biohaven®

DAYS MATTER™

Corporate Presentation

January 2025

Forward-Looking Statement

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 clinical trials for our taldefgrobep alfa, troriluzole, BHV-2100, BHV-7000, BHV-8000, BHV-1300, BHV-1310, BHV-1510 and BHV-1530 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-1400, BHV-1500, and BHV-1600. 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, 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; the timing and outcome of expected regulatory filings; complying with applicable US regulatory requirements; the potential commercialization of Biohaven's product candidates; the potential for Biohaven’s product candidates to be first-in-class or best-in-class therapies; and the effectiveness and safety of Biohaven's product candidates. 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 is 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.

DAYS MATTER™

biohaven®

TWO YEARS SINCE SPIN-OFF

biohaven®

DIVERSIFIED
into top areas of
INNOVATION

- IMMUNOLOGY & INFLAMMATION
- NEUROLOGY
- OBESITY
- ONCOLOGY
- CARDIOVASCULAR
- RENAL
- RARE DISEASE

Focused on Days Matter™
COMMERCIALIZATION OF NOVEL TXs

INCREASED MARKET CAP
10X

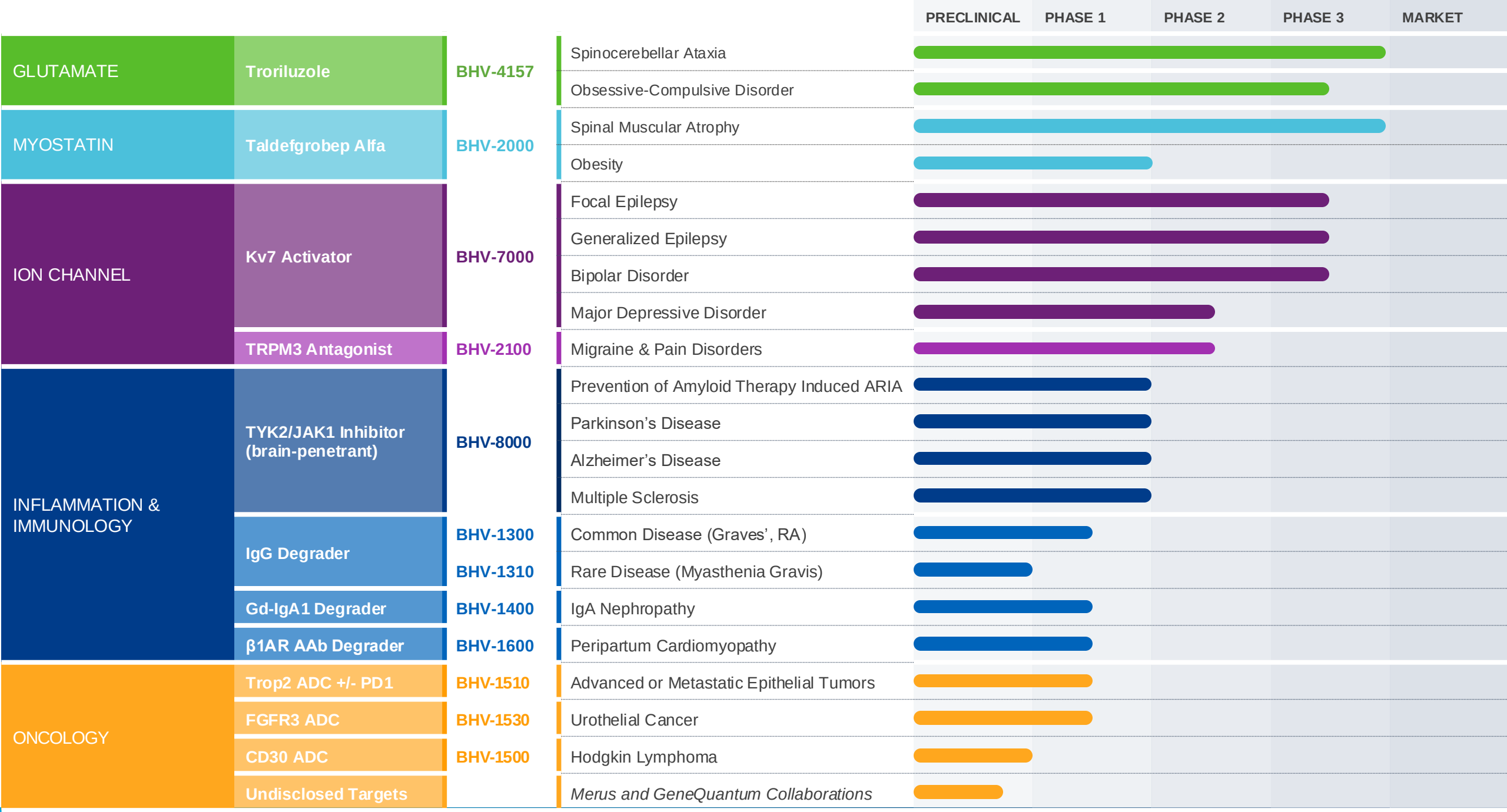
POSITIONED FOR
FUTURE VALUE CREATION

ADVANCING CANCER TREATMENTS
with strategic partnerships

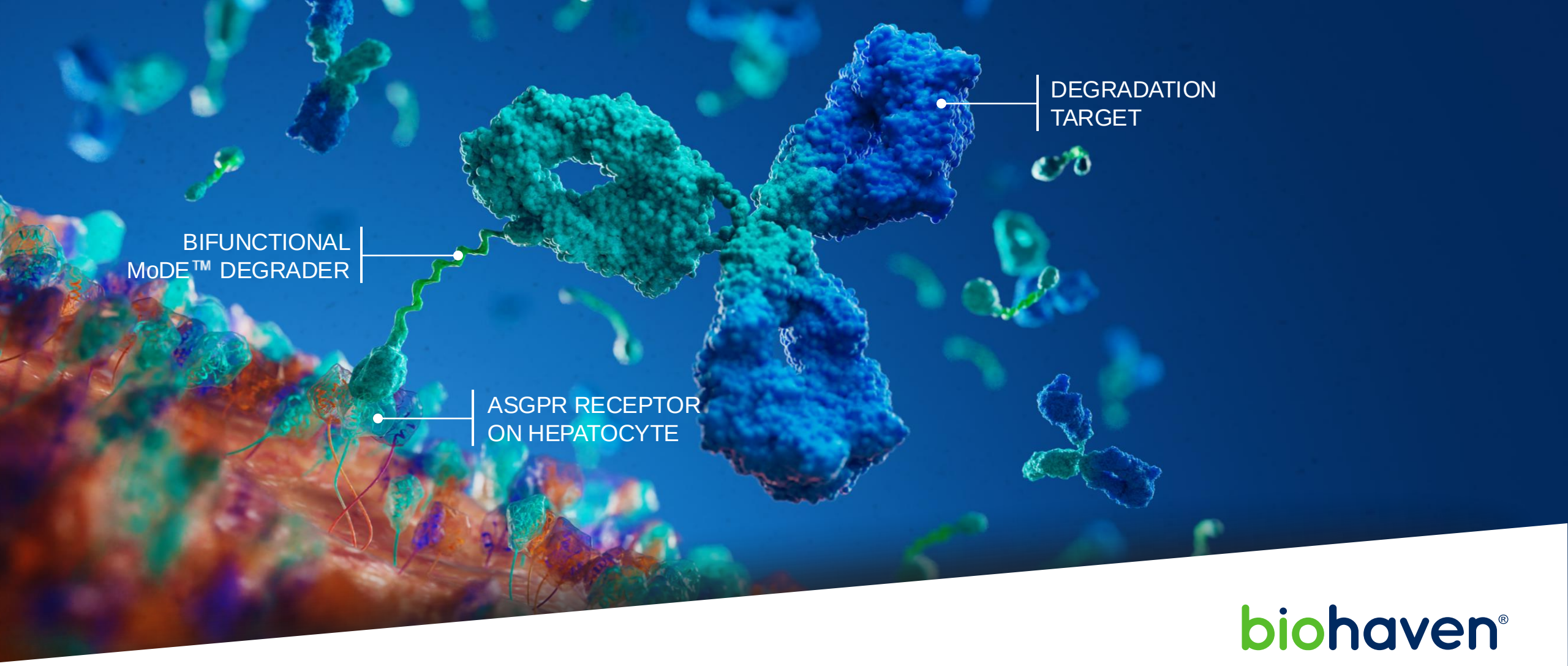
PIONEERING
therapies for rare diseases including
SMA & SCA

CLINICALLY VALIDATED NEXT-GEN TRAP™ DEGRADERS
Targeted removal of aberrant proteins

Integrated
DISCOVERY ENGINE



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



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EXTRACELLULAR DEGRADERS

RAPID AND SELECTIVE REMOVAL OF DISEASE-CAUSING PROTEINS

MoDE™ Platform: Degraders Designed for Real-life and to Preserve Healthy Immune Functioning

- Maximizes selectivity to treat disease while minimizing side effects
- Short half-life enables concomitant administration with Fc-biologics
- Allows for subcutaneous and autoinjector formulations

Advancing Next-Generation TRAP™ (Targeted Removal of Aberrant Proteins) Degraders:

- Only degrades specific disease-causing targets while leaving healthy immune system completely intact
- New Phase 1 clinical trial data demonstrates deep, rapid, and selective lowering of very specific targeted species

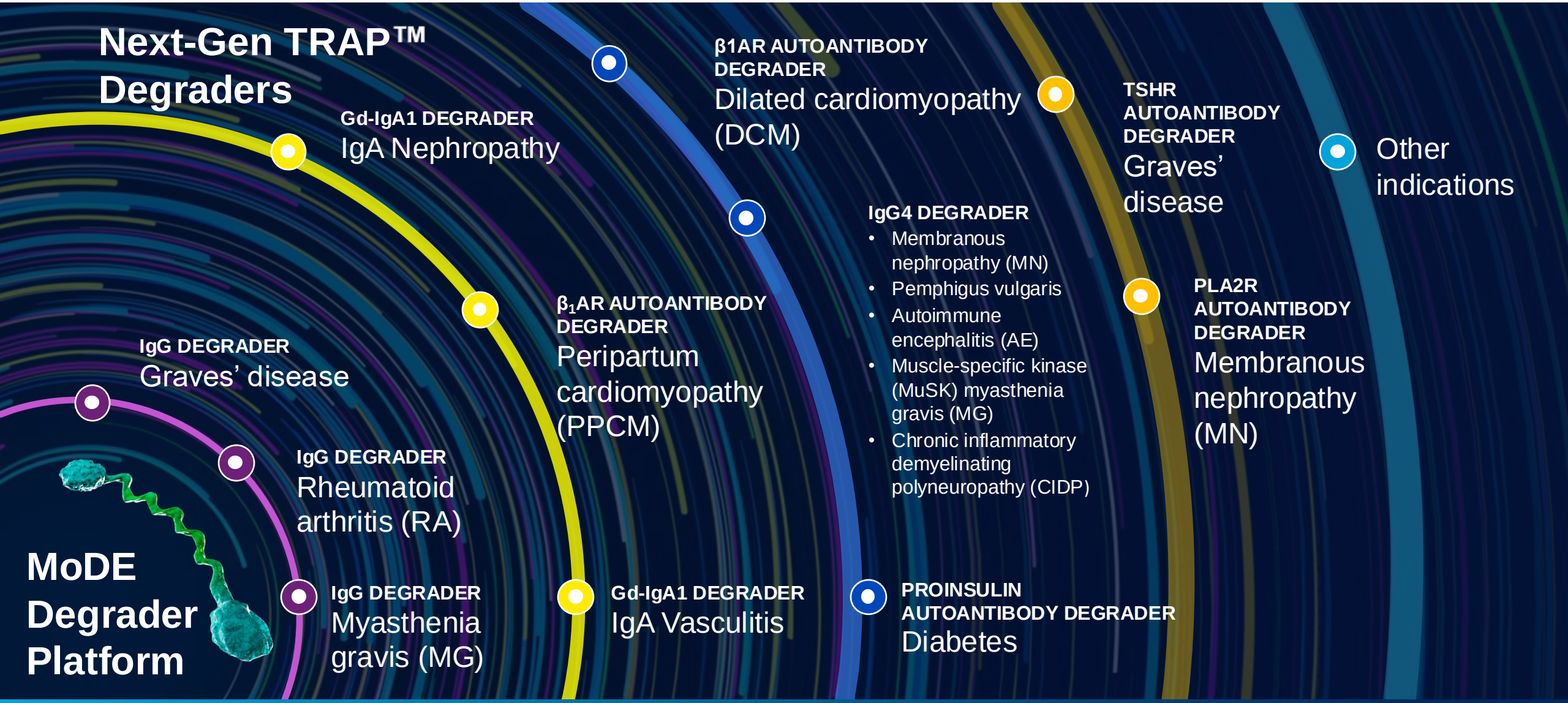
3 Exciting New Indications

IgA Nephropathy | Peripartum Cardiomyopathy | Graves' Disease

BREAKING NEWS

Emerging clinical data with BHV-1400 shows rapid, deep, and selective removal of only galactose-deficient IgA1 while preserving healthy immune function

MoDE™ Degrader Platform Technology: Driving Toward Targeted Removal of Disease-Causing Proteins



Degrader Platform Technology

FAST AND DEEP
Removes disease-causing proteins within hours

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

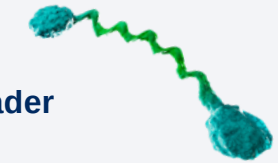
SELECTIVE
Designed to target specific pathogenic species for maximal efficacy and minimal side effects

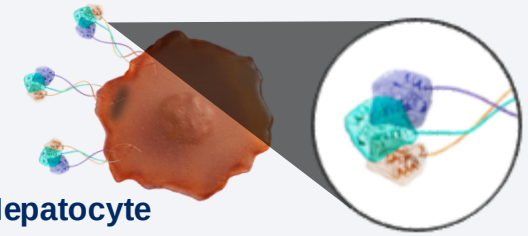
TUNABLE
- Level of degradation carefully modulated by dose level and frequency
- Employs body's natural mechanism for removal of senescent proteins

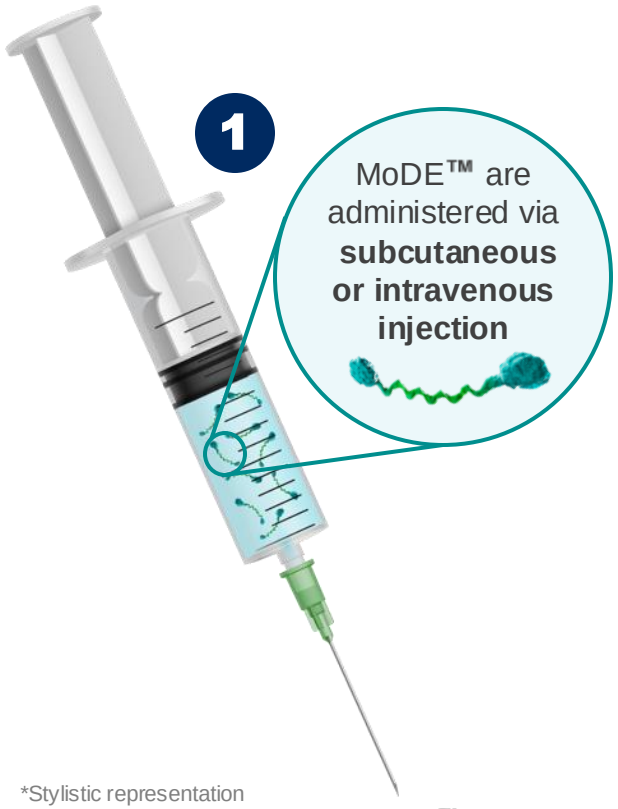
biohaven®

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

Legend

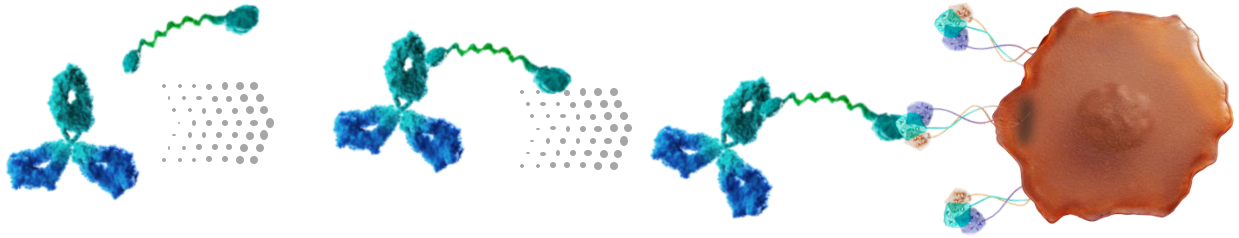






2

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



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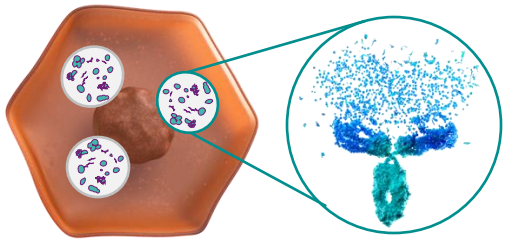
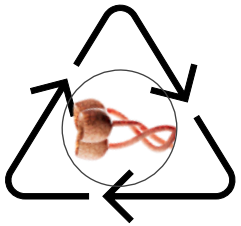


- Internalized target is rapidly degraded in hepatic lysosomes
- Degree of target degradation is precisely controlled

4



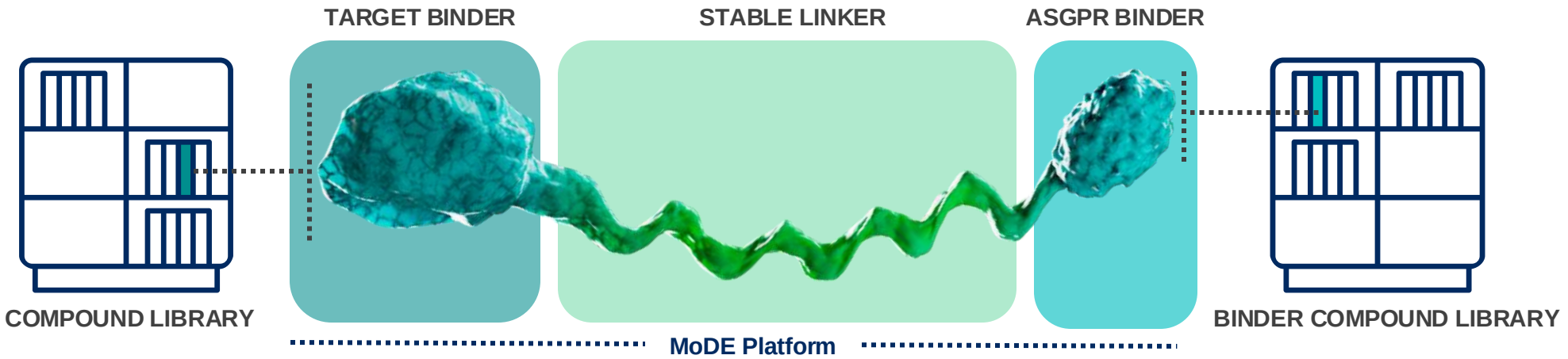
- ASGPRs are rapidly recycled
- Optimized safety and efficacy is achieved through balancing of relative affinities for ASGPR and target protein

*Stylistic representation

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

A Transformational MoDE Drug Platform: Molecular Degraders of Extracellular Proteins (MoDE™)

Precisely balanced components selected for optimal efficacy, safety, and product profile



- Efficiently removes immune targets causing disease
- Fast onset and potential for > 90% deep reduction in target
- Selective targeting of proteins avoids immunosuppression
- Ability to adjunctively dose Fc biologics
- Accelerate IND timelines (12–18 mo)

IND, Investigational New Drug Application.

