the end of pregnancy or in the months following delivery
  - No other cause of heart failure identified
- Incidence of PPCM varies widely in the United States — reported to range from ~1:1000 to 1:4000 live births

Risk Factors

- <1 month postpartum
- Age > 30 years
- Black race
- Hypertensive disorders
- BMI >25
- Multiple gestations

Symptoms

- Dyspnea
- Decreased exercise tolerance
- Orthopnea
- Edema
- Paroxysmal nocturnal dyspnea
- Fatigue
- Chest pain
- Palpitations

Signs

- Tachycardia
- Evidence of volume overload

Adapted from: Hesson, A., Davis, M.B. (2023). Peripartum Cardiomyopathy

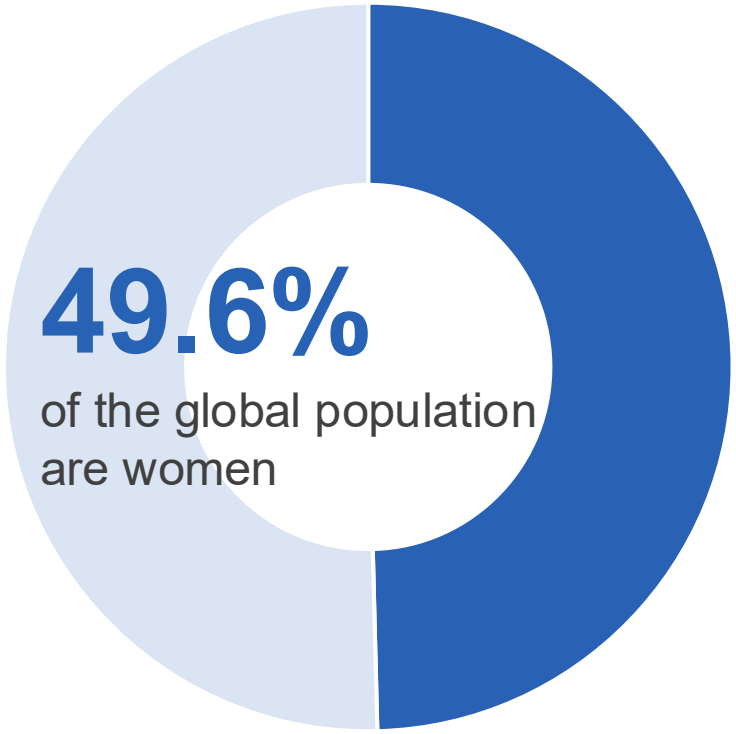
Treatment of Peripartum Cardiomyopathy: A Call to Action[1]

- US Maternal mortality is on the rise and reached its highest levels since 1965. It far exceeds the rates of other industrialized nations
- The primary contributor is cardiovascular disease, which includes PPCM with associated long-term mortality rates ranging from 7-20% in the US[2]
- PPCM often affects young, otherwise healthy women, many of whom suffer persistent life-altering symptoms of heart failure and ~10% progress to require mechanical support (LVAD) or heart transplantation

> *Women with PPCM are **suffering from a devastating disease without any disease specific therapy**.*

1. Ricardo Cardona-Guarache, MD, MPH, and Jordana Kron, MD. *Canadian Journal of Cardiology* 31 (2015)1418-1420; 2. Davis MB, Arany Z, McNamara DM, Goland S, Elkayam U. Peripartum Cardiomyopathy: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2020;75(2):207-221.DOI: 10.1016/j.jacc.2019.11.014.3.

Treatment of Peripartum Cardiomyopathy: A Call to Action[1]



29%
of patients enrolled in HF trials are women

2
RCTs performed in PPCM in the past 10 years

0
FDA-approved medications

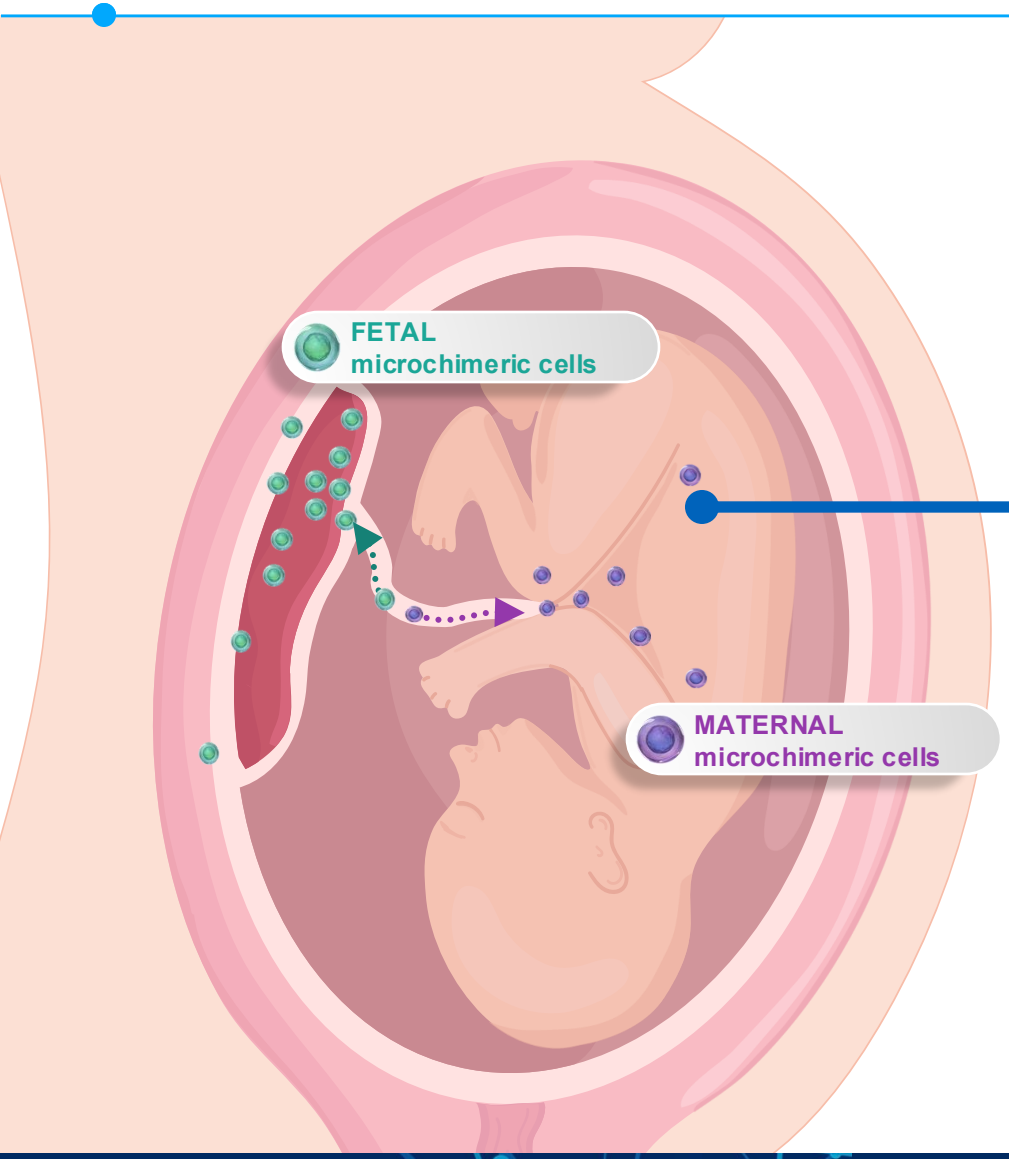
Women are underrepresented in clinical trials and even fewer studies have incorporated PPCM patients

1.Ricardo Cardona-Guarache, MD, MPH, and Jordana Kron, MD. *Canadian Journal of Cardiology* 31 (2015)1418-1420

KEY POINT

A Call to Action makes the case that we need to better understand the science and develop treatments that addresses the underlying cause of the disease

Peripartum Cardiomyopathy: Origin of Anti-Cardiac Autoantibodies



PREGNANCY

- Adaptive changes during pregnancy to tolerate paternal-fetal antigen
- Increased maternal immunotolerance
- Many autoimmune disorders (RA, MS) tend to have lower relapse rates during pregnancy

DELIVERY

- Peak cell traffic between fetus and mother

POSTPARTUM

- Reduction of immunotolerance
- Marked increase in flares of autoimmune diseases in peripartum period (correlates with onset of PPCM)

Gleicher N, Elkayam U. Peripartum cardiomyopathy, an autoimmune manifestation of allograft rejection? *Autoimmun Rev.* 2009 Mar;8(5):384-7. doi: 10.1016/j.autrev.2008.12.003. Epub 2008 Dec 16. PMID: 19087892.