KEY POINT

Biohaven's MoDE platform is rapidly generating drug candidates for multiple diseases

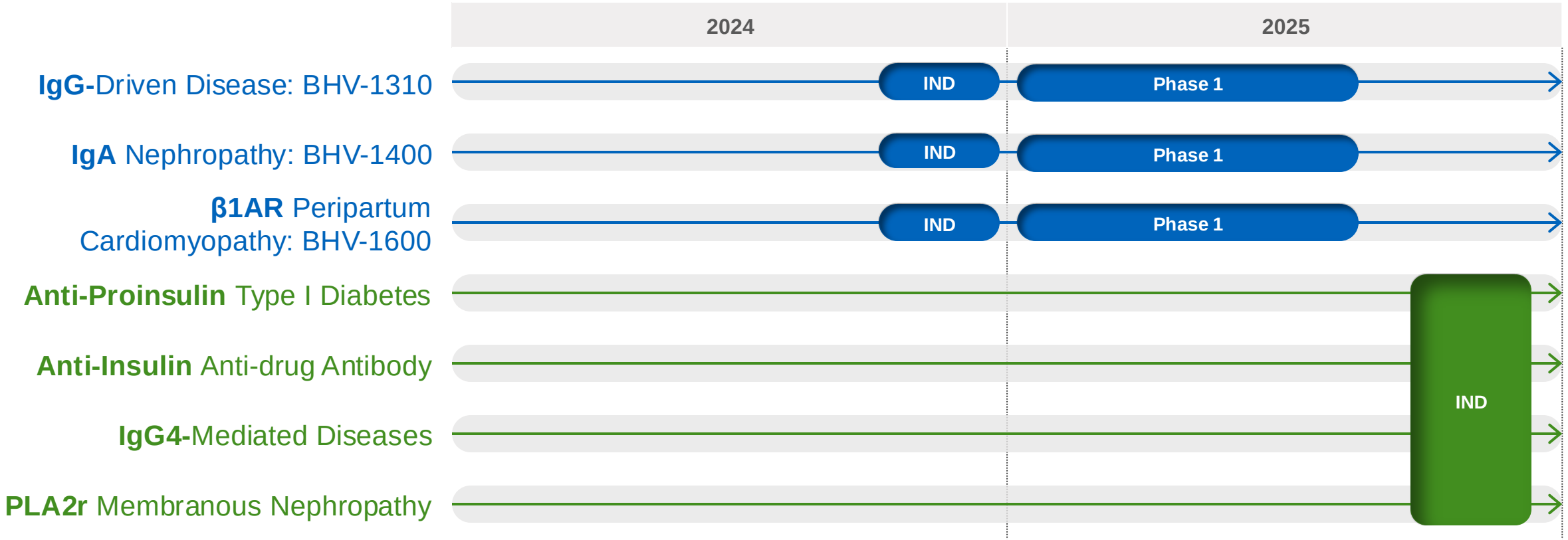
Positive Differentiation Predicted for Bispecific Degraders Over Competition

Antibody lowering therapeutic modalities

Drug Modality	Discovery cycle time	Speed of onset	Depth of Ig-lowering	Administer with SoC	Immuno-suppression
IgG Degraders	●●●●	●●●○	●●●○	●●●○	●○○○
Autoantibody-specific degraders	●●●●	●●●○	●●●○	●●●○	○○○○
FcRN-inhibitor	●●○○	●○○○	●●○○	●○○○	●●○○
Imlifidase	●●○○	●●●●	●●●●	●●●○	●●●●
BLyS/APRIL-i	●○○○	●○○○	●●○○	●●●○	●●●○

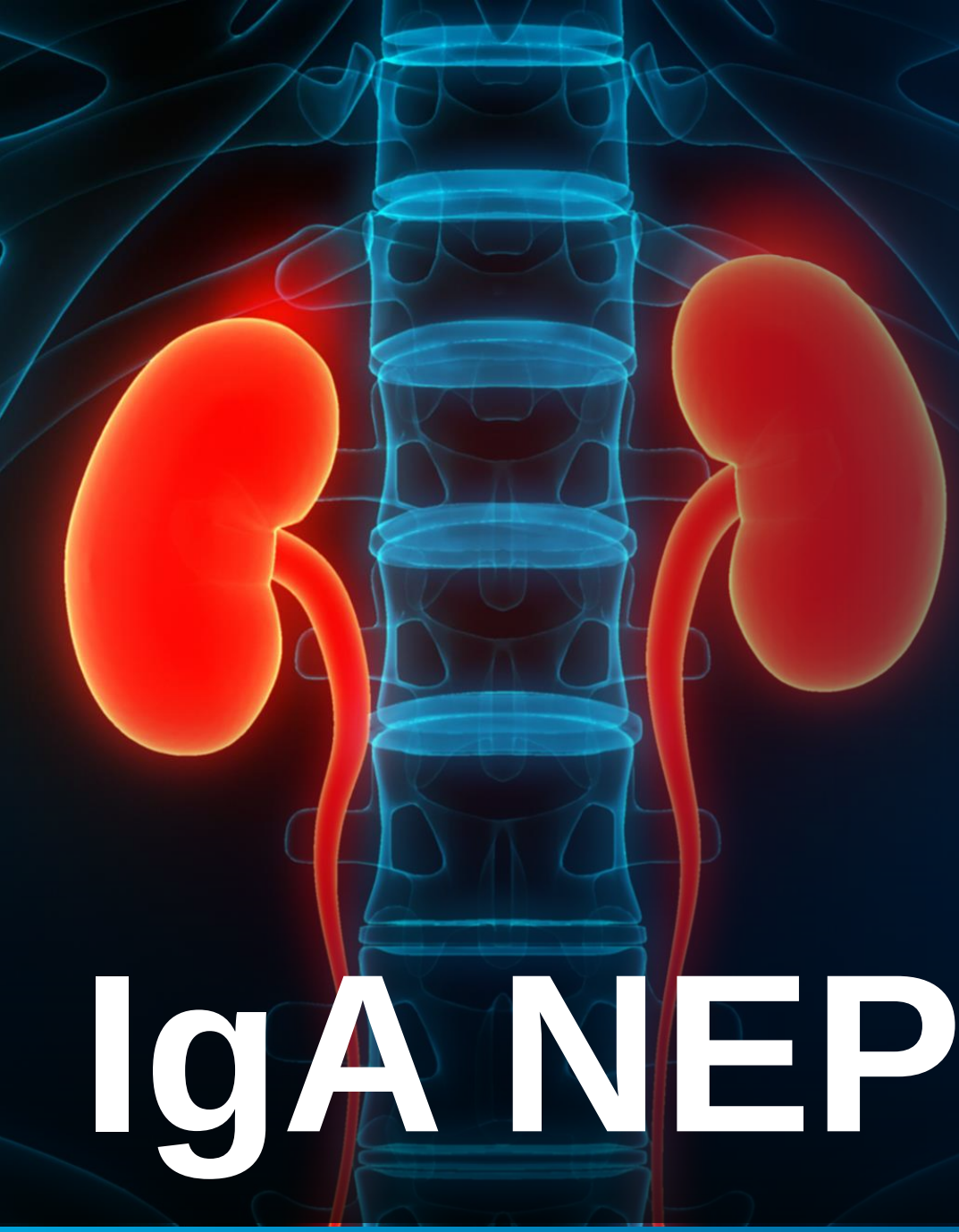
Scoring of properties represent qualitative projections, based on MOA and available data.

MoDEs: Multiple Asset Opportunities and Potential Timelines



KEY POINTS

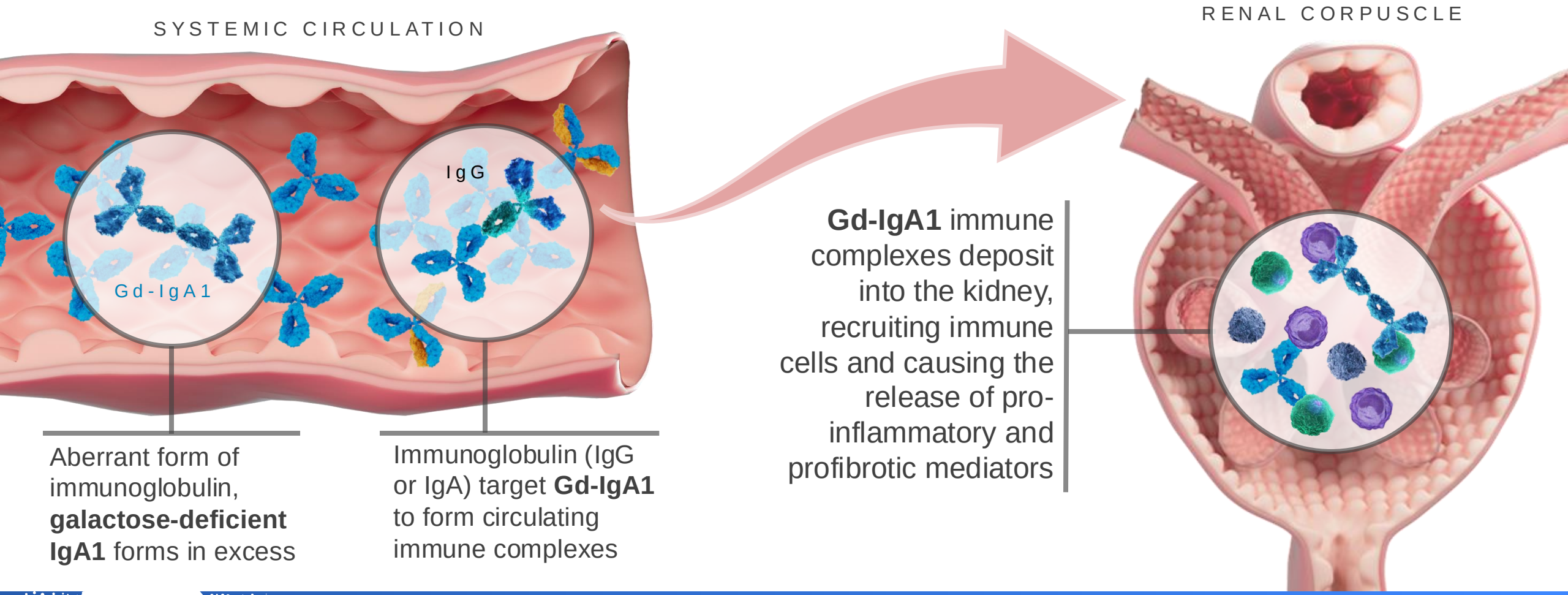
- Three MoDEs on schedule for IND this year
- Four new targets announced and rapidly progressing



- ✓ BHV-1400: Potential to treat by removing pathogenic species without chronic immunosuppression
- ✓ Robust science indicating disease is galactose-deficient IgA1-driven
- ✓ Biomarker endpoint with well-established accelerated approval pathway

IgA NEPHROPATHY

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



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

Immunoglobulin (IgG 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

KEY POINT

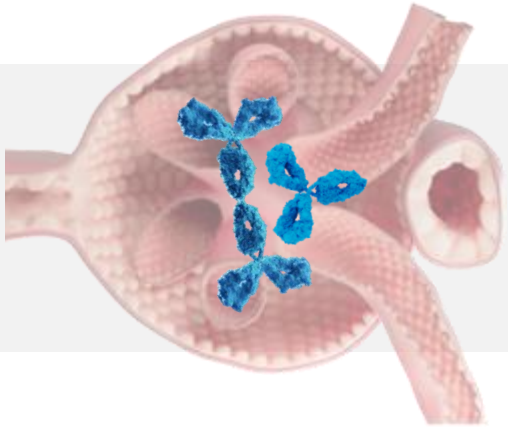
No therapy selectively targets the pathogenic nidus of disease, Gd-IgA1...
UNTIL NOW

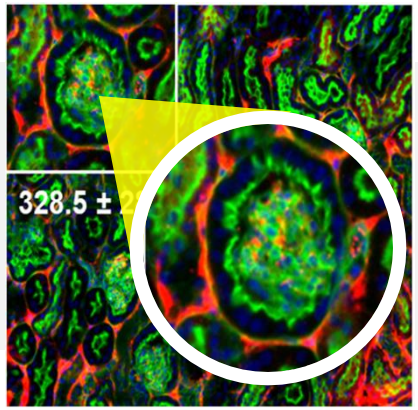
BHV-1400 Rapidly Removes Galactose-Deficient IgA1 from Circulation and from the Renal Glomerular Mesangium *in vivo* in Pre-Clinical Studies

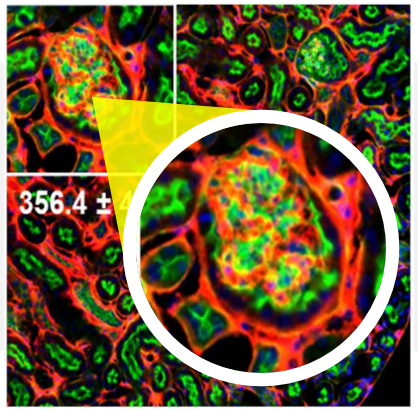
RENAL CORPUSCLE

1 HOUR **6 HOUR**

Gd-IgA1
+ **Vehicle**

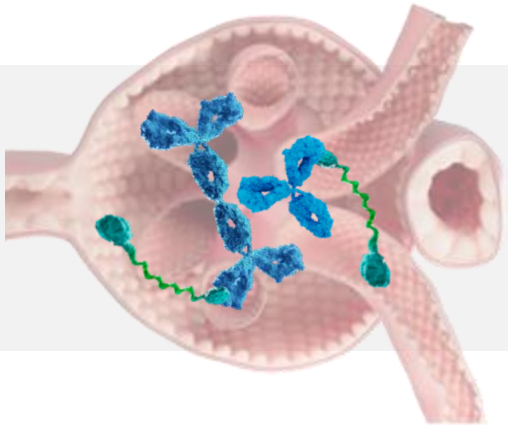


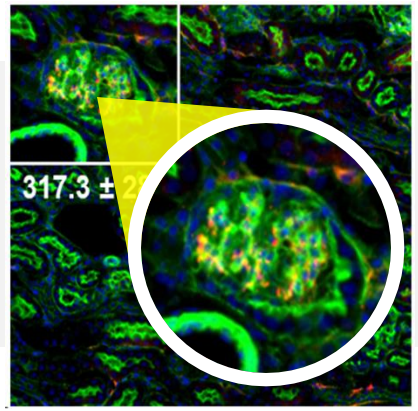


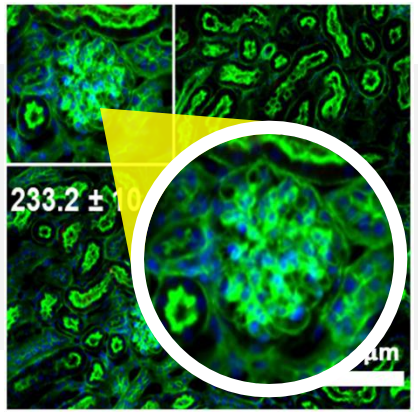


In the Absence of BHV-1400, Galactose-Deficient IgA1 (red) Accumulates in the Renal Glomerulus

Gd-IgA1
+ **BHV-1400**

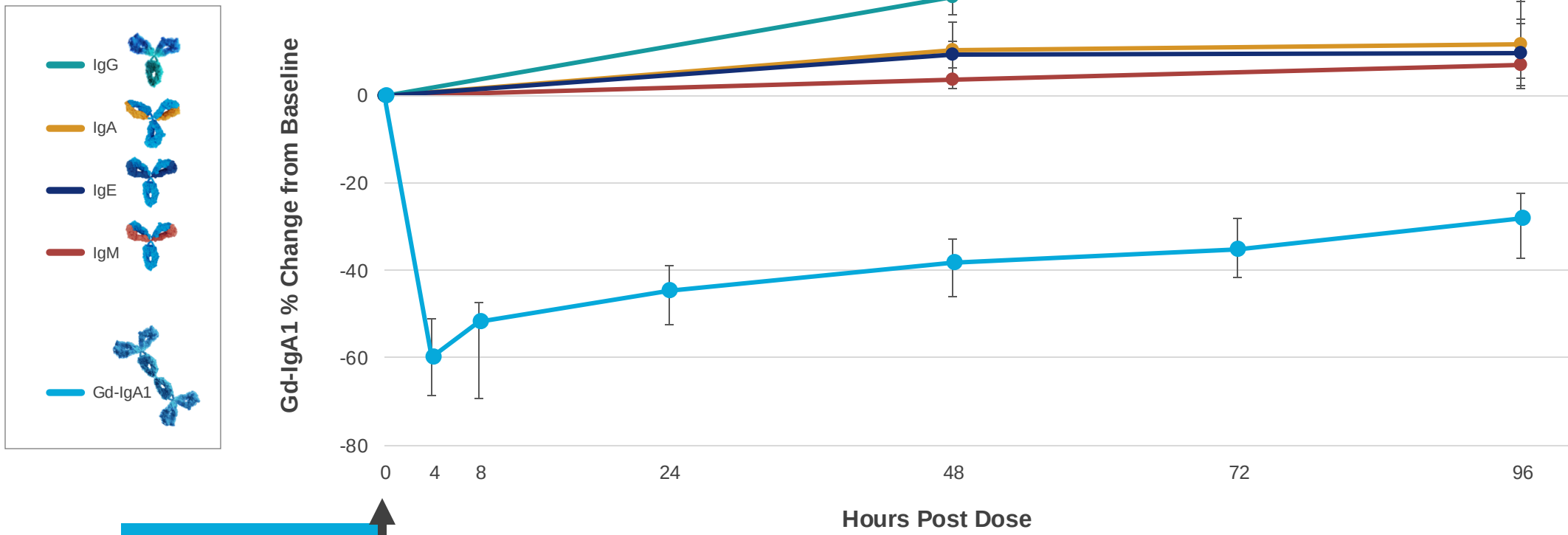






BHV-1400 Rapidly Clears Galactose-Deficient IgA1

Preliminary Phase 1: Selective and Deep Removal of Gd-IgA1 Within Hours



BHV-1400 125 mg Single dose

> 60% Gd-IgA1 LOWERING within 4 hours

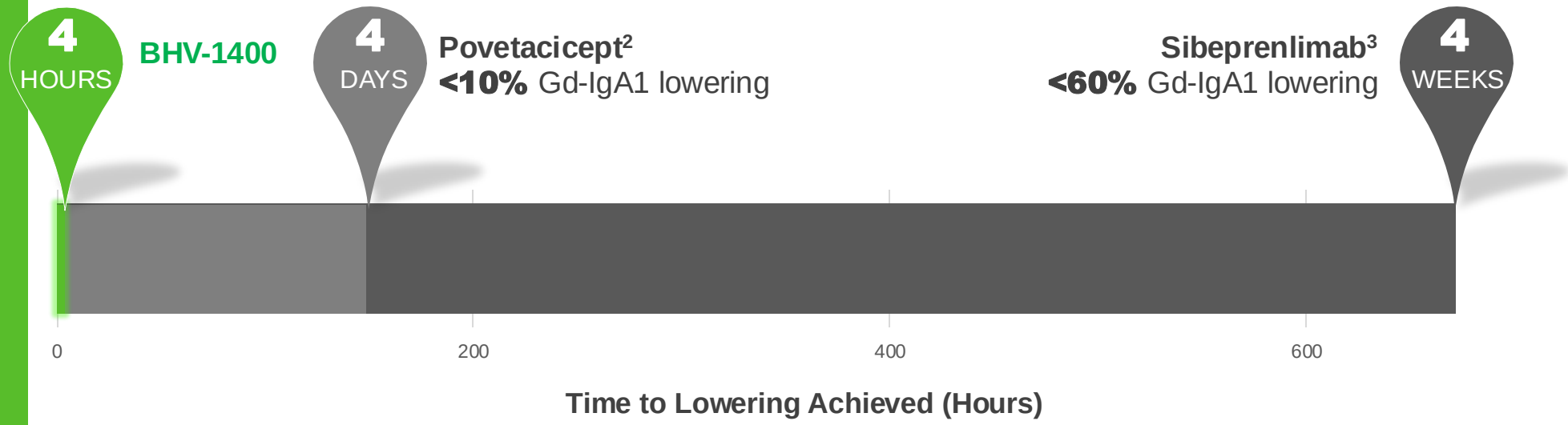
BREAKING NEWS

BHV-1400 at the lowest SAD cohort rapidly and selectively removes 60% of Gd-IgA1 while preserving normal immunoglobulins (IgG, IgE, IgA, IgM)

BHV-1400 Degrades Gd-IgA1 Rapidly: Timeline of Earliest Reported Gd-IgA1 Lowering Across Key Market Competition

BHV-1400

60% Gd-IgA1 lowering in 4 hours[1]



1. Lowering numbers reported for the median from the first and lowest BHV-1400 SAD cohort and for mean lowering for the highest dose SAD cohorts for Sibeprenlimab (12.0 mg/Kg) and Povetacicept (960 mg) 2. Davies et al. A first-in-human, randomized study of the safety, pharmacokinetics and pharmacodynamics of povetacicept, an enhanced dual BAFF/APRIL antagonist, in healthy adults. Clin Transl Sci. 2024 Nov;17(11):e70055. doi: 10.1111/cts.70055. PMID: 39494621; PMCID: PMC11532938. 3. Mathur et al. Safety, tolerability, pharmacokinetics, and pharmacodynamics of VIS649 (sibeprenlimab), an APRIL-neutralizing IgG2 monoclonal antibody, in healthy volunteers. Kidney In Rep. 2022 Feb 8; 7(5): 993-1003. doi: 10.1016/j.ekir.2022.01.1073. PMID: 35570983; PMCID: PMC9091613.

KEY POINT

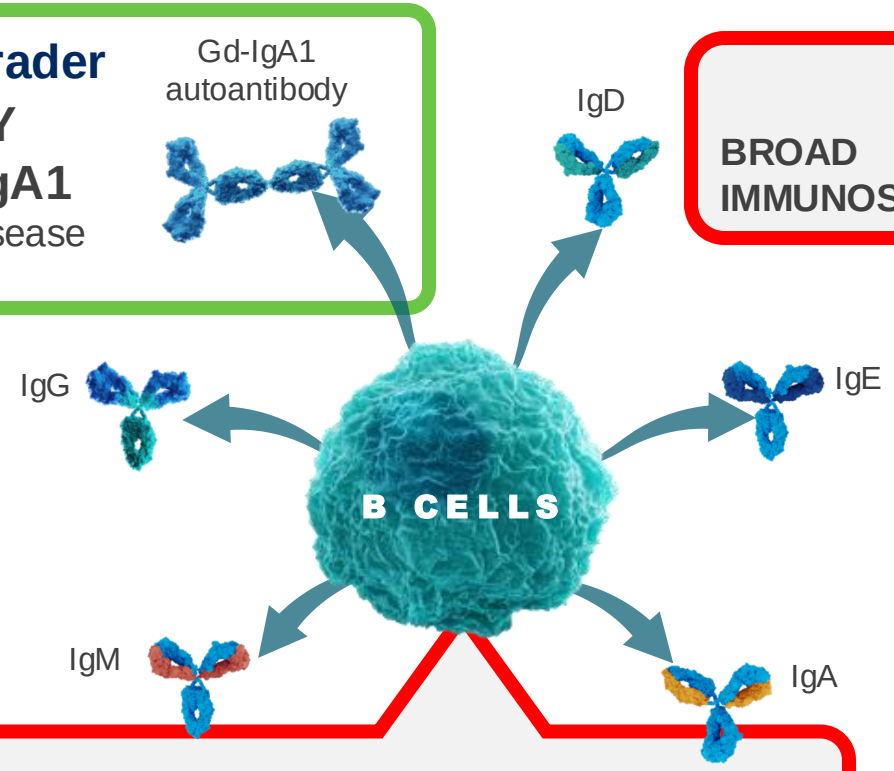
Lowest dose of BHV-1400 tested shows deep reductions of Gd-IgA1 within hours

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

biohaven TRAP™ Degrader

BHV-1400 SELECTIVELY DEGRADES ONLY Gd-IgA1

Targeting the pathogenesis of disease without immunosuppression



BROAD IMMUNOSUPPRESSION

Tarpeyo (calliditas THERAPEUTICS)

INHIBITS COMPLEMENT SYSTEM

With broad immunosuppression

Fabhalta (NOVARTIS)

RO7434656 (IONIS, Roche)

Ravulizumab (Ultomiris) (CHINOOK THERAPEUTICS, NOVARTIS)

TARGET B CELLS

with global immunoglobulin suppression

Povetacicept (ALPINE Immunosciences, VERTEX)

Atacicept (vera therapeutics)

Sibeprenlimab (Otsuka)

Zigakibart (CHINOOK THERAPEUTICS, NOVARTIS)

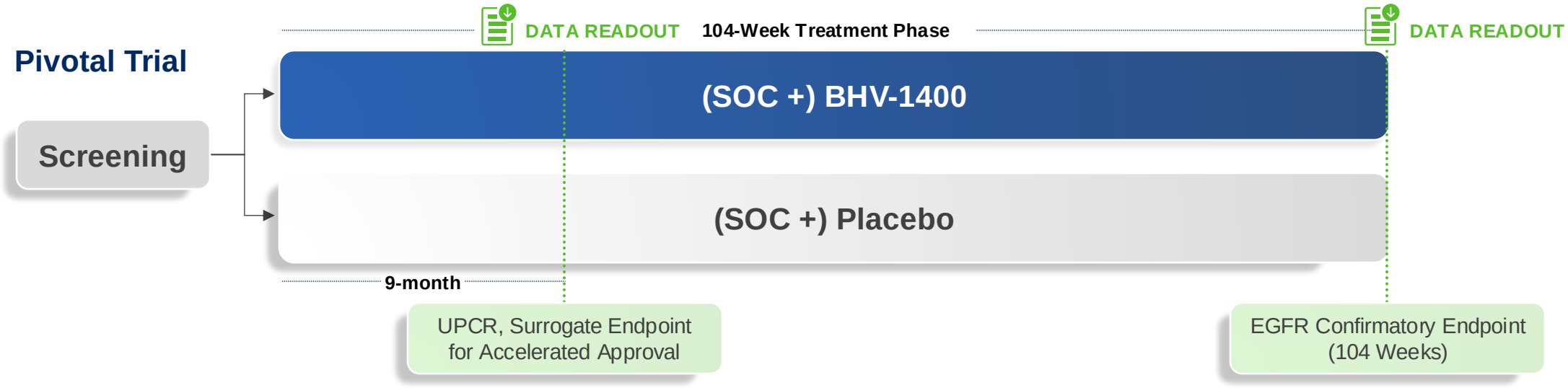
Felzartamab (Biogen)

TARGET ENDOTHELIN RECEPTOR

Filspari (TRAVERE THERAPEUTICS)

Astrasentan (CHINOOK THERAPEUTICS, NOVARTIS)

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



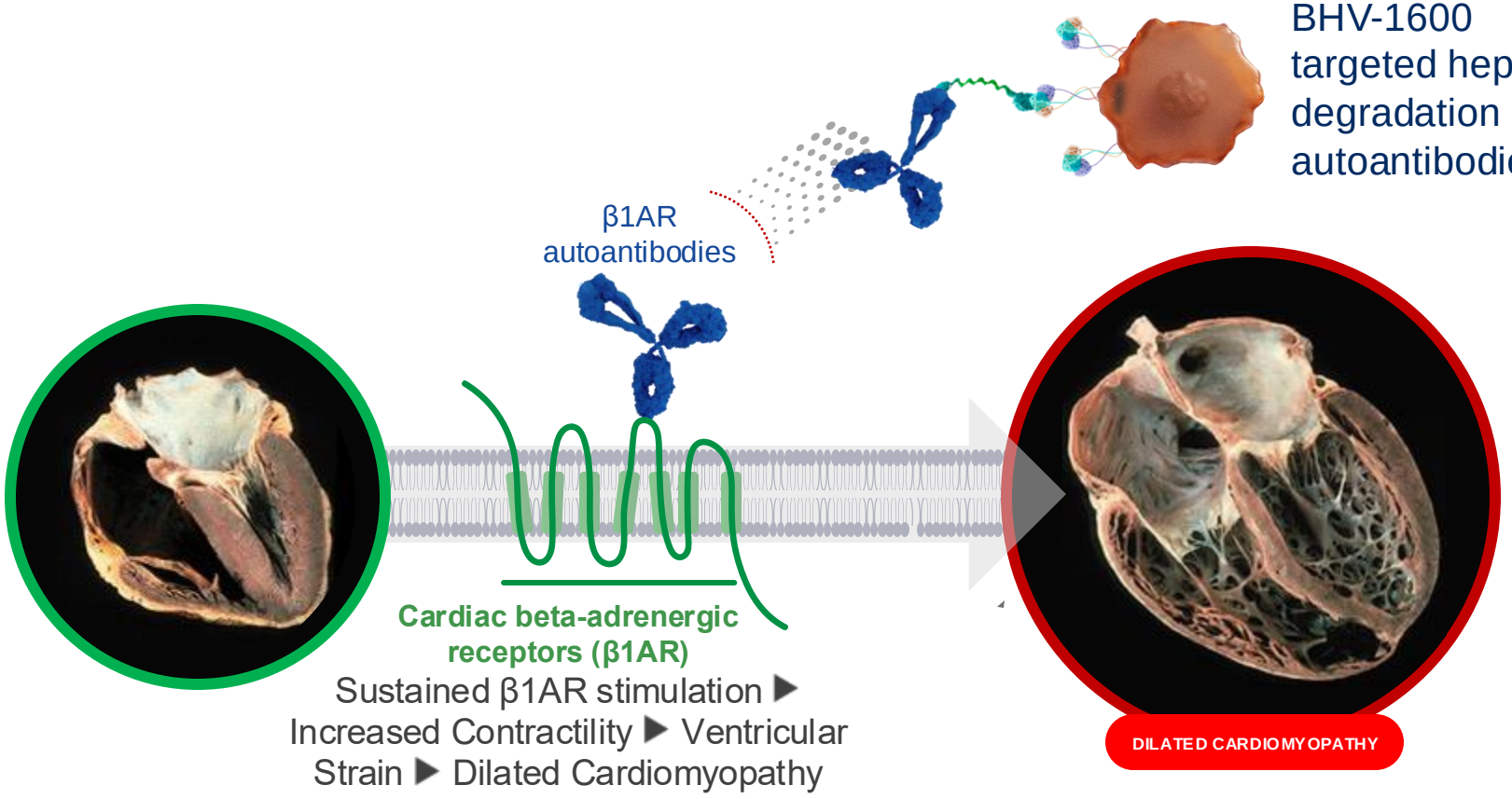
KEY POINT

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

- ✓ BHV-1600: Potential to treat through selective removal of pathogenic autoantibody without chronic immunosuppression
- ✓ High unmet need: rare disease affecting new mothers with no approved treatment
- ✓ Robust science highlighting ß1AR-autoantibodies as pathogenic
- ✓ Biomarker endpoint with FDA-aligned path forward for accelerated approval

PERIPARTUM CARDIOMYOPATHY

BHV-1600, a Novel Investigational Treatment for Peripartum Cardiomyopathy



PERIPARTUM CARDIOMYOPATHY:

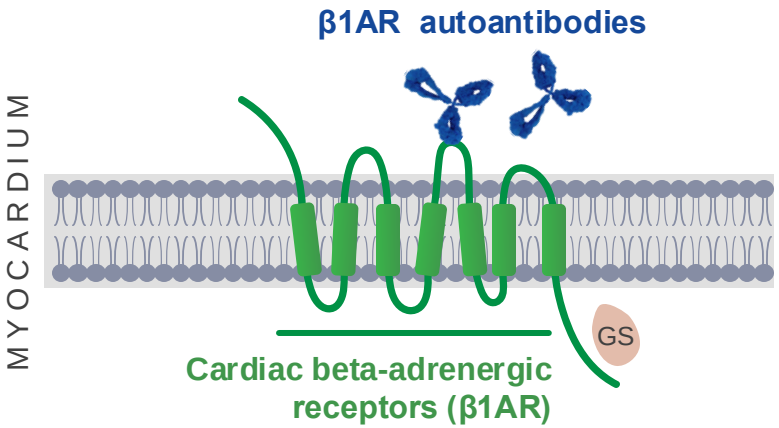
- A rare disease with high unmet need
- Maternal mortality highest since 1965 and primary contributor is PPCM with mortality rates reported up to 20%
- 10% go on to require mechanical support (LVAD or heart transplant)
- BHV-1600 degrades ß1AR autoantibodies to potentially prevent irreversible heart failure

KEY POINT

BHV-1600 degrades ß1AR autoantibodies to potentially prevent permanent heart failure in previously healthy mothers

BHV-1600 Selectively Depletes β1-Adrenergic Receptor Autoantibodies

Agonistic β1AR Autoantibodies Drive Cardiac Pathology[1,2]



Sustained myocardial stimulation

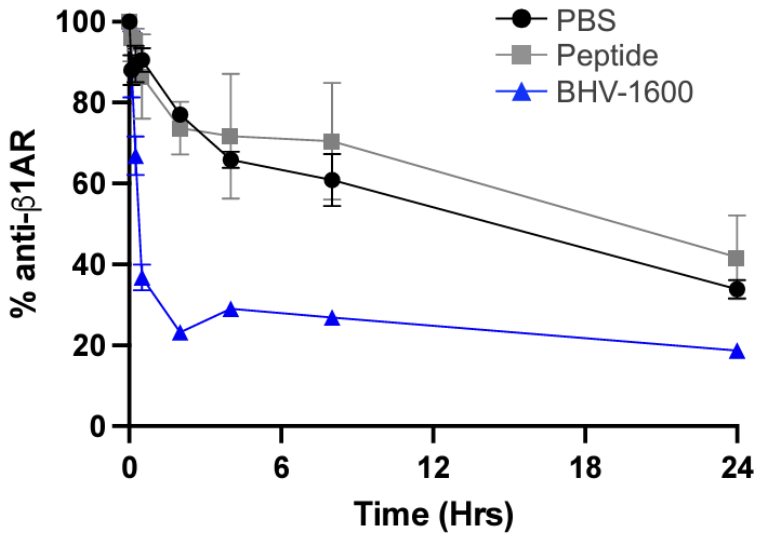
↓

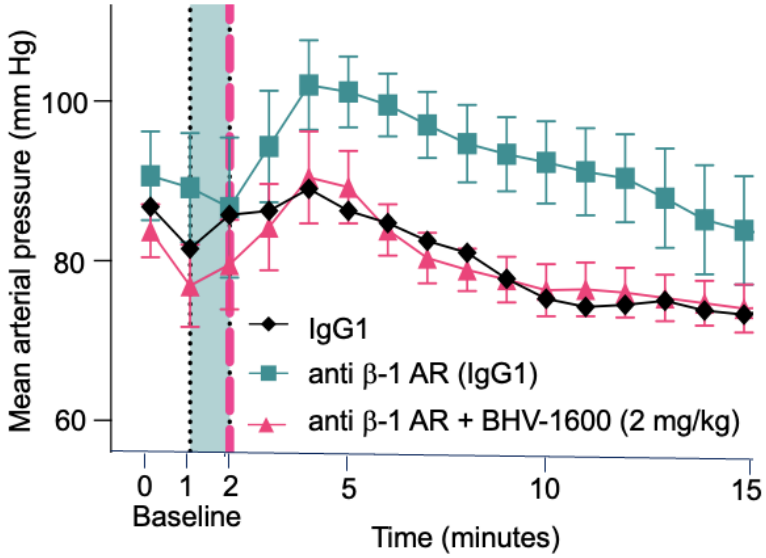
Increased heart rate and contractility

↓

Dilated cardiomyopathy/heart failure

Pre-clinical Data: β1AR Autoantibody Clearance and Functional Improvement

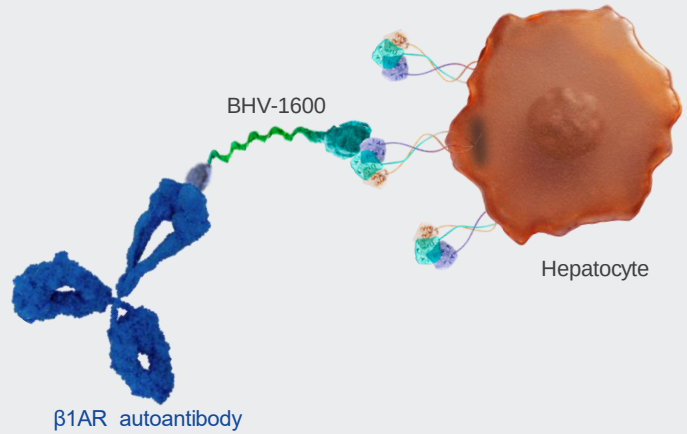




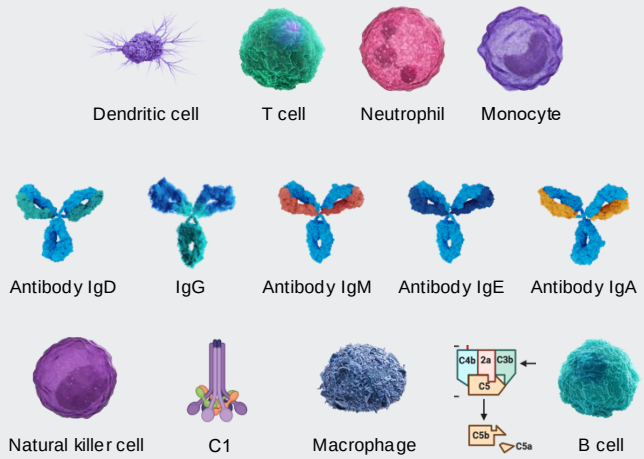
Ongoing Phase 1 Preliminary Clinical Data

- **First-in-human dosing with BHV-1600 has been safe and well-tolerated to date with two cohorts dosed**
- **All AEs have been mild, with no SAEs**
- **Laboratory data demonstrate optimal safety profile:**
  - No clinically relevant changes in white blood cells or immunoglobulins IgG, IgA, IgE, and IgM
  - No clinically significant reductions in albumin, liver function test abnormalities, or increases in cholesterol compared to baseline
- **Study ongoing 1H 2025**

BHV-1600, designed to selectively degrade **ß1AR autoantibodies** to treat PPCM



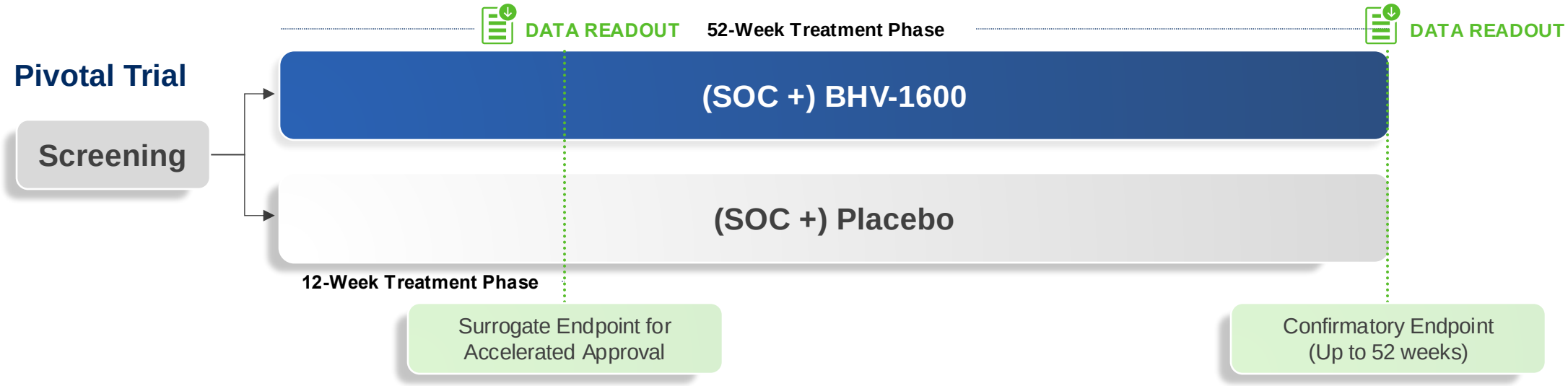
While Preserving Immunity

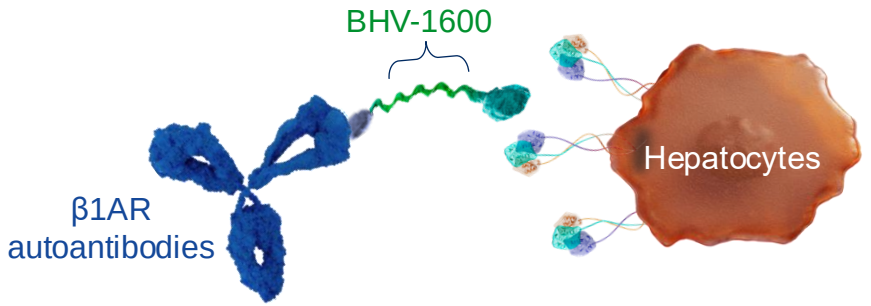


KEY POINT

BHV-1600 selectively targets ß1AR autoantibodies to treat PPCM with Optimal Safety Profile