PPCM: Prevalence of β1AR Autoantibodies

- Primary source: 60% of PPCM patients had β1AR Abs
- Increased titer of β1AR autoantibodies correlated with:
  - Elevated NT-proBNP, Left Ventricular Dimensions and NYHA severity score
  - Decreased LVEF and LVFS
- β1AR AAbs were an independent risk factor for the onset of PPCM

Correlation Between Serum Anti–β1AR-AAB Levels and Other Parameters

	Frequency of autoantibody		Titer of autoantibody	
	Spearman coefficient	*P* value	Spearman coefficient	*P* value
NYHA FC	0.892	<0.001	0.702	<0.001
NT-proBNP (pg/mL)	0.567	<0.001	0.581	<0.001
Echocardiographic data				
Left-ventricular EDD (mm)	0.578	<0.001	0.525	0.001
Left-ventricular ESD (mm)	0.601	<0.001	0.496	0.002
Ejection fraction (%)	-0.561	<0.001	-0.568	<0.001
Fractional shortening (%)	-0.488	<0.001	-0.499	0.002

Doi: 10.1371/journal.pone.0086770.t004

NYHA FC, New York Heart Association functional class; **NT-proBNP**, N-terminal pro-brain natriuretic peptide; **EDD**, end-diastolic diameter; **ESD**, end-systolic diameter

The correlation between peripartum cardiomyopathy and autoantibodies against cardiovascular receptors. Liu J, Wang Y, Chen M, Zhao W, Wang X, et al. PloS one, 2014 (1), e86770. doi: 10.1371/journal.pone.0086770

Targeting the Role of Autoimmunity in PPCM

Current treatment for PPCM

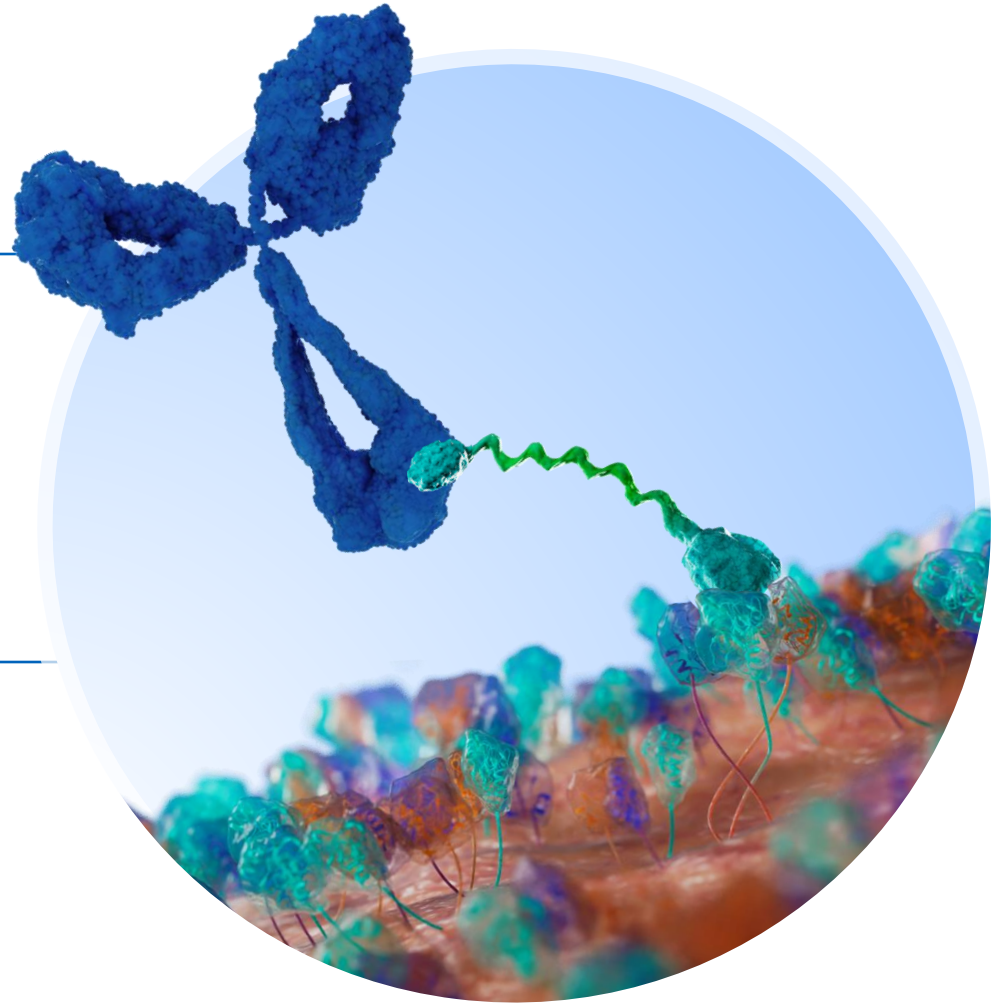
- Guideline-Directed Medical Therapy: No disease specific therapy

Treatment goals in PPCM

- Intervene early
- Treat acute heart failure
- Prevent further myocardial injury and restore baseline normal cardiac function

β1AR AAbs present in PPCM

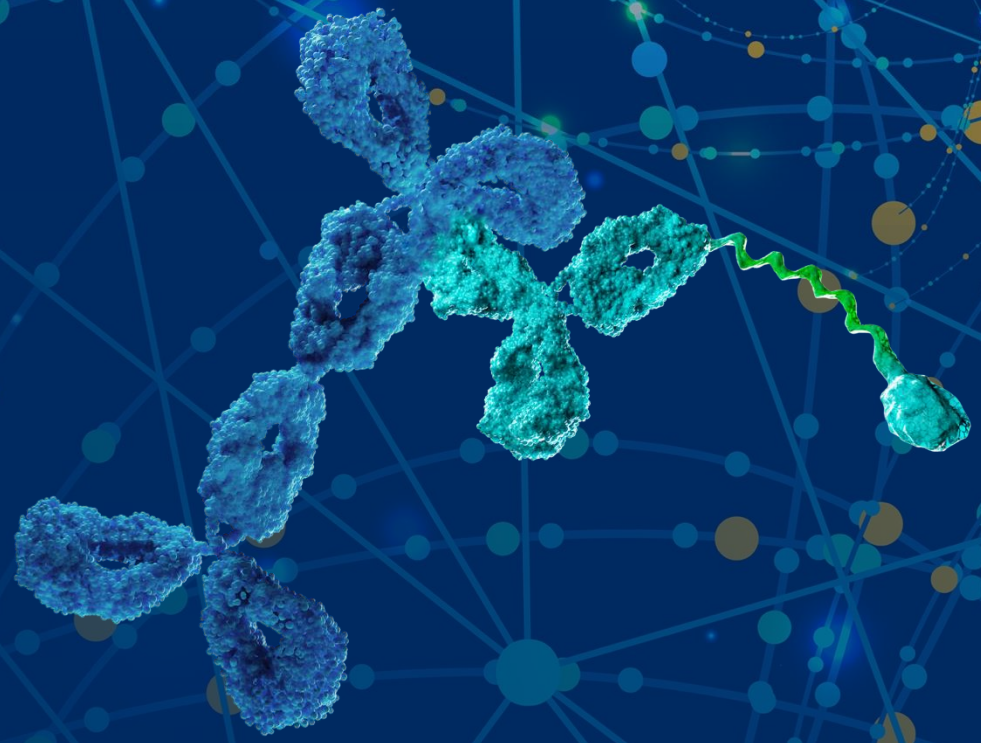
- Increased titers correlate with more severe disease
- β1AR autoantibodies are a potential target to provide PPCM patients with their first disease specific therapy