Harnessing Efficient Trial Design to Address a High Unmet Need





KEY POINT

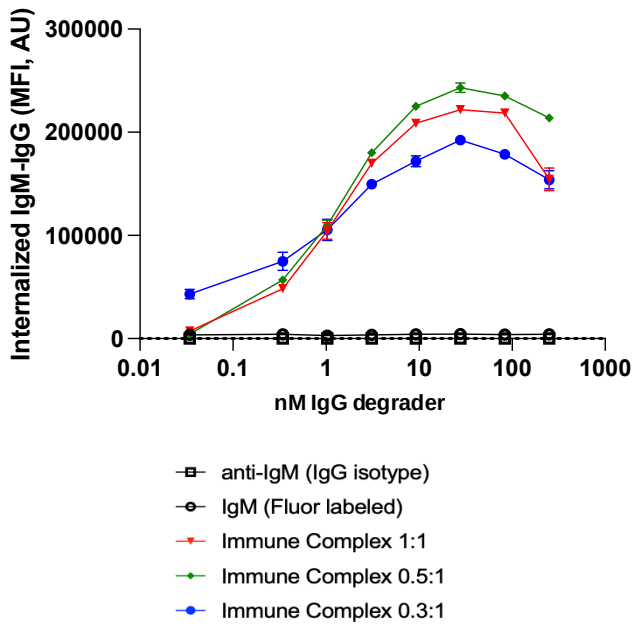
Completed INTERACT meeting with FDA regarding accelerated approval pathway to bring a much-needed therapeutic to women with PPCM efficiently

- ✓ BHV-1300: Potential to transform clinical paradigm to improve patient lives
- ✓ Robust science indicating disease is IgG1 antibody-mediated
- ✓ Easily measured biomarker endpoint
- ✓ Potential first or second to market with strong commercial opportunity

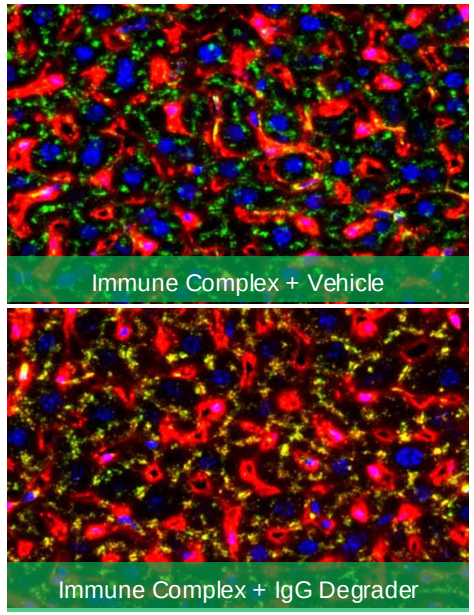
GRAVES' DISEASE

IgG Degraders Remove Disease Relevant Immune Complexes (IC)

In Vitro Lowering of IgM/IgG ICs

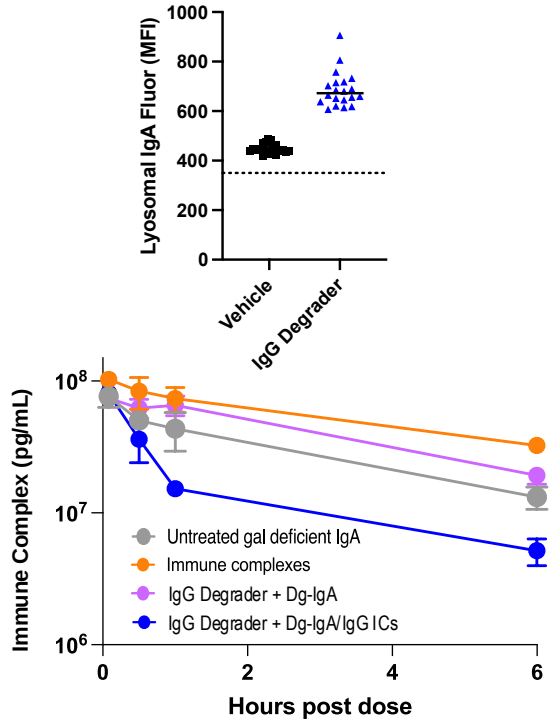


Dg-IgA1/IgG ICs Colocalize with Lysosome (LAMP1) via BHV-1310



Staining: DAPI / IgA1 / LAMP-1
Combined (IgA1/LAMP-1)

In Vivo ICs are Efficiency Removed in Mice

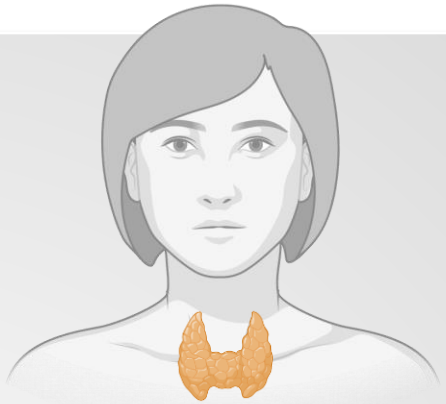


Dg-IgA1, Surrogate for natural form of galactose-deficient IgA1 (Gd-IgA).

KEY POINT

- First evidence of degraders directly removing IgM/IgG, IgG/IgG, Dg-IgA/IgG complexes *in vivo*

Seventy Years of Research Demonstrate the Pathogenicity of TSH Receptor Autoantibodies in Graves' Disease (GD)

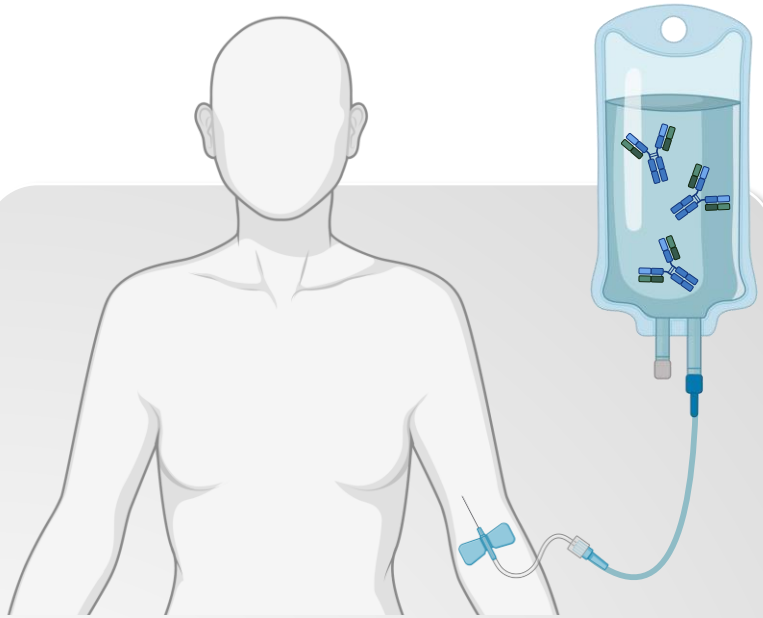


1950s

"Long-Acting Thyroid Stimulator," (TSH receptor autoantibody) identified in the serum of GD patients

1960s

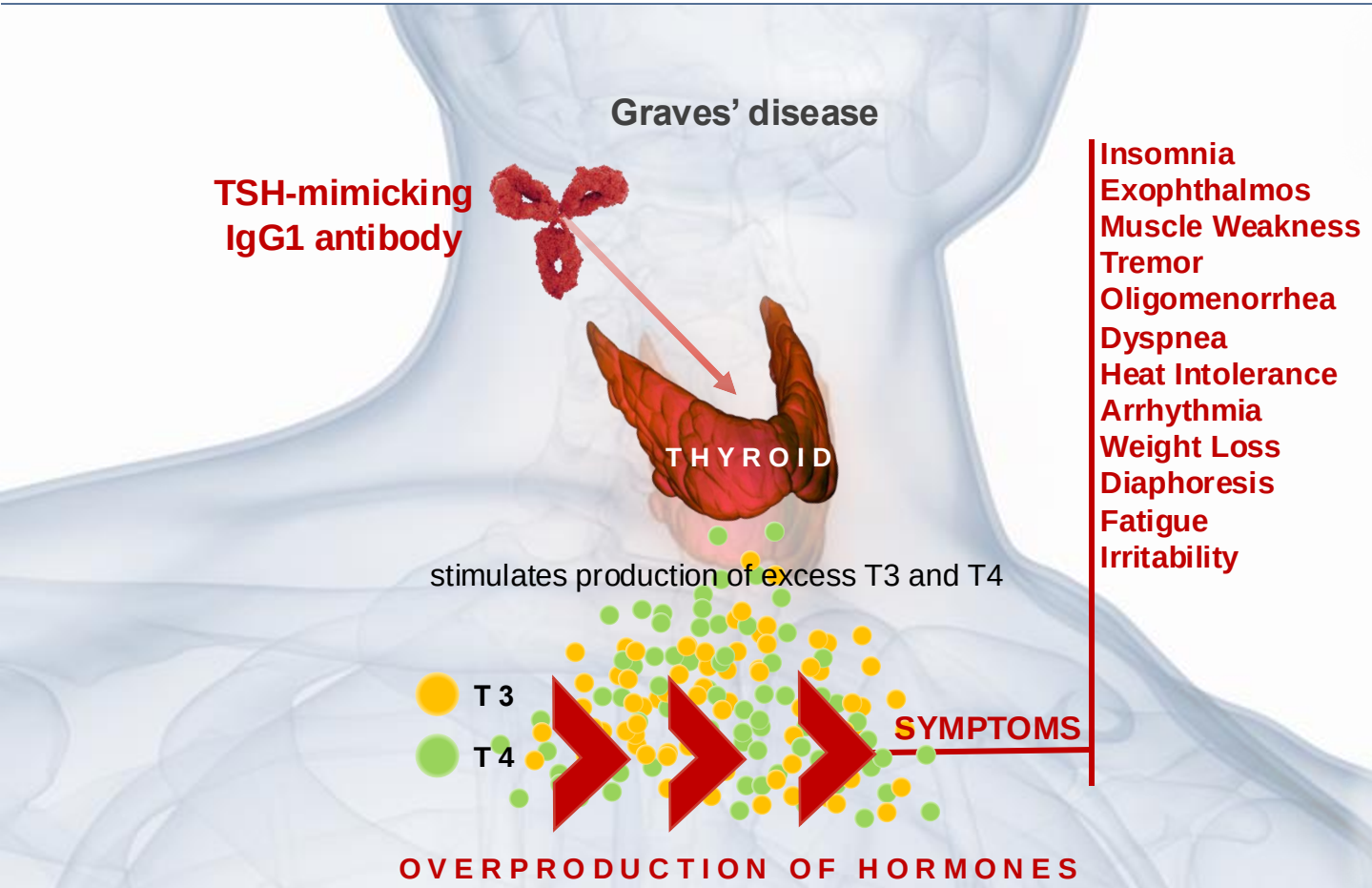
TSH receptor autoantibodies are detected in serum of neonates with hyperthyroid mothers with GD



1970s

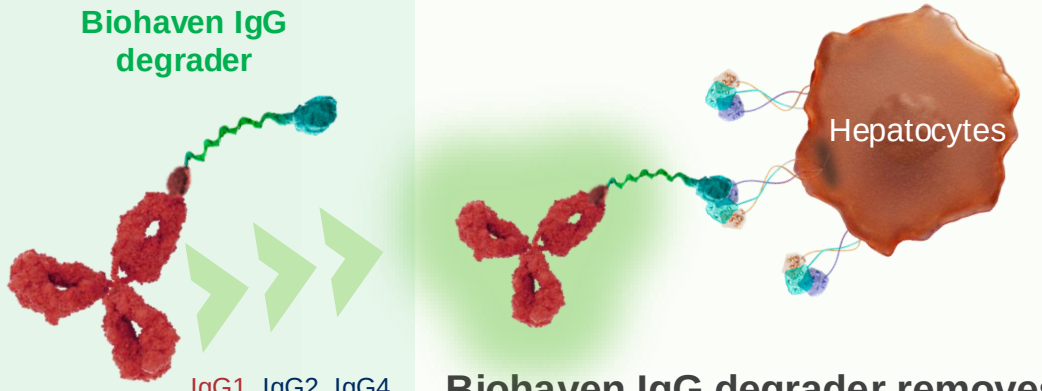
Passive transfer of TSH receptor autoantibodies into healthies prove definitively to stimulate the thyroid

Biohaven IgG1,2,4 Degrader Platform: A Novel Therapeutic for the Treatment of Graves' Disease



- Insomnia
- Exophthalmos
- Muscle Weakness
- Tremor
- Oligomenorrhea
- Dyspnea
- Heat Intolerance
- Arrhythmia
- Weight Loss
- Diaphoresis
- Fatigue
- Irritability

IgG Degrader designed to selectively degrade **IgG1,** IgG2, and IgG4 to treat Graves'



…while preserving IgG3 and Innate Immune Response

KEY POINT

Biohaven IgG degrader removes TSHR-IgG1 autoantibodies with goal of treating Graves' disease

Redefining Possibilities in Graves' Disease Treatment: Treat the Mechanism of Disease, Spare Patients their Thyroid

"Why lose my thyroid?"

"Why expose myself to radiation?"

"Why trade HYPERthyroidism for HYPOthyroidism?"

"A drug that causes fatal agranulocytosis and liver failure is probably not one I want to take."

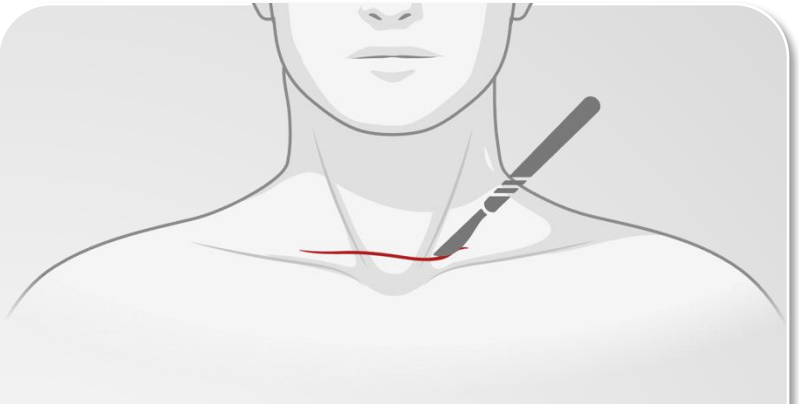
LIMITATIONS OF ANTI-THYROID THERAPY (ATD)

- Does not treat the underlying autoimmune disease
- Are associated with birth defects
- Side effects include liver toxicity, agranulocytosis, hypothyroidism, allergic reactions, etc.
- Other treatment options like ablation or surgery invasive and causes permanent hypothyroidism resulting in life-long need for thyroid hormone replacement

KEY POINT

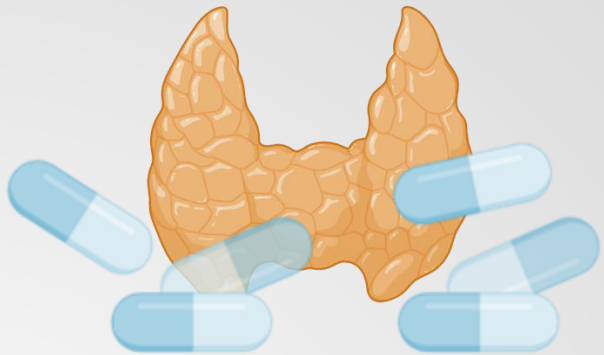
BHV-1300 targets the underlying autoimmune pathology of Graves' disease to potentially improve disease control and avoid the undesirable adverse effects of ATD's and surgery

Biohaven's Goal Is to Change the Treatment Paradigm in Graves' Disease



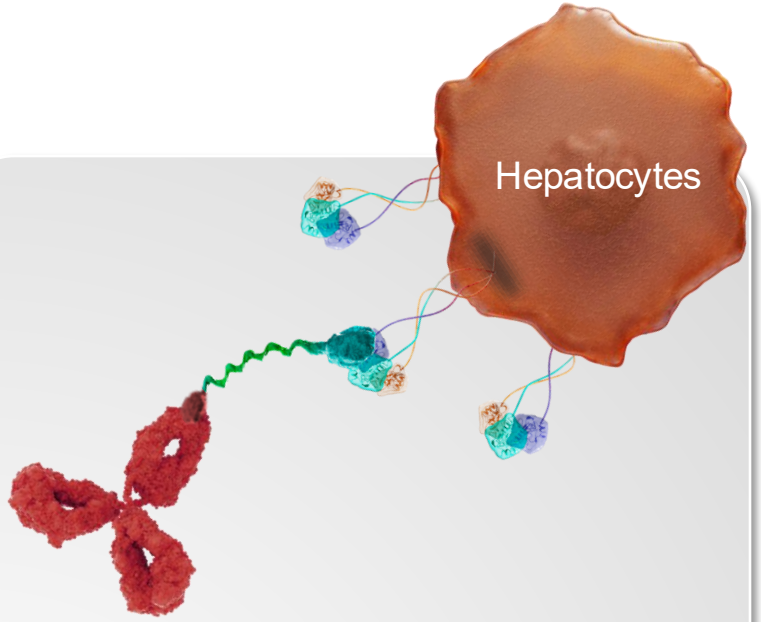
1790s

DeSault performs first successful partial thyroidectomy



1940s

Antithyroid drugs and radioactive iodine (RAI) used as alternative to surgery, chronic thyroid replacement

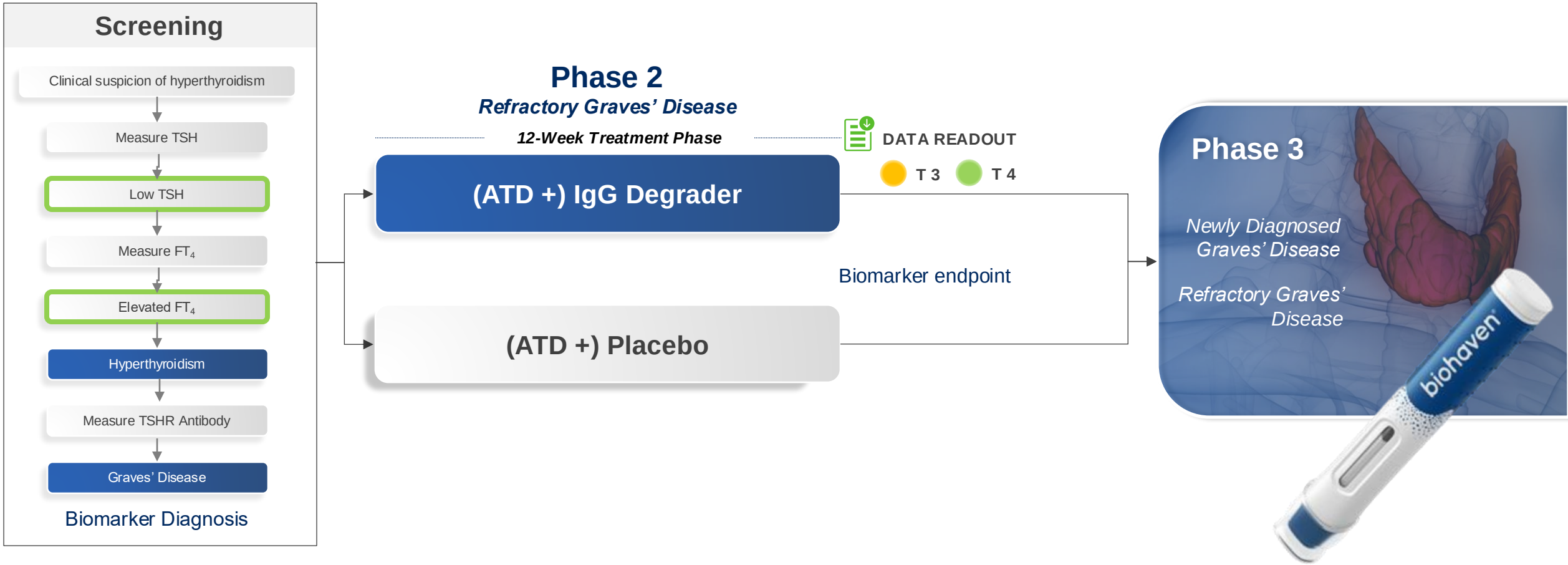


2020s

Biohaven technology redirects TSH receptor autoantibodies to the liver for removal, treating the underlying cause of Graves' disease

TRAb, TSH Receptor Autoantibodies

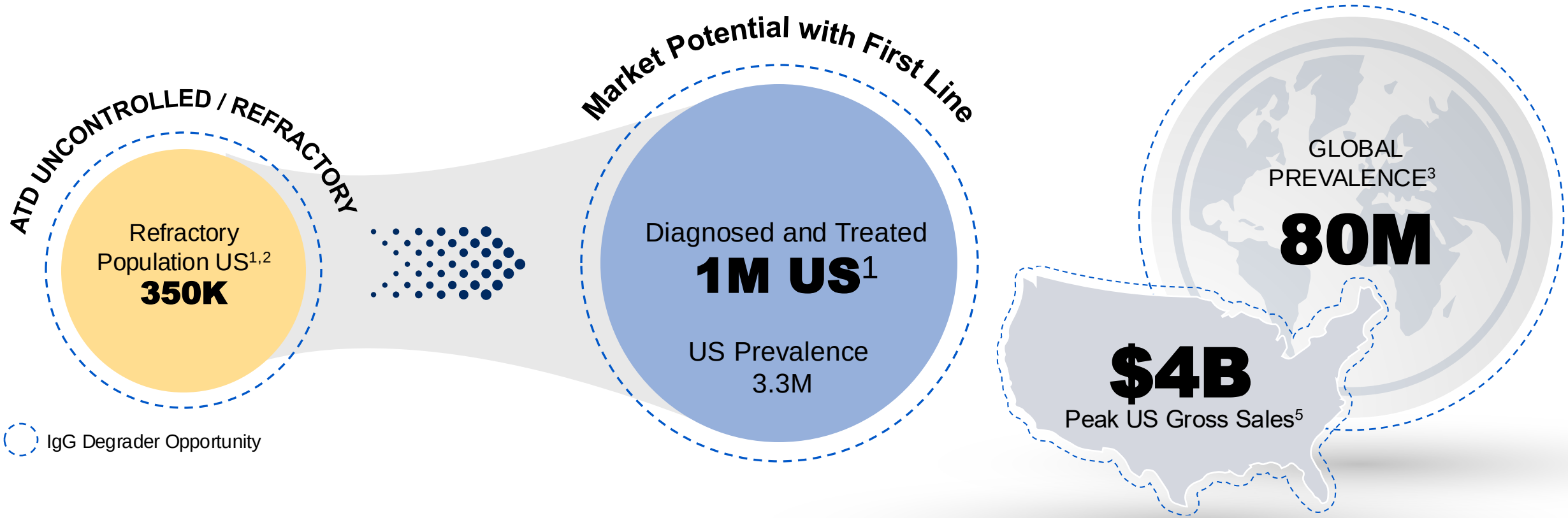
Graves' Disease Mid-2025 with Biomarker Endpoint



KEY POINT

Biomarker-driven diagnosis and endpoints facilitate efficient trial design in Graves' disease patients

Broad Market Strategy to Modify Graves' Disease

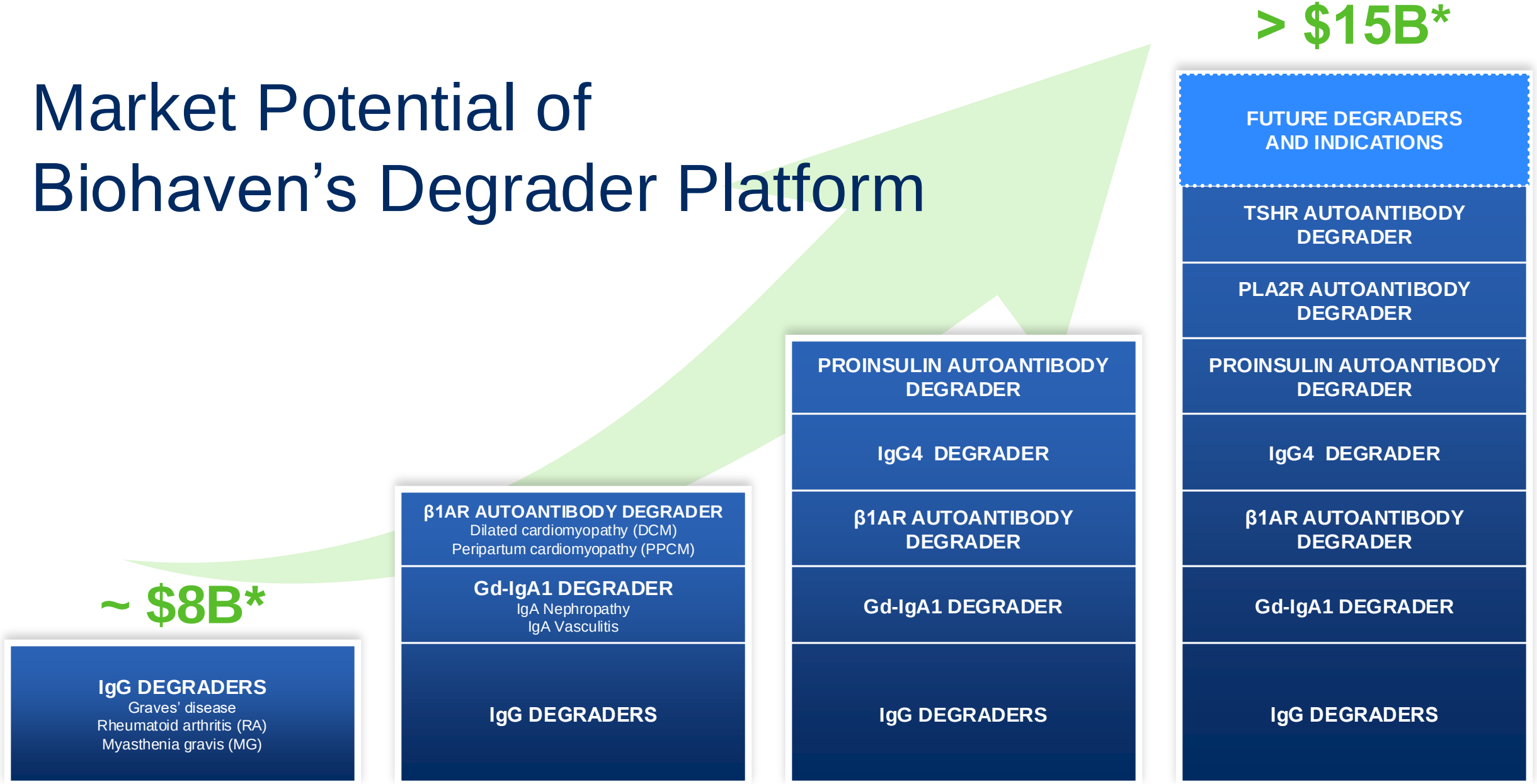


1. Forian Insurance Claims Data Base Analysis Jun 2016-September 2024; 2. Percent of ATD patients refractory or uncontrolled: Sundaresh V, Brito JP, Thapa P, Bahn RS, Stan MN. Comparative Effectiveness of Treatment Choices for Graves' Hyperthyroidism: A Historical Cohort Study. Thyroid. 2017 Apr;27(4):497-505. doi: 10.1089/thy.2016.0343. Epub 2017 Feb 6. PMID: 28049375; PMCID: PMC5385429; 3. NBK448195/NIDDKD. Graves disease. Accessed September 11, 2024. https://www.niddk.nih.gov/health-information/endocrine-diseases/graves-disease; 4. US prevalence and Incidence: Pokhrel B, Bhusal K. Graves Disease. [Updated 2023 Jun 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/; 5. Biohaven Internal Analysis: Peak US Gross Sales

KEY POINT

Degraders redefine care, targeting the autoimmune pathogenesis of disease with the potential to treat across the course of disease

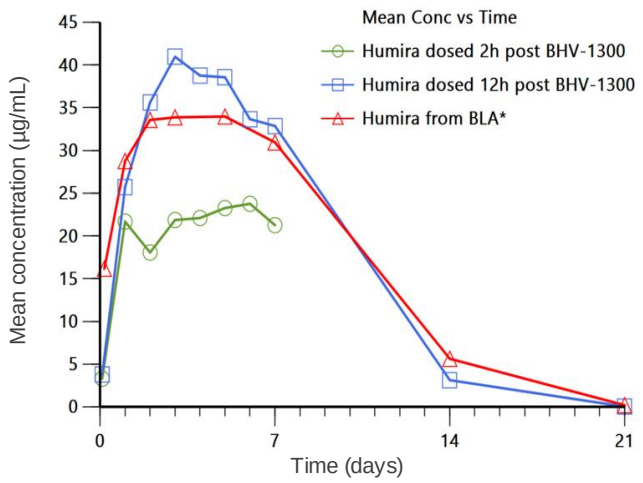
Market Potential of Biohaven's Degrader Platform



* Biohaven Internal Analysis: Peak US Gross Sales

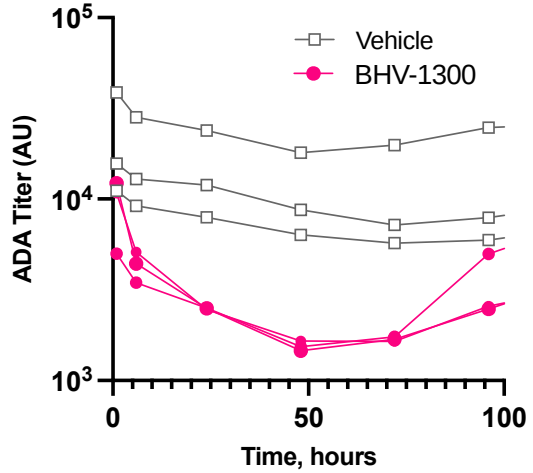
IgG Degradation Improves Efficacy of Biologics Through Removal of ADAs

BHV-1300 Compatible With Biologic Therapeutics When Dosed >12h Prior



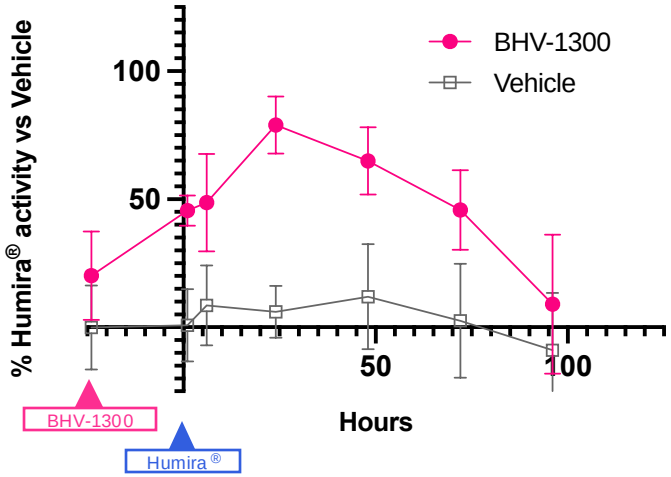
BHV-1300 dosed at 30 mg/kg SC followed by Humira® dosed at 3 mg/kg SC in NHPs

BHV-1300 Effectively Removes ADAs in NHPs



ADAs[1] induced by administration of Humira® are reduced with a single dose of BHV-1300

BHV-1300 Restores Effects of Biologics Through Removal of ADAs (TNFα Neutralization Assay)



Humira® activity measured by TNFα levels BHV-1300 dosed 24h prior to Humira®

* Adapted from BLA 761154, IND 116471, Study no. r-fkb327-01

ADA, Antidrug Antibody; **NHP,** Non-human Primates

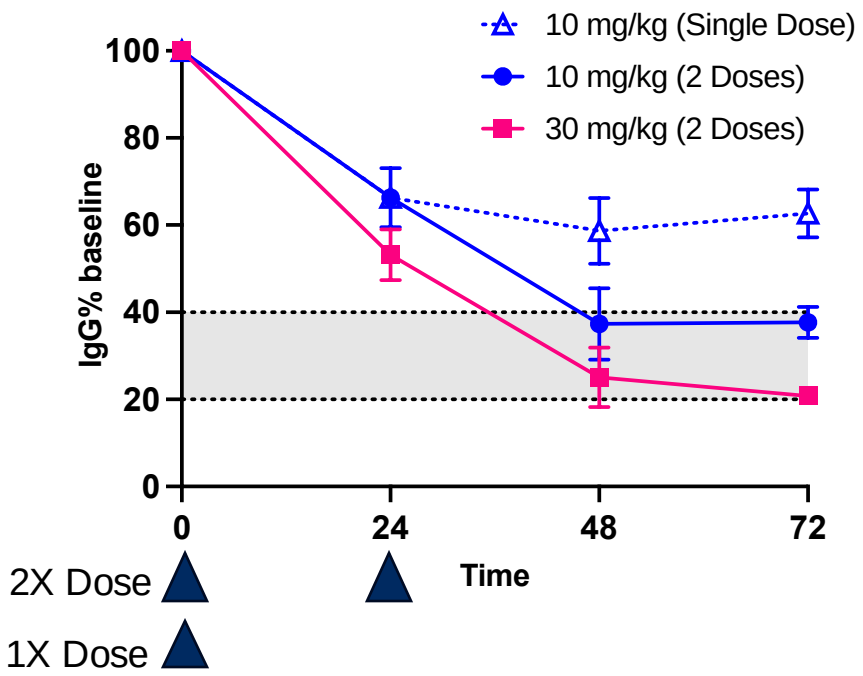
1. Ann Rheum Dis. 2014 Dec;73(12):2178-82.

KEY POINT

BHV-1300 can be co-administered with biologics, removing anti-drug antibodies and restoring efficacy[1]

Consecutive Doses of MoDE Doubles IgG Lowering in NHPs

IgG Lowering to Efficacious Levels (60-80%)
Is Achieved With Consecutive Daily Doses in 2 Days

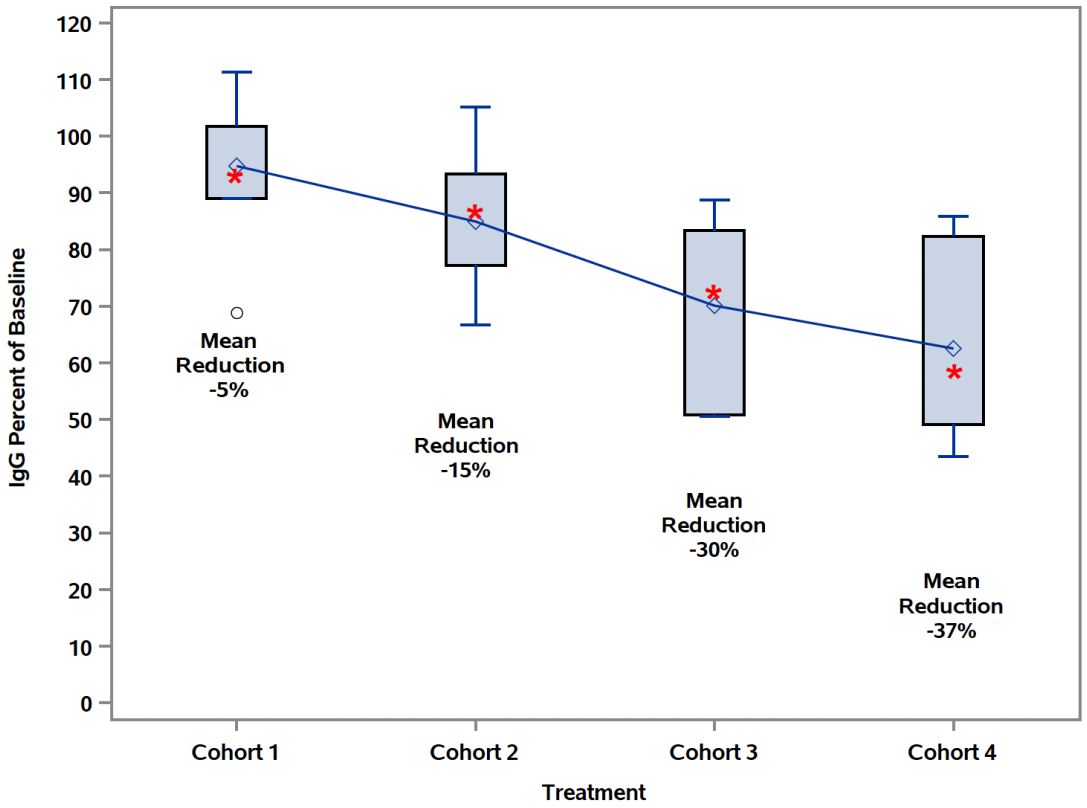


KEY POINT

Unique pharmacology provides flexibility in dosing regimens

Single Doses of BHV-1300 Reduce IgG in Dose-Dependent Manner in Ongoing SAD Study in Healthy Subjects

BHV-1300 Maximum IgG Percent of Baseline Within 96 Hours



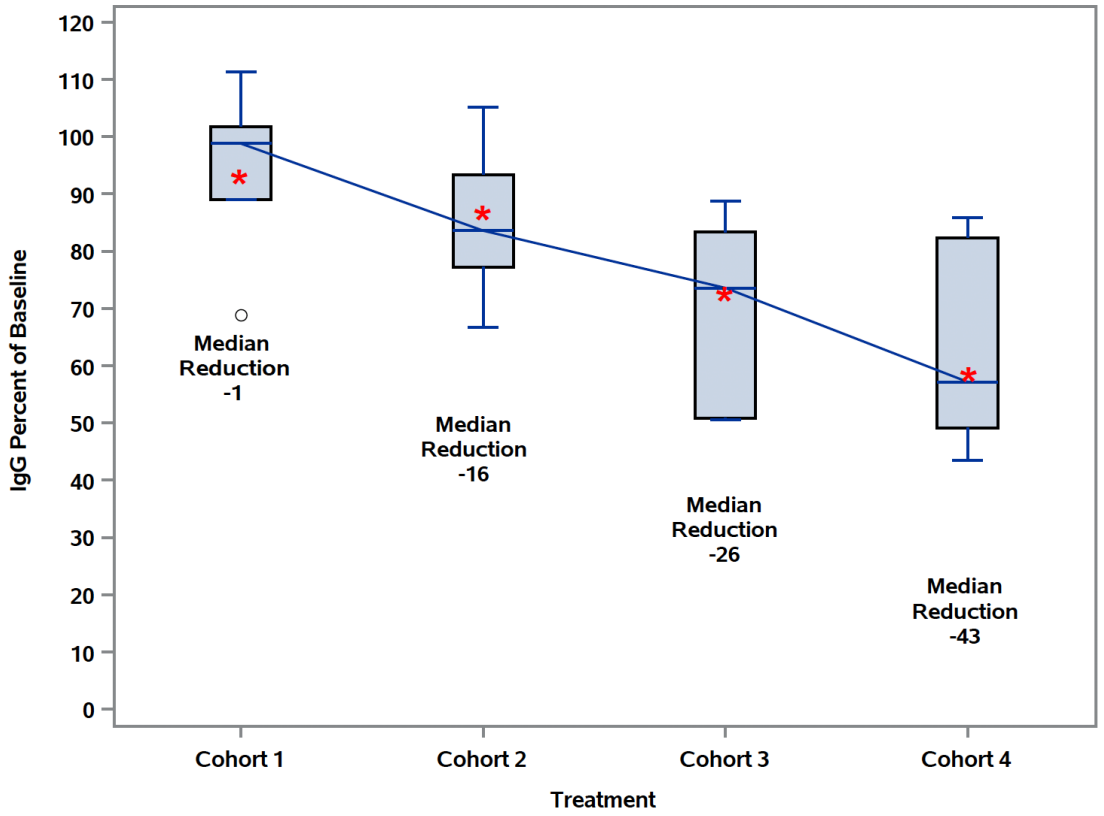
★ Predicted based on modeling

- Dose-dependent sustained lowering through follow-up period
- Based on modeling, anticipate achieving 70-80% IgG reduction when Phase 1 complete

Preliminary data from ongoing Phase 1 Study (as of May 28, 2024).