Tova Gardin, MD, MPP

Chief Translational Officer

biohaven®



Galactose-Deficient IgA1 TRAP™ Degrader: IgA Nephropathy

biohaven®

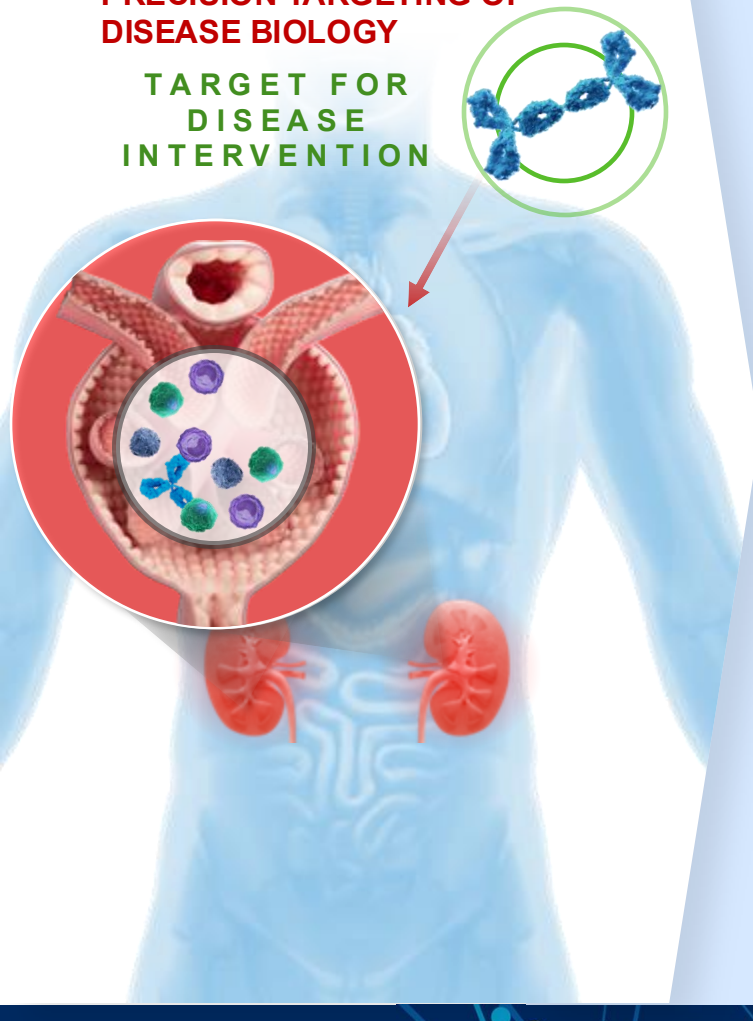
BHV-1400 Selectively Removes Gd-IgA1, the Pathogenic Antibody in IgAN While Sparing Healthy Immunoglobulins

DEGRADERS

Follow the Science

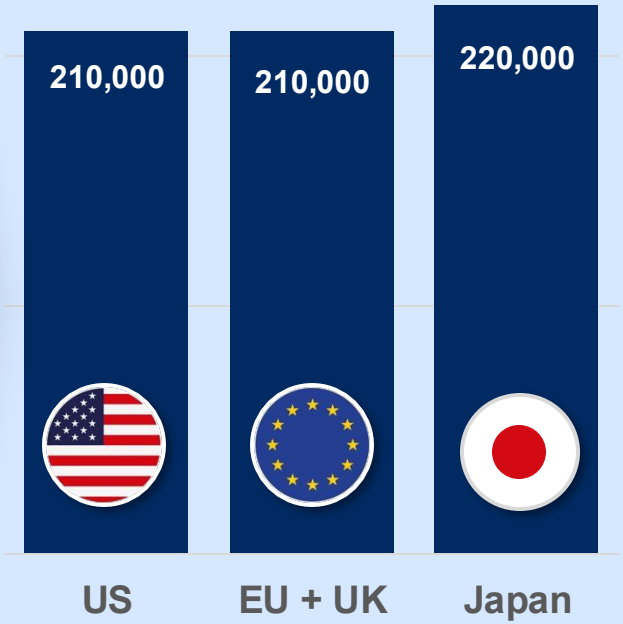
PRECISION TARGETING OF DISEASE BIOLOGY

TARGET FOR DISEASE INTERVENTION



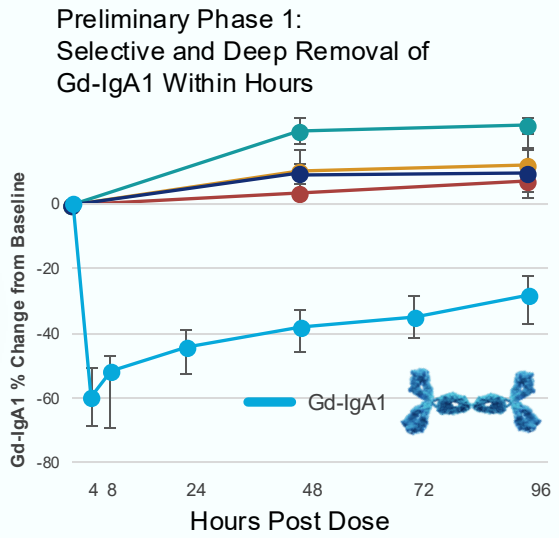
Understand the Need

UNMET NEED & LARGE COMMERCIAL OPPORTUNITY



Demonstrate Early Efficacy

PHASE 1 PD ENDPOINT



Phase 1 Pharmacodynamic endpoint predicts **success**, enables **speed**; sparing of healthy immune components predicts improved **safety**

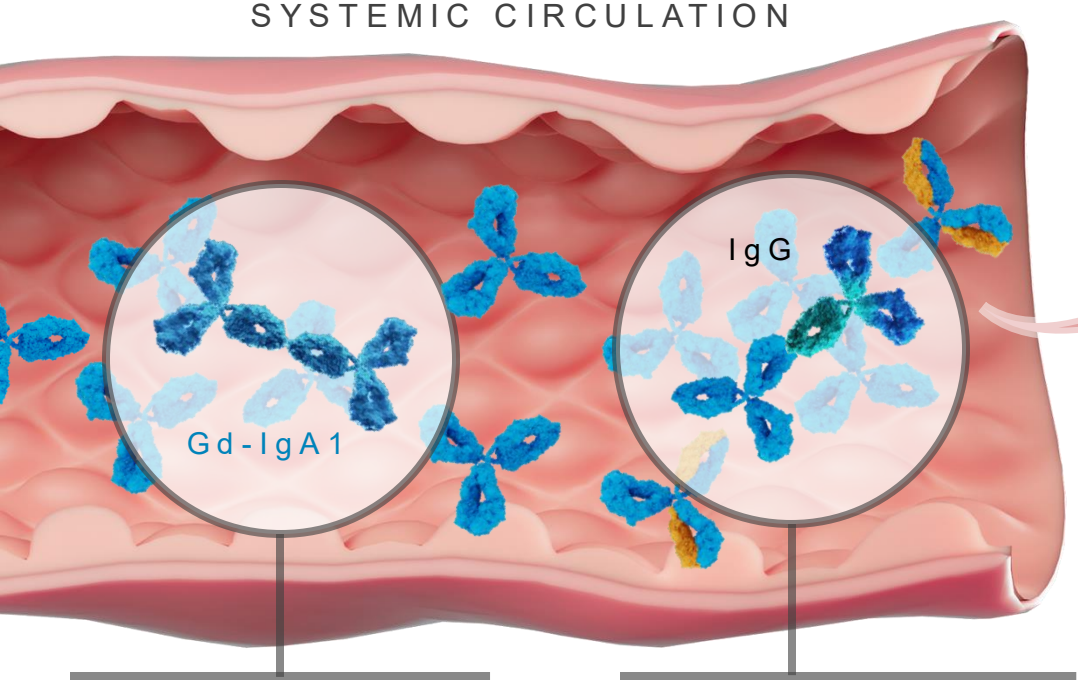
Create Value

PIVOTAL TRIAL TO INITIATE 2026

IgA Nephropathy Is Caused by Excess Production of Galactose-Deficient IgA1 (Gd-IgA1)