Median IgG Lowering Within 96 Hours

BHV-1300 Maximum IgG Percent of Baseline Within 96 Hours



★ Predicted based on modeling

- Fixed or non-weight based dosing for all cohorts
- Data shown represents median values across dose cohorts

Preliminary data from ongoing Phase 1 Study (as of May 28, 2024).

BHV-1300 Is Selective for IgG

- No meaningful reduction of IgM, IgA, or IgE
- No meaningful impact on albumin
- No meaningful impact on low-density lipoprotein cholesterol

Preliminary data from ongoing Phase 1 Study (as of May 28, 2024).

BHV-1300 Is Safe and Well-Tolerated in Healthy Subjects

SC formulation of BHV-1300 used in Phase 1 study delivered exposures higher than the intravenous formulation, enabling the profile of a convenient patient administered auto-injector to attain targeted reduction of IgG.

- No SAEs or severe AEs
- Most AEs were mild, not related, and resolved spontaneously
- No clinically significant ECG changes
- No clinically significant drug-related lab changes
- No hepatotoxicity or clinically significant changes in LFTs

Preliminary data from ongoing Phase 1 Study (as of May 28, 2024).

BHV-1300 Rapidly, Selectively and Safely Lowers IgG in a Dose-Dependent Manner in Healthy Subjects

EFFICACY

- Dose-dependent and rapid onset of IgG lowering within hours
- Dose-dependent sustained lowering through follow-up period
- Based on modeling, anticipate achieving 70-80% IgG reduction in Phase 1 utilizing doses compatible with subcutaneous administration

SELECTIVITY

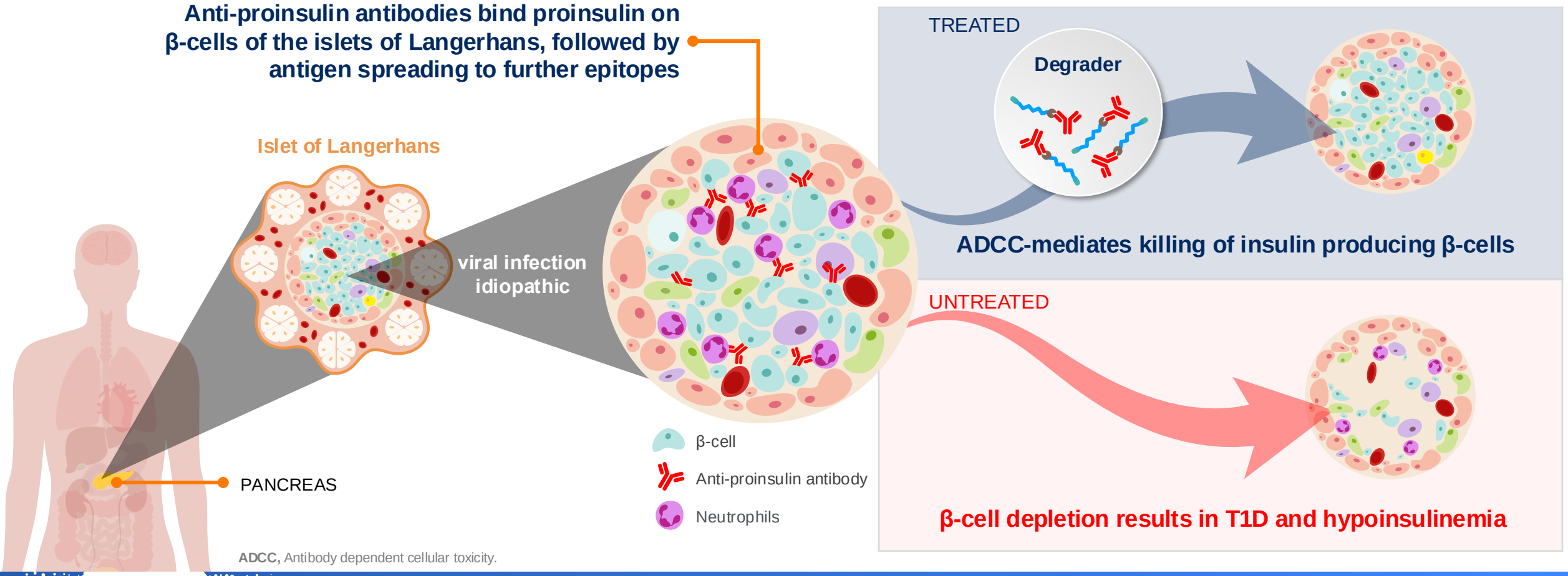
- No meaningful reduction of other immunoglobulins
- No meaningful impact on albumin and low-density lipoprotein cholesterol

SAFETY

- Safe and well-tolerated
- No infusion reactions
- No hepatoxicity or clinically significant changes in LFTs

Preliminary data from ongoing Phase 1 Study (as of May 28, 2024).

Removal of Proinsulin Autoantibodies Halts Progression of Nascent Type 1 Diabetes (T1D)



ADCC, Antibody dependent cellular toxicity.

KEY POINTS

THERAPEUTIC HYPOTHESIS Lowering of antibodies early in course of disease may prevent loss of β-cells and stop cascading events which lead to Type 1 Diabetes

Degraders Bind to Insulin and Proinsulin Autoantibodies, Resulting in Uptake, Hepatic Degradation and Correction of Glucose Homeostasis

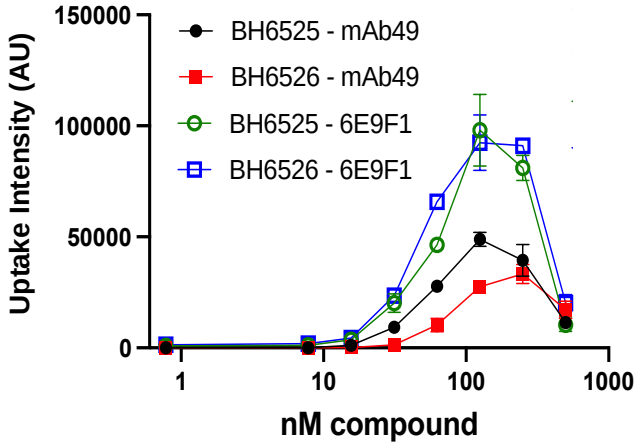
Biochemistry Selectivity (Insulin Autoantibody)

EC50 (nM)

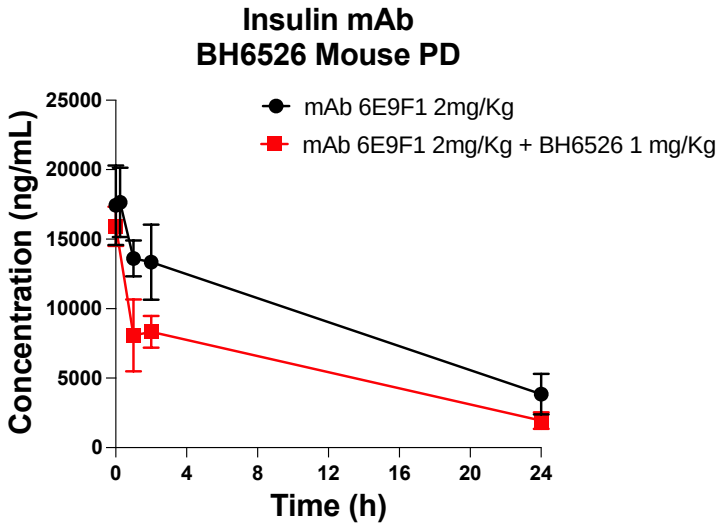
	BH6525	BH6526
mAb49	39.68	67.21
6E9F1	39.13	37.61

mAb49: Human anti-Insulin antibody
6E9F1: Mouse anti-Insulin antibody

Cellular Autoantibody Uptake



In Vivo Autoantibody Reduction



- Anti-insulin and anti-proinsulin autoantibody MoDEs form ternary complexes, show *in vitro* uptake and drive *in vivo* clearance without binding insulin receptors or IGF1R
- Robust and selective lowering of these autoantibodies shown in mouse PK/PD experiments
- Evaluation underway in efficacy studies and preliminary toxicology

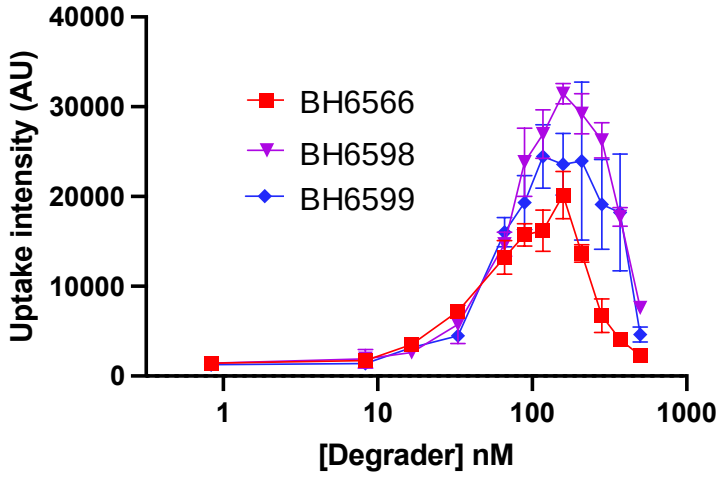
Specific Degraders Designed to Efficiently Remove Only IgG4

IgG4-Specific Degraders Bind Only Human IgG4 with 100X Selectivity

Binding Affinity

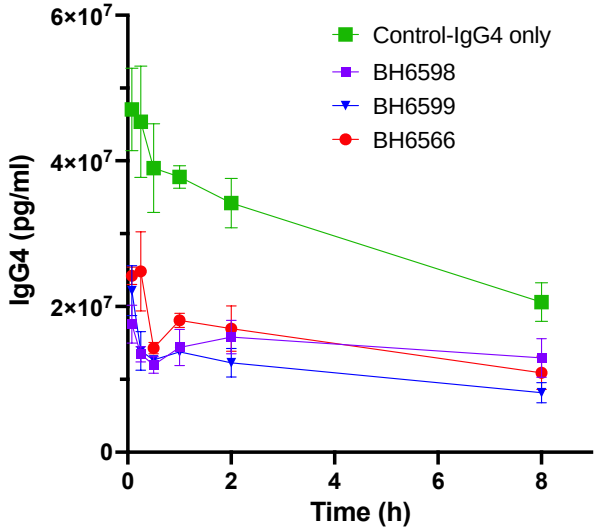
	Native hIgG1	Native hIgG2	Native hIgG3	Native hIgG4
BH6566	>1000	>1000	>1000	36
BH6598	>1000	>1000	>1000	33
BH6599	>1000	>1000	>1000	43

Cellular IgG4 Uptake



In Vivo IgG4 Reduction

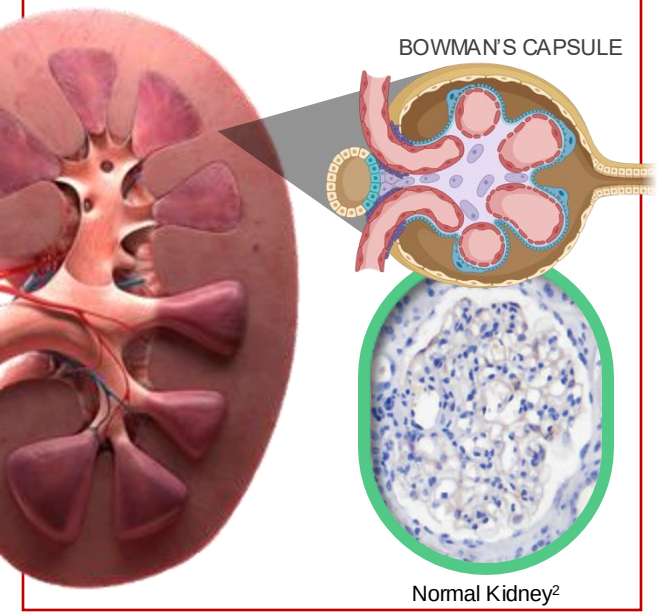
(single dose, 1 concentration POC)



- IgG4 selective degraders identified
- Robust and selective lowering of IgG4 in mouse PK/PD experiment
- Evaluation underway in disease relevant efficacy studies and preliminary toxicology

Selective Targeting of Anti-Phospholipase A2 Receptor (PLA2r) Antibodies for Idiopathic Membranous Nephropathy (IMN)

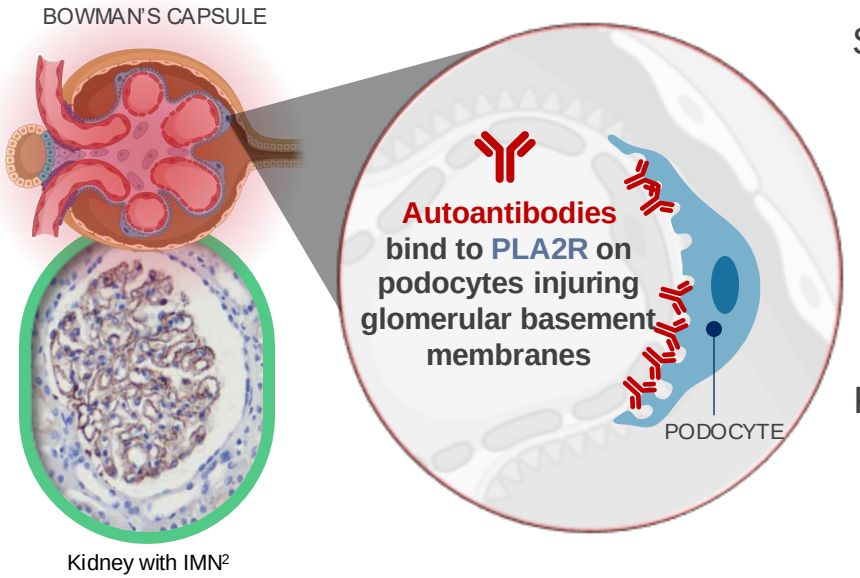
HEALTHY KIDNEY



NEPHROTIC KIDNEY

70–80% of IMN patients have high anti-PLA2r levels[1]

Anti-PLA2r autoantibodies levels are strongly associated with disease severity in IMN



Subepithelial immune complex deposits

▼

Podocyte injury, thickening of basement membrane

▼

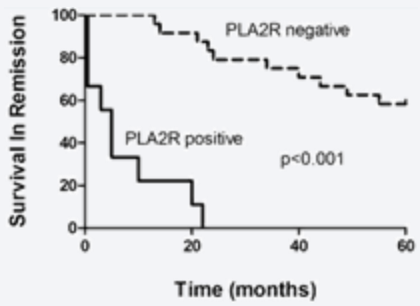
Proteinuria and hyperlipidemia

▼

Kidney failure

Currently no specific therapies to treat IMN[2]

- Rituximab or cyclophosphamide + glucocorticoids are first-line therapies but have serious side effects
- Combination of plasmapheresis with SoC shows more favorable outcomes[3,4]



Patients rendered anti-PLA2r negative by immunosuppression have greater disease remission

1. Beck, L.H.; Bonegio, R.G.B.; Lambeau, G.; Beck, D.M.; Powell, D.W.; Cummins, T.D.; Klein, J.B.; Salant, D.J. M-Type Phospholipase A 2 Receptor as Target Antigen in Idiopathic Membranous Nephropathy. *N. Engl. J. Med.* 2009, *361*, 11–21. 2. Adapted from *Kidney International* (2012) 82, 797–804 3. Rovin BH, Adler SG, Barratt J, Bridoux F, Burdge KA, Chan TM, et al. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int (2021) 100(4, Supplement):S1–276. doi: 10.1016/j.kint.2021.05.021. 4. Bennani HN, et al.,*J. Pers. Med.* 2024, *14*(3), 249. 5. Lu H et al. Medicine(Baltimore) 2019 May; 98(18): e15303.

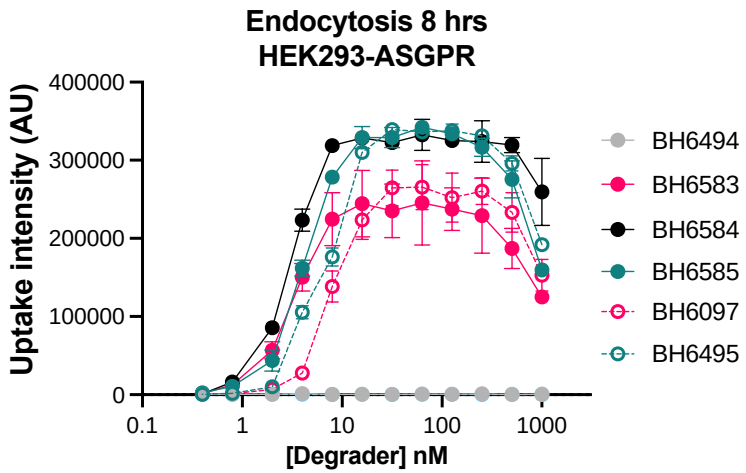
PLA2r Antigen-Specific MoDEs Rapidly Remove Pathogenic Autoantibodies

Biochemical Selectivity

Binding Affinity (nM)

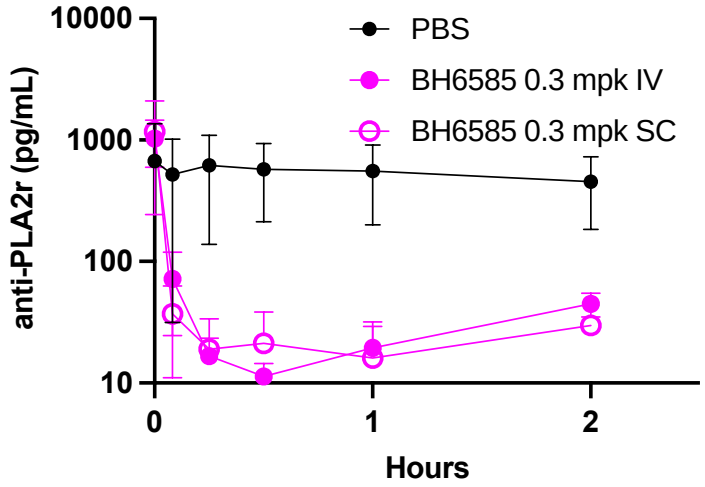
	Anti-PLA2r
BH6494	0.3
BH6583	10 ± 3
BH6584	3 ± 0.3
BH6585	7 ± 1
BH6097	23 ± 1
BH6495	7