DEGRADERS

SYSTEMIC CIRCULATION

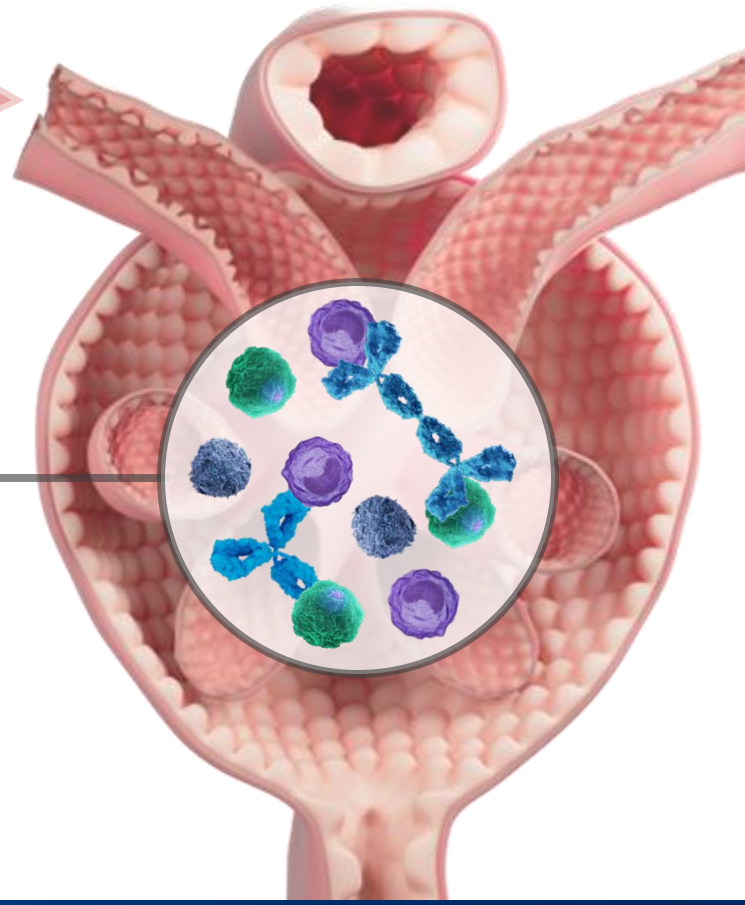


Aberrant form of immunoglobulin, **galactose-deficient IgA1** forms in excess

Immunoglobulin (IgG, IgM or IgA) target **Gd-IgA1** to form circulating immune complexes

Gd-IgA1 immune complexes deposit into the kidney, recruiting immune cells and causing the release of pro-inflammatory and profibrotic mediators

RENAL CORPUSCLE

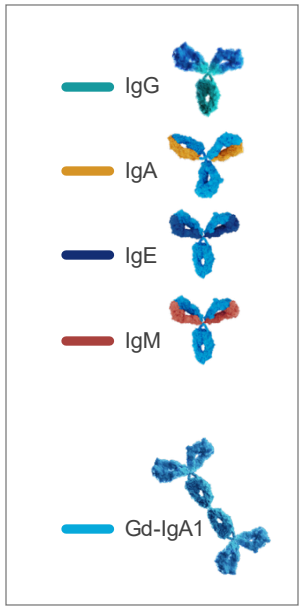


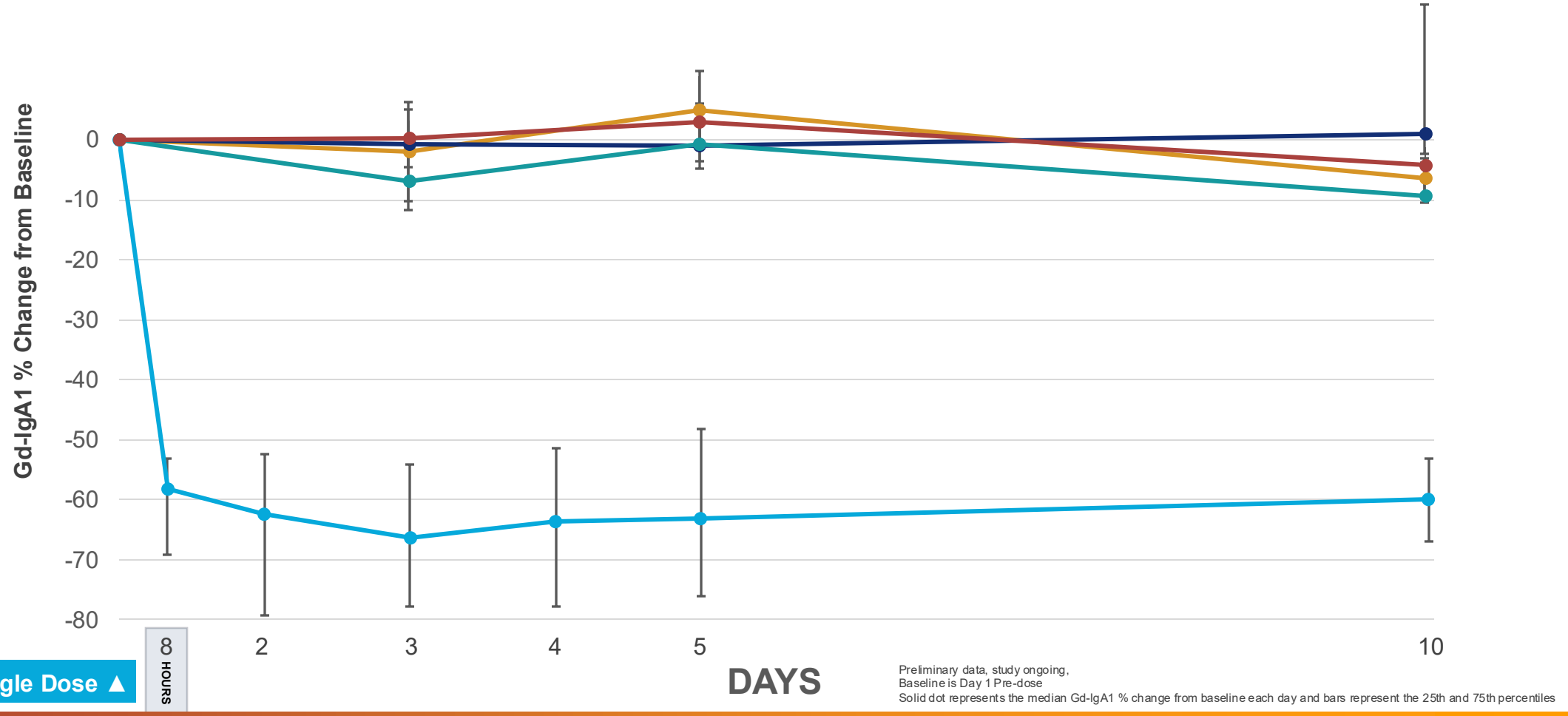
KEY POINT

No therapy selectively targets the pathogenic nidus of disease, Gd-IgA1... **UNTIL NOW**

BHV-1400: Single Subcutaneous Dose Delivers *Rapid, Selective, Deep and Sustained* Removal of Gd-IgA1

DEGRADERS





BHV-1400 500 mg SC Single Dose ▲

Preliminary data, study ongoing,
Baseline is Day 1 Pre-dose
Solid dot represents the median Gd-IgA1 % change from baseline each day and bars represent the 25th and 75th percentiles