Cellular Autoantibody Uptake



*BH6494 lacks ASGPR binder

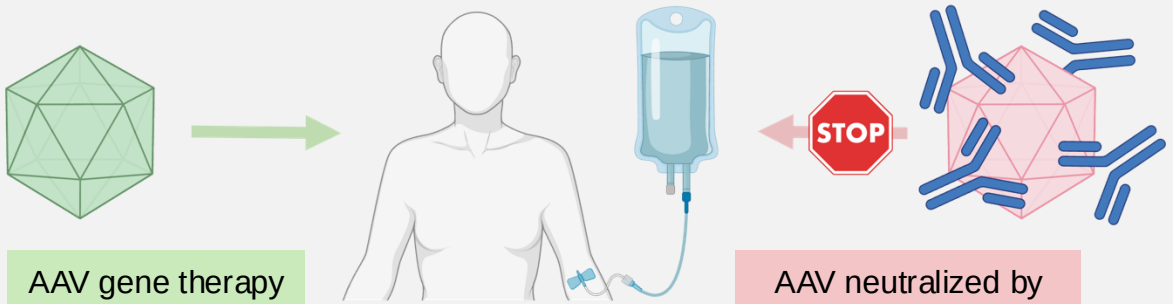
In Vivo Autoantibody Reduction



KEY POINTS

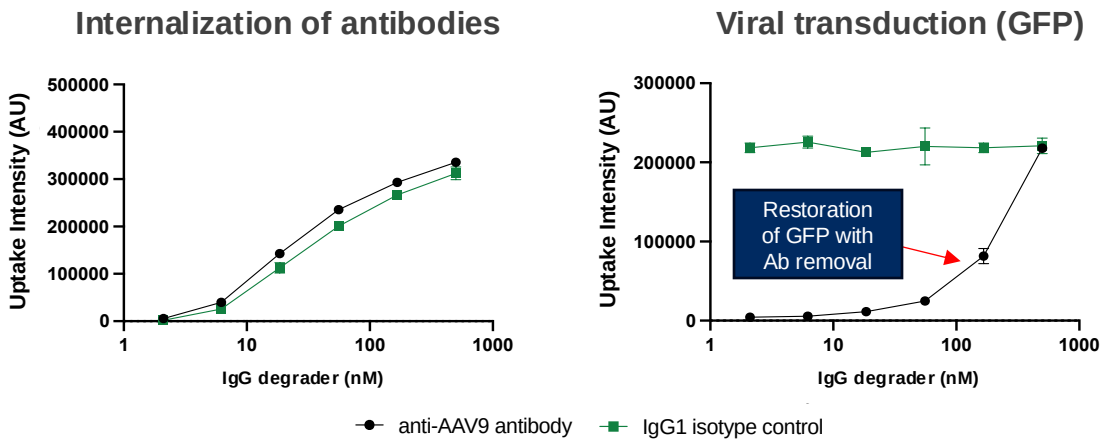
Deep reductions in anti-PLA2r autoantibodies will prevent further glomerular injury

Removal of Neutralizing Antibodies to Capsids to Optimize Gene Therapy Uptake and Allow Repeat Administration



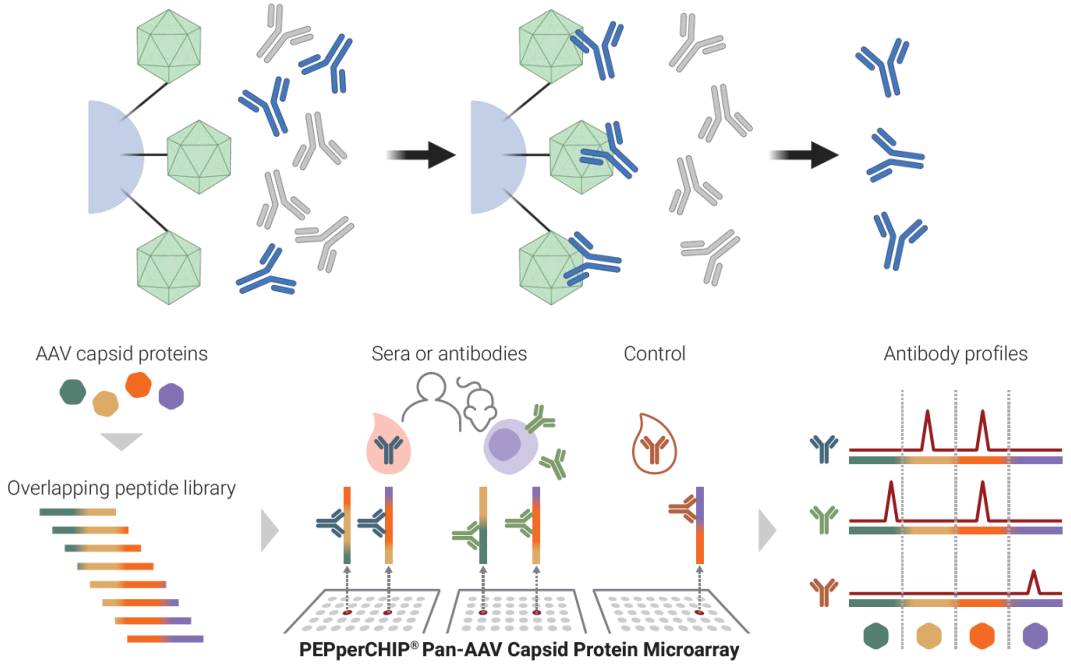
Preexisting anti-AAV antibodies limit the use of AAV-based gene therapy

POC Using GFP Viral Transduction

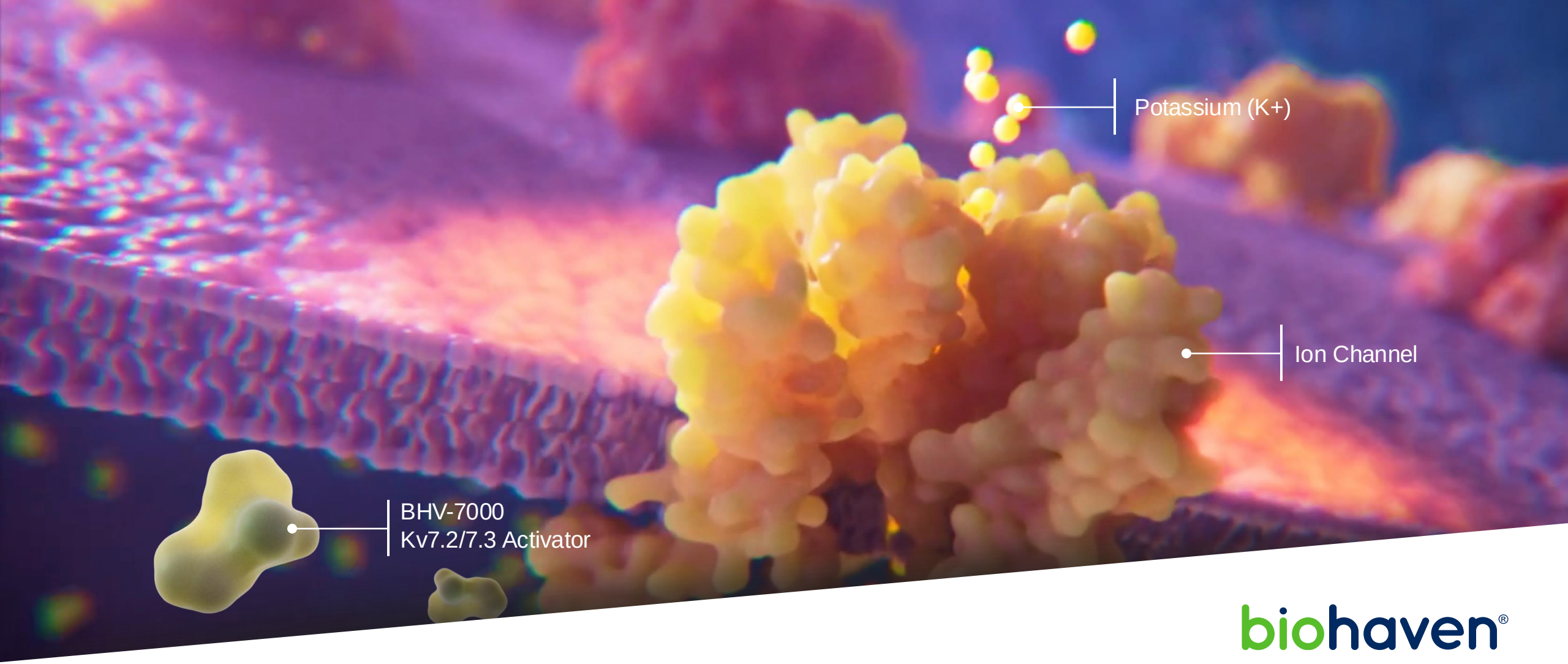


Discovery of Dominant Epitopes for Anti-AAV Antibodies

Enrich anti-AAV antibodies (blue) with immobilized capsids identify binders using array of display techniques



Peptide binders which bind comprehensive antibody populations can be quickly converted to MoDEs



biohaven®

Ion Channels

First-in-Clinic TRPM3 Antagonist — Novel Mechanism for the Treatment of Migraine and 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 such as hyperthermia

Phase 1 Study Data Supports Evaluation in Pain

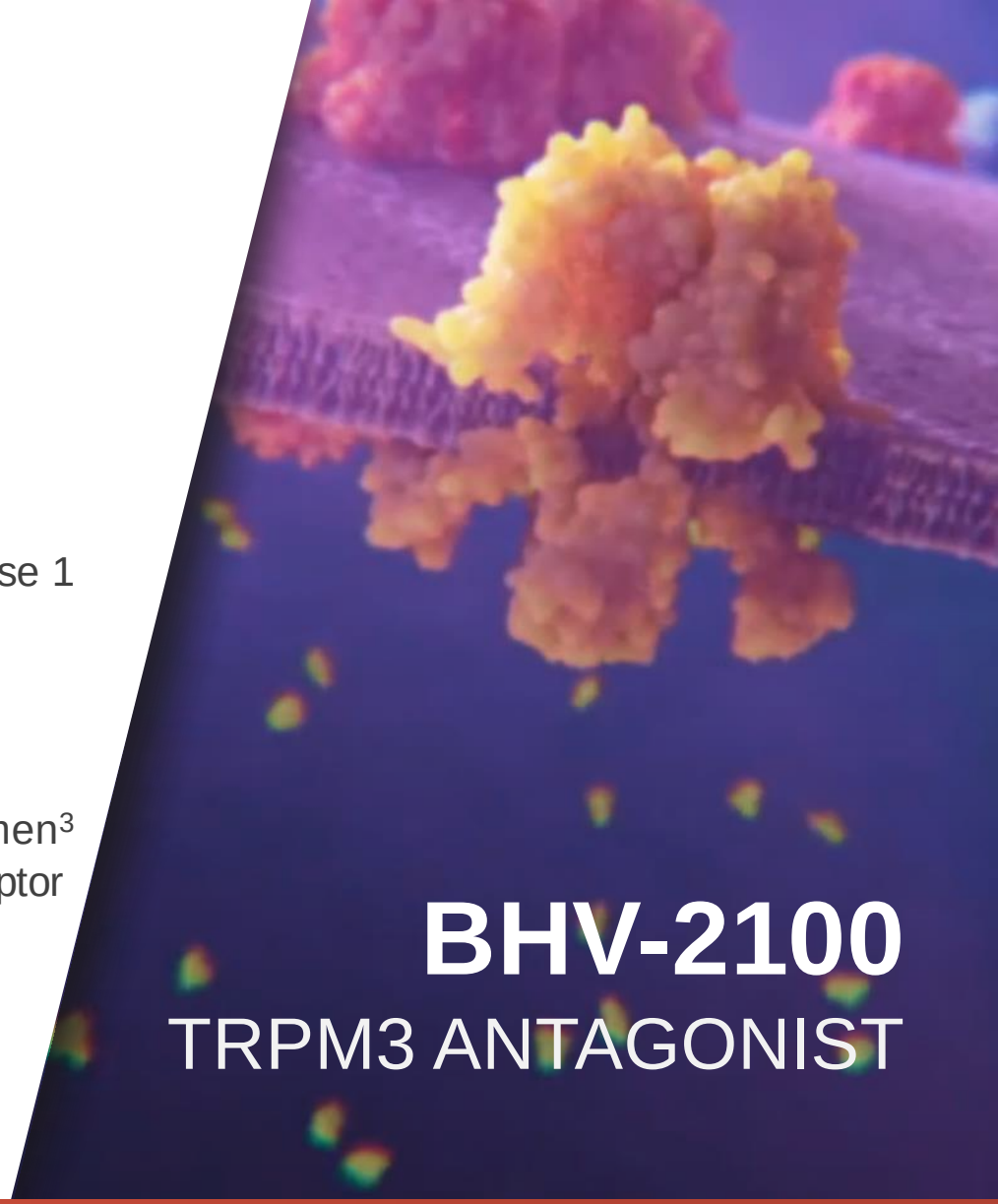
BHV-2100 demonstrated excellent safety/tolerability and favorable PK in Phase 1

Significant Unmet Need Remains

- The CDC estimates the prevalence of chronic pain to be 20%[1]
- The global opioid crisis highlights the unmet needs in pain management[2]
- Migraine is 2nd leading cause of disability worldwide, 1st among young women[3]
- 30–40% of patients do not respond to treatments that block CGRP or its receptor

Milestones Achieved

- Laser-evoked potential proof-of-concept trial for pain initiated in 2H 2024
- Proof of concept trial for acute treatment of migraine initiated in 2H 2024



1. Volkow, N.D. and W.J. Koroshetz, Nat Rev Neurol, 2019. 15(5): p. 301-305.; 2. Steiner TJ et al, J Headache Pain. 2020 Dec 2;21(1):137;
3. Cohen SP, Vase L, Hooten WM. Lancet 2021;397(10289):2082-2097.

BREAKING NEWS

Emerging data with BHV-2100 in laser heat-induced pain and brain evoked potentials validates the TRPM3 inhibitor class in the treatment of pain

BHV-7000, Potential Best-in-Clinic Selective Kv7 Activator, Nears Completion of Pivotal Trials with Blockbuster Potential

Bipolar Disorder
7M Patients

- Novel MOA for bipolar disorder
- Differentiated profile vs. antipsychotics, lithium, and ASMs

Acute bipolar mania topline results expected in 1H 2025

Major Depressive Disorder
21M Patients

- Clinically validated MOA for MDD
- Differentiated profile vs. SSRIs

Topline results expected in 2H 2025

Epilepsy
3.5M Patients

- Clinically validated MOA for epilepsy
- Global Phase 2/3 program ongoing in focal epilepsy (2 trials) and idiopathic generalized epilepsy (1 trial)

1st focal epilepsy study topline results expected in 1H 2026

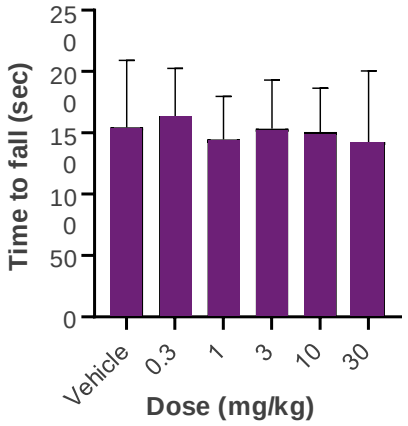
BREAKING NEWS

Pivotal topline results for BHV-7000 development program expected within the next year

Dialing Out $GABA_A$ Receptor Activation Clinically Proven to Reduce CNS Side Effects With Selective Kv7 Activator BHV-7000

PRECLINICAL

No effects on motor performance on rotarod



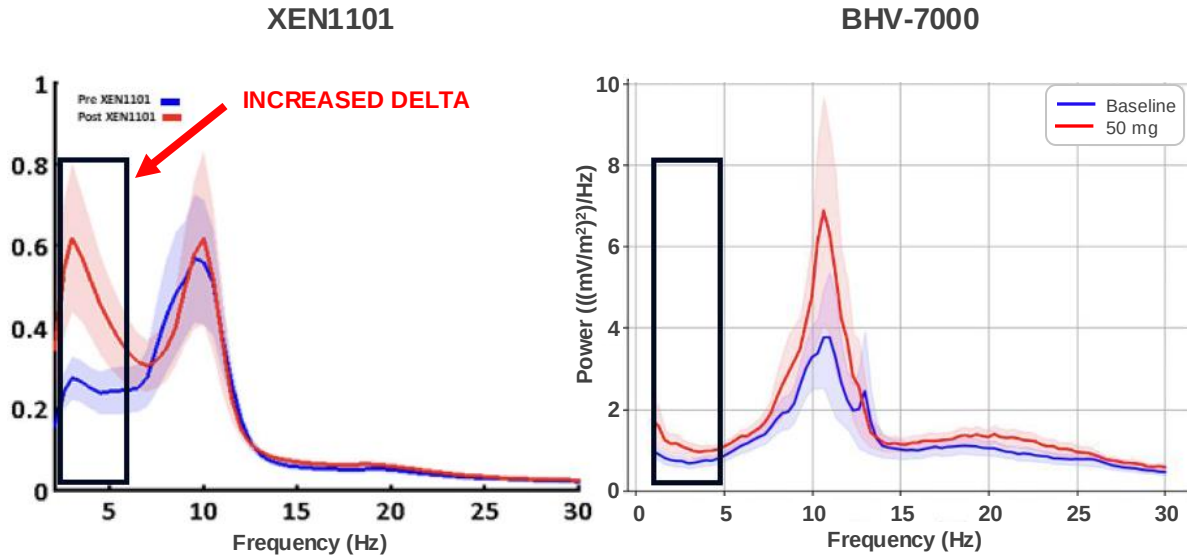
PHASE 1

Not associated with CNS adverse events (AEs) typical of other ASMs in healthy volunteers

Pooled CNS AEs	BHV-7000 MAD Pooled N=29	XEN1101 MAD Pooled N=18
Somnolence	0%	39%
Headache	21%	39%
Balance disorder/ dizziness	10%	34%
Memory impairment	0%	28%
Sensory disturbance	0%	11%
Speech disorder	0%	33%

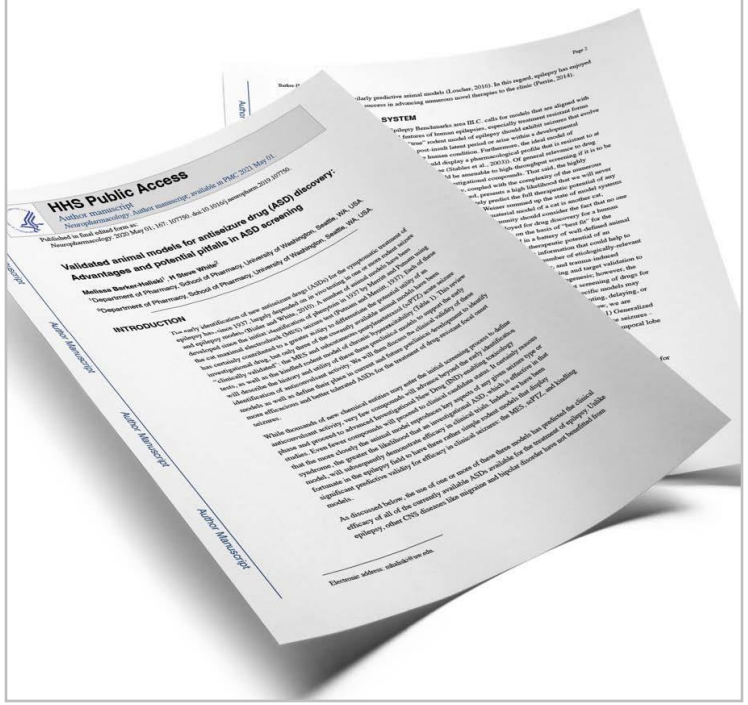
EEG

Significant impact on alpha spectral power confirms target engagement, minimal impact on delta-theta spectral power consistent with lack of somnolence in Phase 1



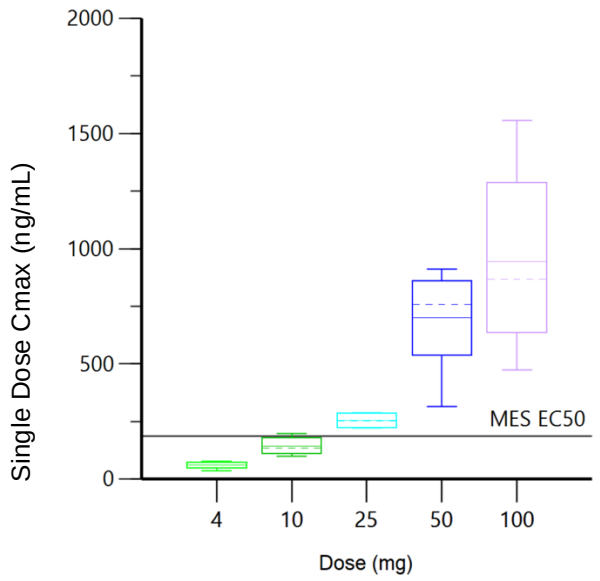
BHV-7000 Profile Allows for Optimizing Efficacy and Safety

MES Predicts Clinical Efficacy

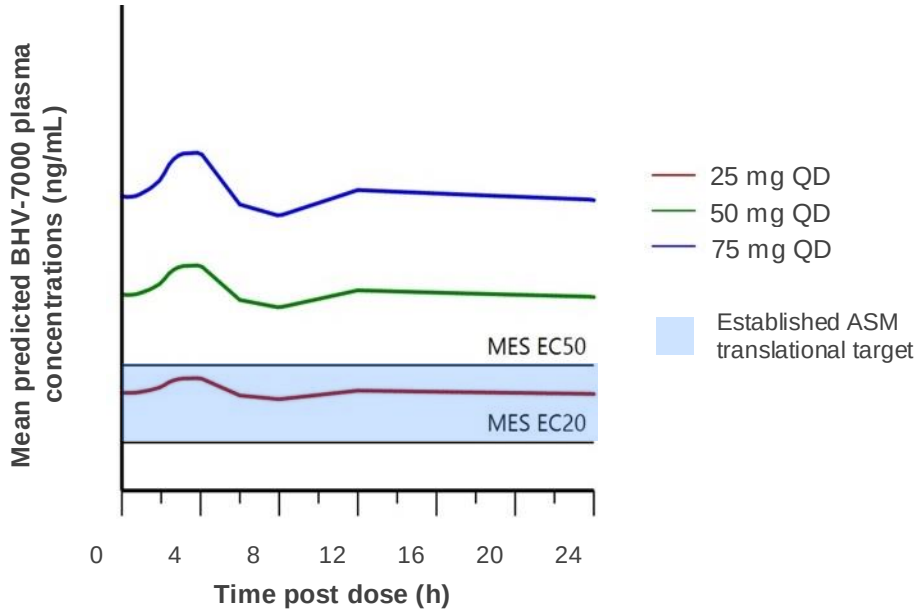


Loscher, 2016.