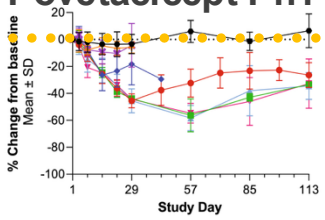
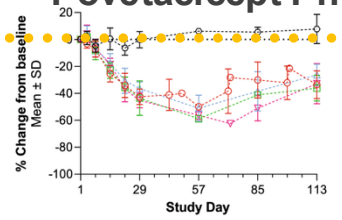
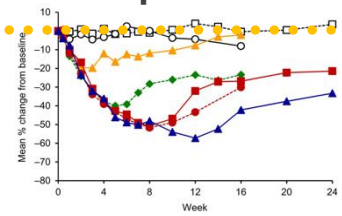
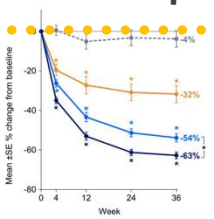
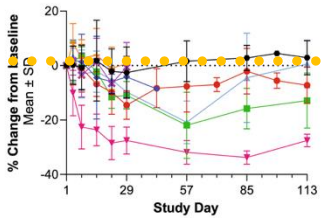
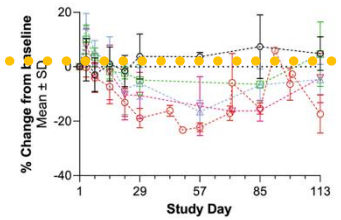
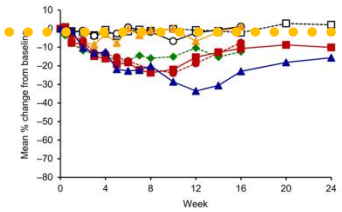
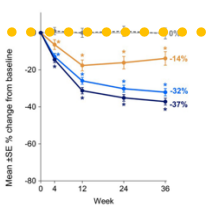
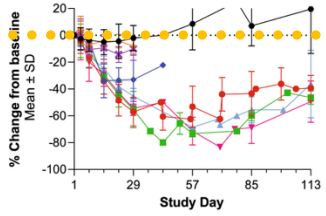
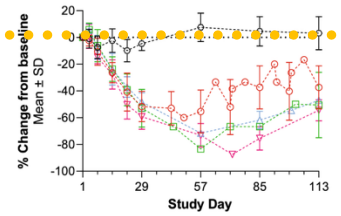
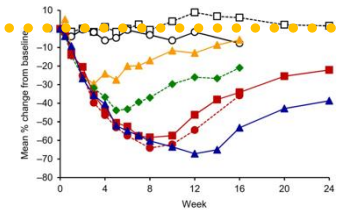
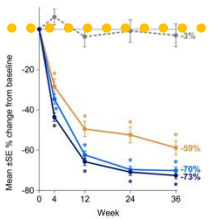
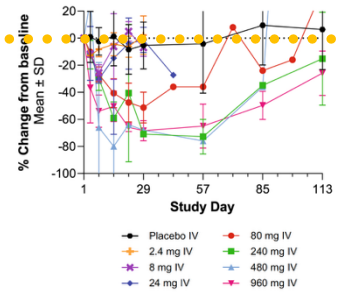
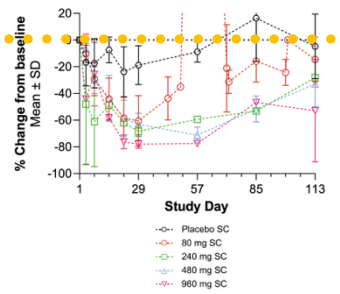
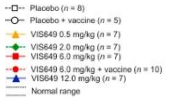
BREAKING NEWS

A single SC dose of BHV-1400 delivers rapid, selective, deep, and sustained reductions in Gd-IgA1 of up to 81% and without suppression of healthy immunoglobulins

BHV-1400 TRAP™ Degrader Targets Gd-IgA1 with Precision Without Reducing Healthy Immunoglobulins

DEGRADERS

BHV-1400 Single Dose SC

		Povetacicept Ph1 IV[1]	Povetacicept Ph1 SC[1]	Sibeprenlimab Ph1[2]	Atacicept[3]
No change in IgA	Drop from baseline IgA				
No change in IgG	Drop from baseline IgG				
No change in IgM	Drop from baseline IgM				
No change in IgE	Drop from baseline IgE				

BASELINE

1. https://pmc.ncbi.nlm.nih.gov/articles/PMC11532938/pdf/CTS-17-e70055.pdf 2. https://pmc.ncbi.nlm.nih.gov/articles/PMC9091613/ 3. https://www.kidney-international.org/article/S0085-2538(24)00236-9/fulltext

High Selectivity Predicts Improved Safety

DEGRADERS

	BHV-1400	**Tarpeyo®** (budesonide)	**Vanrafia®** (astrasentan)	**Filspari®** (sparsentan)	**Fabhalta®** (iptacopan)
Risk Evaluation and Mitigation Strategies (REMS)	**Not anticipated**	**NO**	**NO**	**YES**	**YES**
Black Box	**Not anticipated**	**NO**	**YES** embryo-fetal toxicity	**YES** hepatotoxicity and embryo-fetal toxicity	**YES** serious infections caused by encapsulated bacteria
Targets	**Selectively targets disease causing protein**	Targets glucocorticoid receptors	Targets endothelin receptor	Targets ETAR and AT1R	Targets complement Factor B

BHV-1400: Selective Removal of Disease-Causing Gd-IgA1 without Immunosuppression Compared to Competitors

DEGRADERS

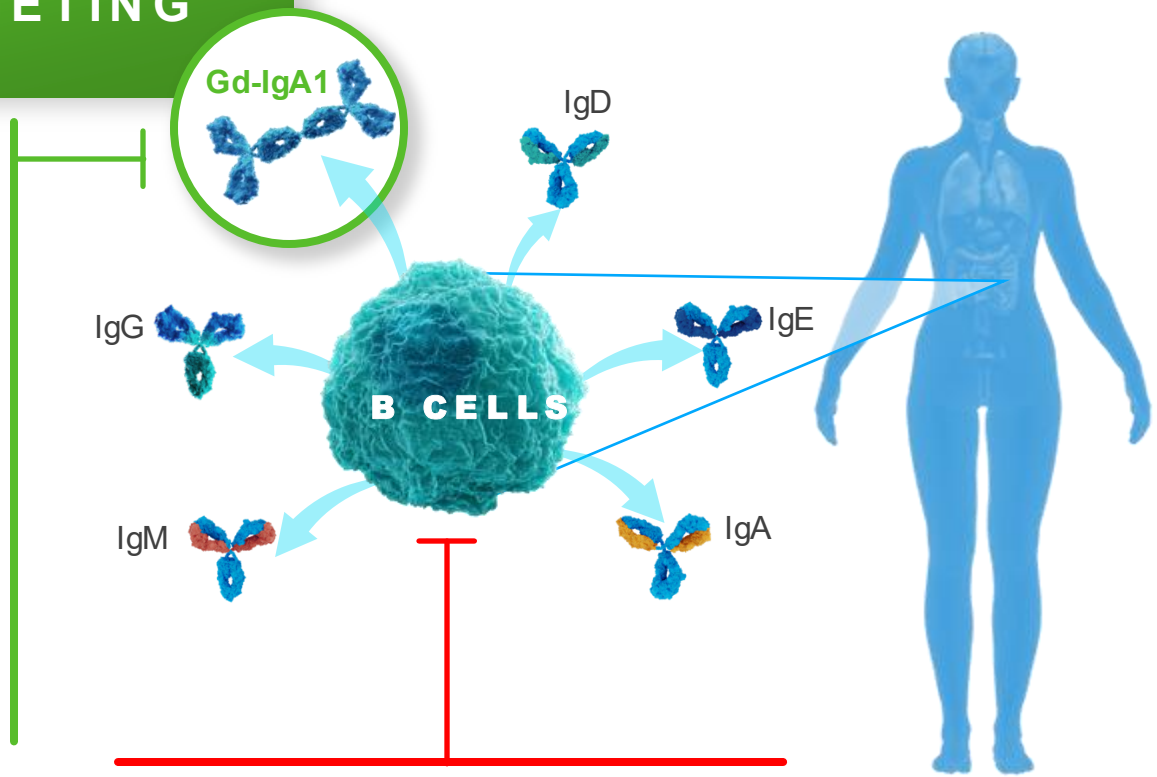
PRECISION TARGETING

biohaven

TRAP™ Degrader

BHV-1400 SELECTIVELY DEGRADES ONLY Gd-IgA1

Targeting the pathogenesis of disease without immunosuppression



TARGET B CELLS
with global immunoglobulin suppression

Povetacicept — ALPINE immunosciences, VERTEX

Atacicept — vera therapeutics

Sibeprenlimab — Otsuka

Zigakibart — CHINOOK THERAPEUTICS, NOVARTIS

Felzartamab — Biogen

BROAD IMMUNOSUPPRESSION

TARPEYO®
calliditas THERAPEUTICS

INHIBITS COMPLEMENT SYSTEM
with broad immunosuppression

FABHALTA® — NOVARTIS

RO7434656 — IONIS, Roche

ULTOMIRIS® — ALEXION, AstraZeneca

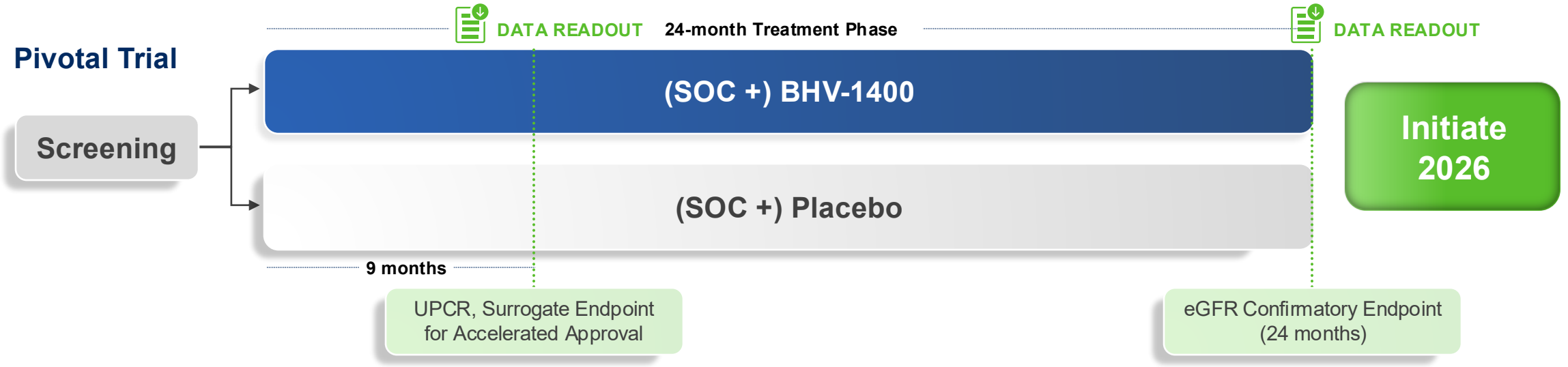
TARGET ENDOTHELIN RECEPTOR

FILSPARI® — TRAVERE THERAPEUTICS

VANRAFIA® — CHINOOK THERAPEUTICS, NOVARTIS

Harnessing Efficient IgAN Trial Design to Address a High Unmet Need
BHV-1400 Phase 2/3 Study Design

DEGRADERS



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Male and female adults with biopsy proven IgA nephropathy
SAMPLE SIZE	500 participants randomized 1:1
TREATMENT	BHV-1400 500 mg SC Q2Wk vs Placebo Q2Wk
TREATMENT DURATION	24-month treatment period
KEY ENDPOINTS	Change in UPCR at 9 months (AA), Annualized total eGFR slope

KEY POINT

Accelerated approval pathway to bring a selective, disease-specific therapeutic to treat IgAN

Professor Jonathan Barratt, PhD, FRCP

The Mayer Professor of Renal Medicine,
Department of Cardiovascular Sciences

UNIVERSITY OF LEICESTER

Galactose-Deficient IgA1 TRAP™ Degrader: IgA Nephropathy

biohaven®

Panel

MODERATOR

Tyler Van Buren
Equity Analyst
TD Cowen

PANELISTS

Tova Gardin, MD, MPP
Chief Translational Officer
Biohaven

Terry F. Davies, MD
Florence and Theodore Baumritter Professor of Medicine
Chief Emeritus, Division of Endocrinology, Diabetes and Bone Diseases
Icahn School of Medicine at Mount Sinai

Volkan Granit, MD, MSc
Senior Medical Director,
Head of Neuromuscular Disease
Biohaven

Brian McGuire, MD
Medical Director
Biohaven

Kayle Shapero, MD, PhD
Brown University Health Cardiovascular Institute
Clinical Assistant Professor of Medicine
Alpert Medical School of Brown University

Professor Jonathan Barratt, PhD, FRCP
The Mayer Professor of Renal Medicine, Department of Cardiovascular Sciences
University of Leicester

David Spiegel, MD, PhD
Professor of Chemistry and Pharmacology
Yale University

Dennis G. Moledina, MD, PhD
Associate Professor of Medicine (Nephrology)
Yale School of Medicine

Bruce Car, DVM, PhD, DACVP
Chief Scientific Officer
Biohaven

BHVN
LISTED
NYSE

Bruce Car, DVM, PhD, DACVP

Chief Scientific Officer

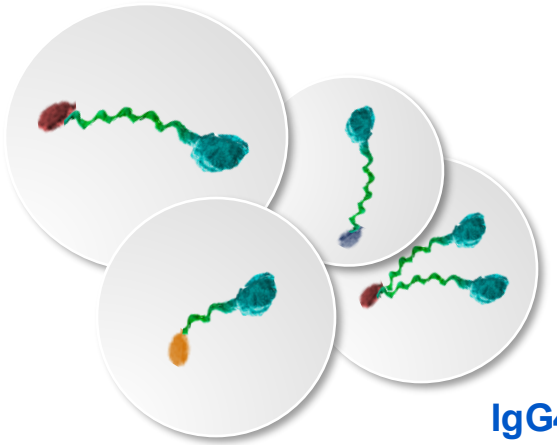
biohaven®

Discovery

biohaven®

Biohaven Discovery Provides Pipeline Sustainability and Optionality

DISCOVERY



DEGRADER PORTFOLIO
MoDEs™, TRAPs™, New Degrader Technology

	preDC	DC*
IgG4: BHV-1450		✓
IgG-Driven Disease: BHV-1320		✓
Anti-PLA2r: Nephropathy		✓
Anti-Proinsulin: Type I Diabetes		✓
Anti-TSHR: Graves' Disease	✓	
Multiple Early Targets	✓	
Technology Build		

SMALL MOLECULES AND BIOLOGIC THERAPEUTICS

preDC	DC*	
	✓	**Kv7.2/3**: Central Backups
	✓	**Kv7**: Peripheral Smooth Muscle
	✓	**TRPM3**: Peripheral and CNS Penetrant
✓	✓	**Neuroscience**: Undisclosed Targets
✓	✓	**Troriluzole**: Backups
✓		**Oncology**: Undisclosed ADC Targets
	✓	**Myostatin Inhibitor**: Backup

*named or planned development candidate within current quarter

KEY POINT

Discovery drug platforms have delivered 6 INDs and multiple drug candidates in 3 years

Degrader Platform Dramatically Shortens Timelines and Reduces Costs

DISCOVERY

Beyond 1300,1310, 1400,1600…

IgG4

Anti-PLA2r

Anti-TSHR

Anti-Proinsulin

IgM

AAV9

< 2 years

Efficient Safety Assessment

Streamlined Efficacy Evaluation

Modular Drug Design and Synthesis

IND **Clinical** **Commercial**

Allows for aggressive IP filing while preserving commercial exclusivity

IgG4, Immunoglobulin G4; **PLA2r**, phospholipase A2 receptor; **TSHR**, thyroid-stimulating hormone receptor; **IgM**, Immunoglobulin M; **AAV9**, adeno-associated viral.

KEY POINT

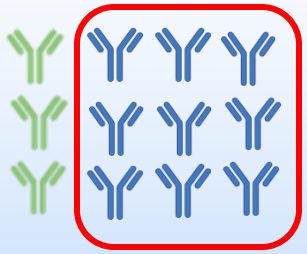
Degrader platform produces high value assets with unmatched speed

Expanding the Degrader Platform Into Focused Research Areas

DISCOVERY

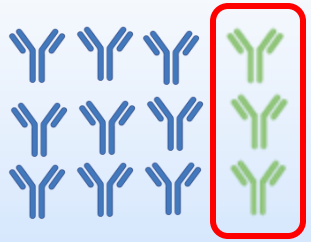
- **Neuro and Neuromuscular**: MG, MuSK, CIDP, LRP4, Guillain Barré, MS, MOGAD, NMO*
- **Renal**: IgAN, PLA2r, IgG4, GBM, nephrin-1, cortico-interstitial fibrosis, ADAs*
- **Hematology**: Gammopathies, TTP, wAIHA, CAG, IgA1 and ANCA-associated vasculitis*

Aligning Disease Indications with Appropriate Degrader Technology



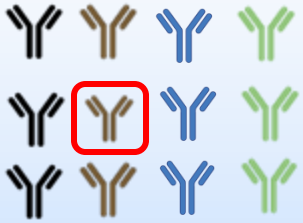
MoDE™ pan-IgG

e.g., Graves'



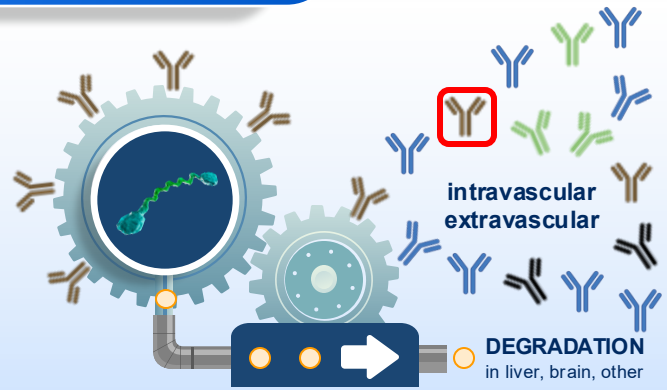
MoDE IgG Subclass

e.g., MuSK myasthenia gravis



TRAP™ Targeting AAb

e.g., Type I Diabetes



Novel Approaches

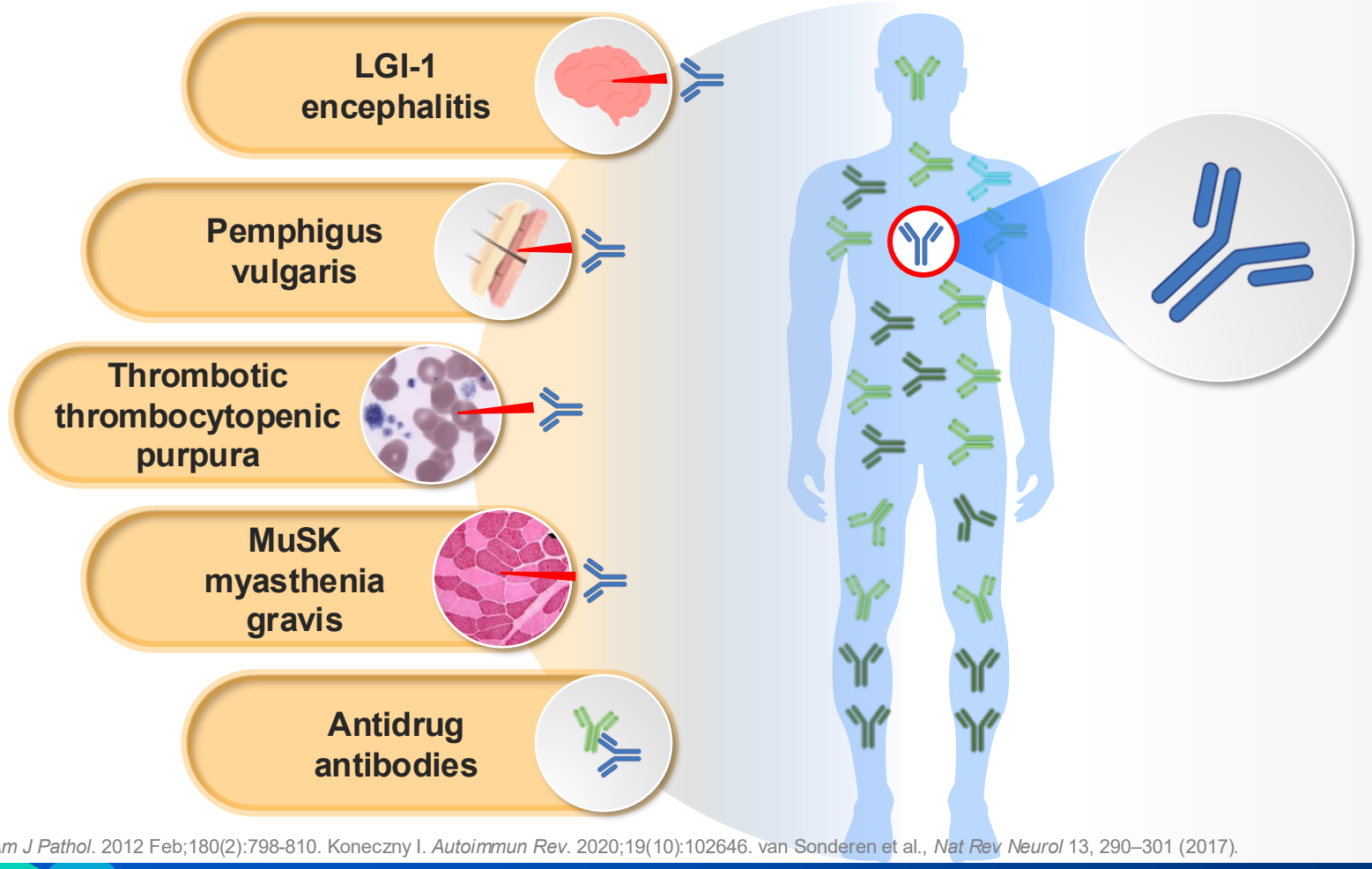
e.g., Light chain gammopathy

*Indications are exemplary, many of which are early programs

MG, Myasthenia gravis; **MuSK**, muscle-specific kinase; **CIDP**, chronic Inflammatory demyelinating polyneuropathy; **LRP4**, low-density lipoprotein receptor-related protein 4; **MS**, multiple sclerosis; **MOGAD**, myelin oligodendrocyte glycoprotein antibody disease; **NMO**, neuromyelitis optica; **IgAN**, IgA nephropathy; **PLA2r**, phospholipase A2 receptor; **IgG4**, Immunoglobulin G4; **ADAs**, Autosomal Dominant Alport Syndrome; **TTP**, thrombotic thrombocytopenic purpura; **wAIHA**, warm autoimmune hemolytic anemia; **CAG**, cytarabine, aclarubicin, and G-CSF; **IgA1**, immunoglobulin A1; **ANCA**, anti-neutrophil cytoplasmic antibodies.

BHV-1450: Deep Removal of IgG4 for IgG4-Mediated Diseases

DISCOVERY



IgG4-related diseases result in target organ inflammation and fibrosis

- Pancreatitis
- Sclerosing cholangitis
- Retroperitoneal fibrosis
- Tubulointerstitial nephritis
- Mikulicz's disease and sclerosing sialodacryoadenitis
- Riedel's thyroiditis
- Interstitial lung disease

Mori S et al., *Am J Pathol*. 2012 Feb;180(2):798-810. Koneczny I. *Autoimmun Rev*. 2020;19(10):102646. van Sonderen et al., *Nat Rev Neurol* 13, 290–301 (2017).

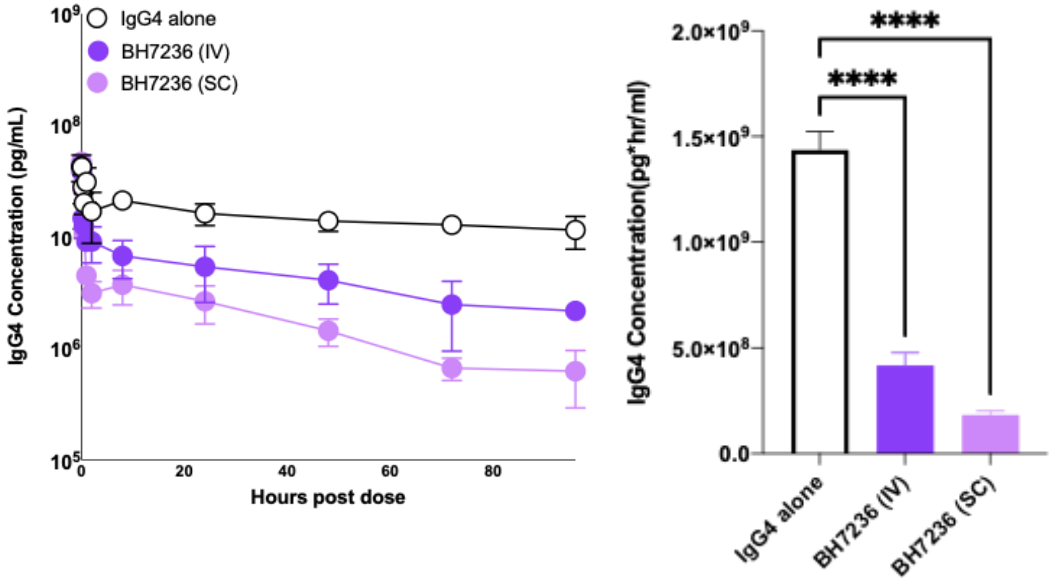
KEY POINT

BHV-1450 degrades the minor (4%) IgG4 subclass. IgG1, IgG2 & IgG3 remain unchanged

BH7236 (BHV-1450): Potent IgG4-Depletion and High SC Bioavailability

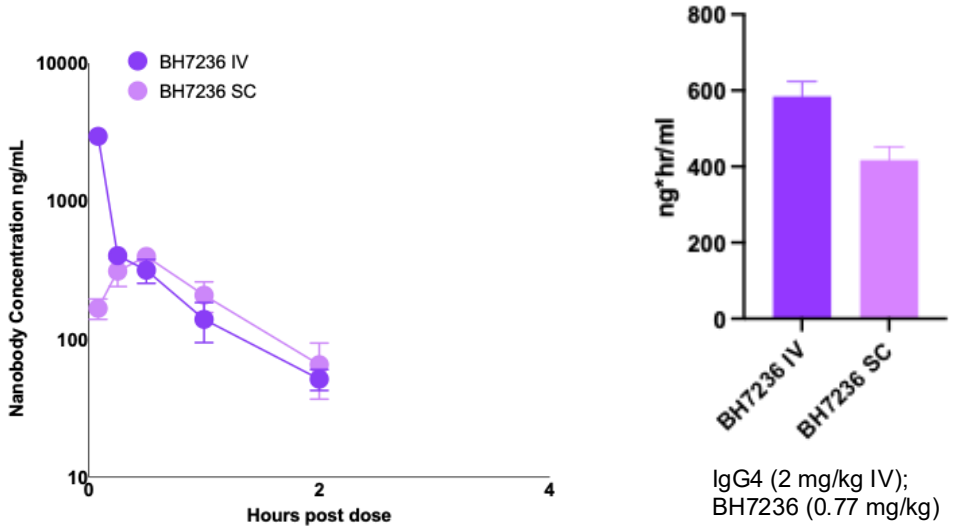
DISCOVERY

PD: IgG4-Depletion in Mice



IgG4 (2 mg/kg IV); BH7236 (0.77 mg/kg)

PK: SC vs IV Bioavailability in Mice

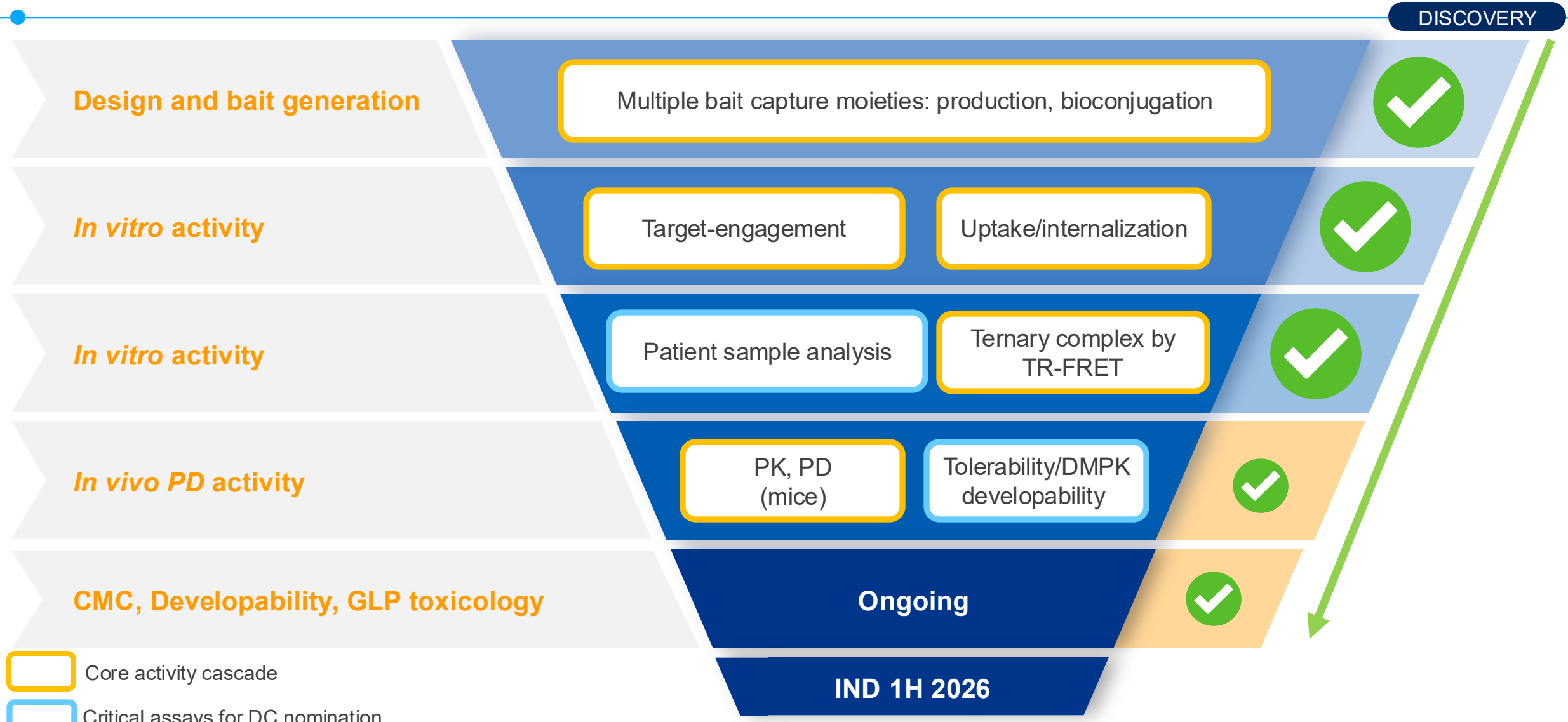


IgG4 (2 mg/kg IV);
BH7236 (0.77 mg/kg)

Lead molecules	Route	PD – IgG4 depletion (%)	PK – (SC/IV) BA (%)	Tolerability (≤100 mg/kg)
BH7236	IV	67	71%	Well-tolerated
	SC	87		

Of 4 optimized leads, BH7236 selected as best candidate for a self injectable device

BHV-1450: Advancing a Versatile IgG4 MoDE™ to Patients



DIVERSIFIED PORTFOLIO

TOP AREAS OF INNOVATION

RARE DISEASE

ONCOLOGY

RENAL

CARDIOVASCULAR

OBESITY

NEUROSCIENCE

IMMUNOLOGY & INFLAMMATION

CLINICALLY VALIDATED MoDE™ AND TRAP™ DEGRADERS

ADVANCING CANCER TREATMENTS

Integrated **DISCOVERY ENGINE**

PIONEERING THERAPIES FOR RARE DISEASES

Working Towards Commercialization of **NOVEL THERAPEUTICS**

biohaven®

INNOVATING
EXECUTING
CREATING VALUE

BHVN LISTED NYSE