Single Doses (up to 100 mg) of Spray-Dried Dispersion Suspension



Phase 2/3 Clinical Trial Doses Provide Broad Coverage of Predicted Therapeutic Target Levels

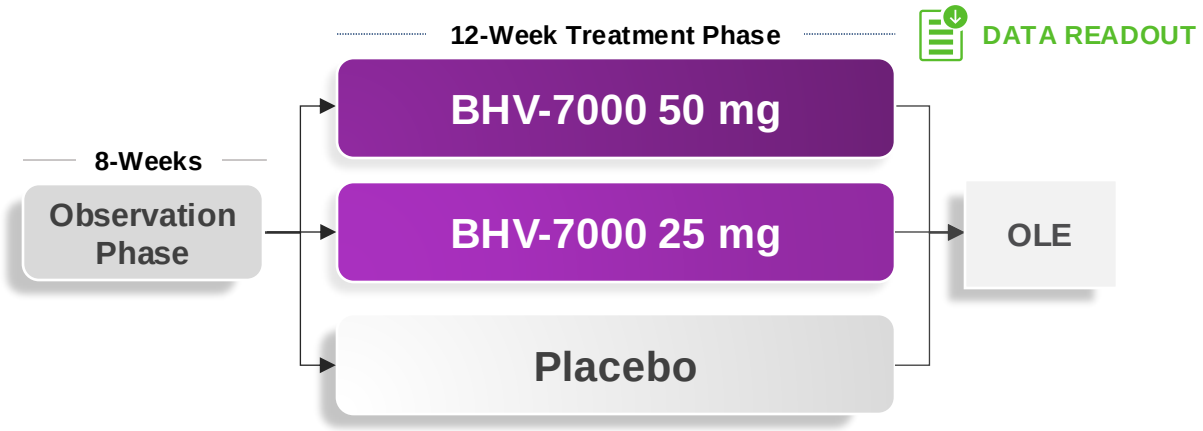


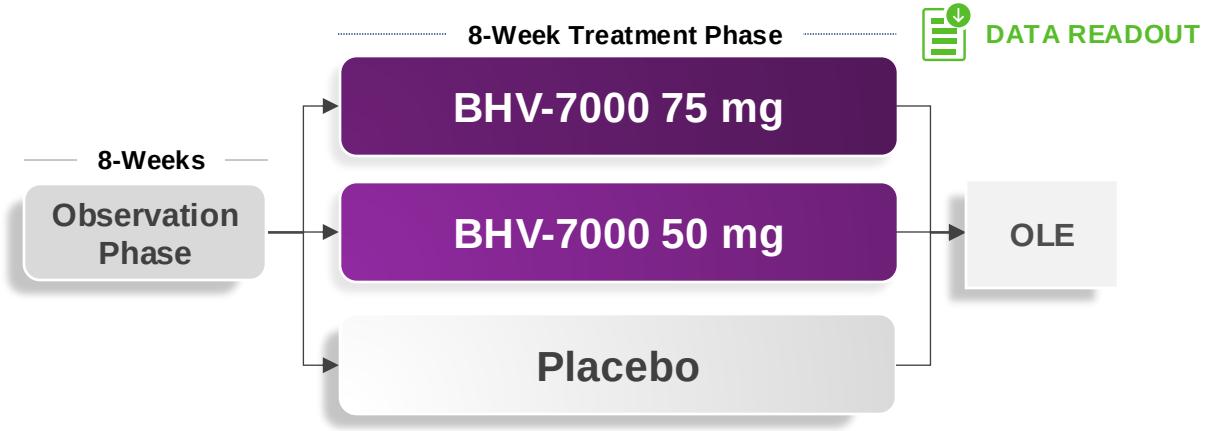
*EC50 based on preclinical maximal electroshock seizure (MES) models.

KEY POINTS

- 5x therapeutic target levels predicted by MES model achieved in Phase 1 studies
- In Phase 1 MAD, no AEs reported with 75 mg ER (highest dose in ongoing Phase 2/3 studies)

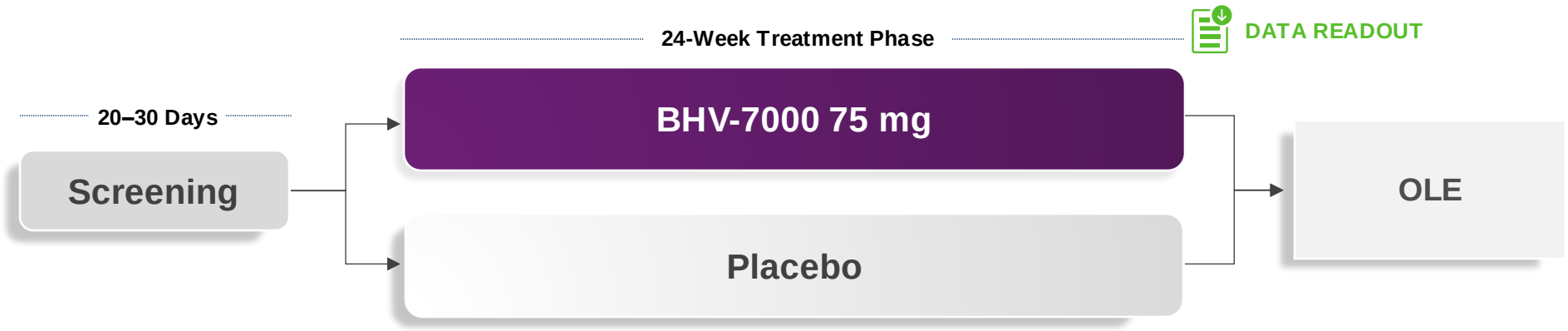
BHV-7000:
Two Phase 2/3 Studies in Focal Epilepsy Are Ongoing





DESIGN	Randomized, double-blind, placebo-controlled trials
POPULATION	Subjects 18-75 years of age with refractory focal epilepsy
SAMPLE SIZE	390 subjects in each study (randomized 1:1:1)
KEY ENTRY CRITERIA	Average of ≥4 observable focal seizures per 28 days
ENDPOINTS	Change in seizure frequency, 50% responder rate, seizure freedom

BHV-7000: Phase 2/3 Study in Idiopathic Generalized Epilepsy Is Ongoing



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Subjects 18-75 years old with idiopathic generalized epilepsy with intractable generalized tonic-clonic seizures
SAMPLE SIZE	242 subjects (randomized 1:1)
TREATMENT	BHV-7000 75 mg vs. placebo
TREATMENT DURATION	Up to 24-week double-blind phase
ENDPOINT	Time to event (2nd day with generalize tonic-clonic seizure)

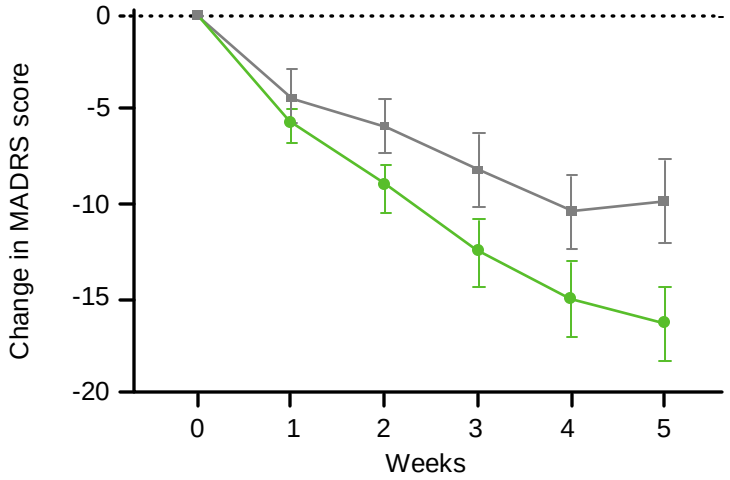
KEY POINT

Pivotal Phase 2/3 IGE study initiated in 1H 2024

BHV-7000:
Kv7 Activation Validated in the Clinic for Major Depressive Disorder

Randomized clinical trials in MDD with two nonselective Kv7 activators have demonstrated potential for rapid onset of clinically meaningful benefit in symptoms of depression and anhedonia

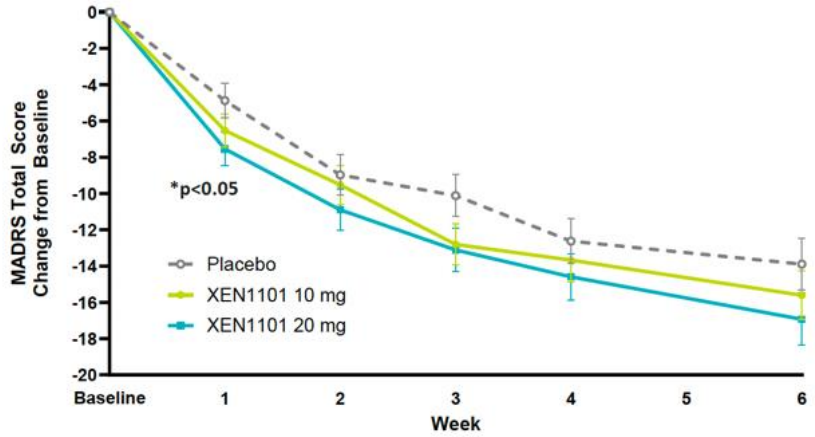
Ezogabine Demonstrated Robust Clinical Benefit (n=45)[1]



- 7.9-point benefit vs. placebo on MADRS (p<0.001)
- 6.9-point benefit vs. placebo on SHAPS (p<0.001)
- **Dose-limiting side effects in 20% of study subjects**

Costi et al, Am J Psychiatry. 2021 May 01; 178(5): 437–446.

XEN1101 Demonstrated Rapid Onset of Clinical Benefit With a Clear Dose Response (n=167)[2]



- 3-point benefit on MADRS (p=0.135) vs. placebo in 20 mg group, at week 1, 2.7-point benefit (p<0.05)
- 2.5-point benefit on SHAPS at week 6 (p<0.05) vs. placebo in 20 mg group
- **Efficacy not optimized likely due to dose limiting tolerability concerns**

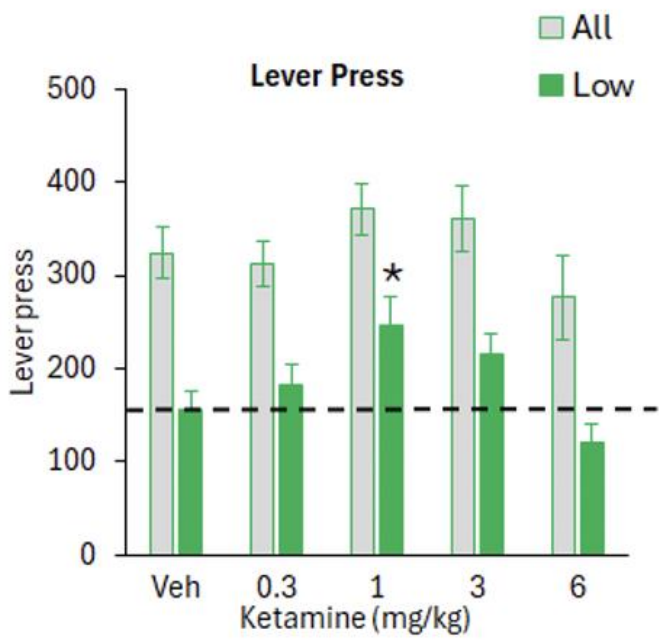
Xenon Pharmaceuticals Corporate update, November 27, 2023

KEY POINT

BHV-7000 has ideal profile for MDD due to **higher potential dose** and lower rates of CNS AEs vs. nonselective Kv7 activators

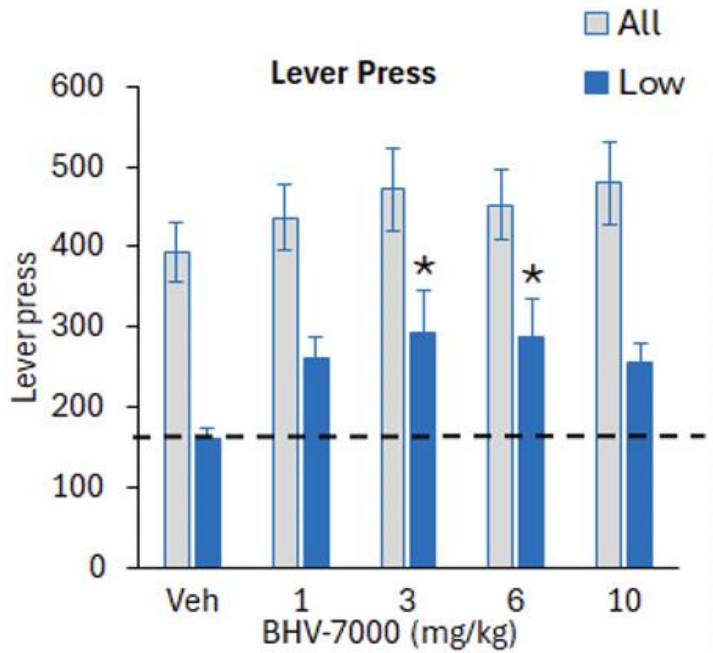
Potential Convergence of Therapeutic Effects of BHV-7000 and Ketamine

Ketamine Effects In 5-Choice Operant Model



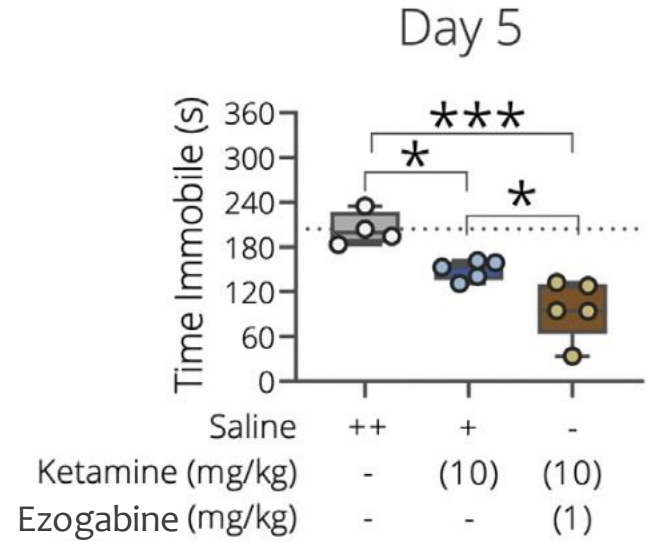
Higgins et al. Front Pharmacol. 2021 Feb 26; 12:640241.

Similar BHV-7000 Effects in 5-Choice Operant Model



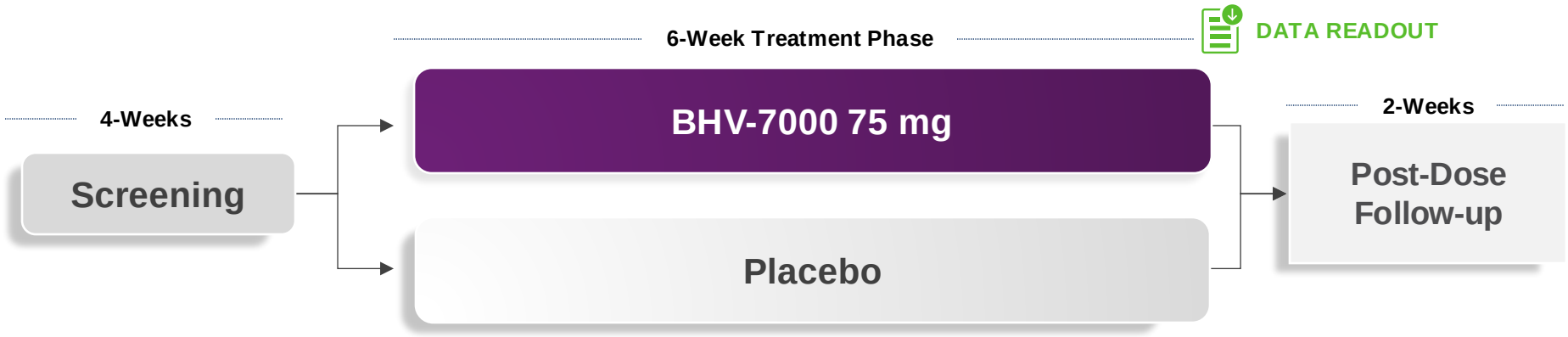
Biohaven data on file.

Ezogabine Enhances Ketamine Efficacy in Forced Swim Test Model



Lopez et al. Neuron. 2022 Jul 20;110(14):2283-2298.e9.

BHV-7000: Phase 2 Study in Major Depressive Disorder Is Ongoing



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

HAM-D, Hamilton Depression Rating Scale; **SHAPS**, Snaith-Hamilton Pleasure Scale; **MADRS**, Montgomery–Åsberg Depression Rating Scale; **CGI-S**, clinical global iimpression, severity; **Q-LES-Q-SF**: Quality of Life, Enjoyment, and Satisfaction Questionnaire-Short Form.

KEY POINT

Pivotal topline results expected in 2H 2025

BHV-7000:
Compelling Evidence for Targeting Kv7 in Bipolar Disorder

Human Genetics

- Bipolar disorder risk is heritable
- Ankyrin G (ANK3) is highly associated bipolar disorder risk gene in GWAS[1,2]
  - Ankyrin G anchors Kv7.2/7.3 channels to neuronal cell membrane[3]
  - Most significant gene-gene interaction in bipolar disorder GWAS is between ANK3 and Kv7.2[4]
- Kv7.2 and Kv7.3 are also directly linked to bipolar disorder risk by several studies[4,5]

Molecular Profiling of Bipolar Disorder Patient Tissues

- Evidence of significant transcriptional, epigenetic and proteomic changes in Kv7 channels in bipolar disorder
  - Bipolar disorder patient brain tissue demonstrates deregulation of Kv7 channels[6,7]
  - Kv7.3 gene DNA methylation patterns are altered, and expression is decreased, in bipolar disorder patients[7]

Preclinical Models

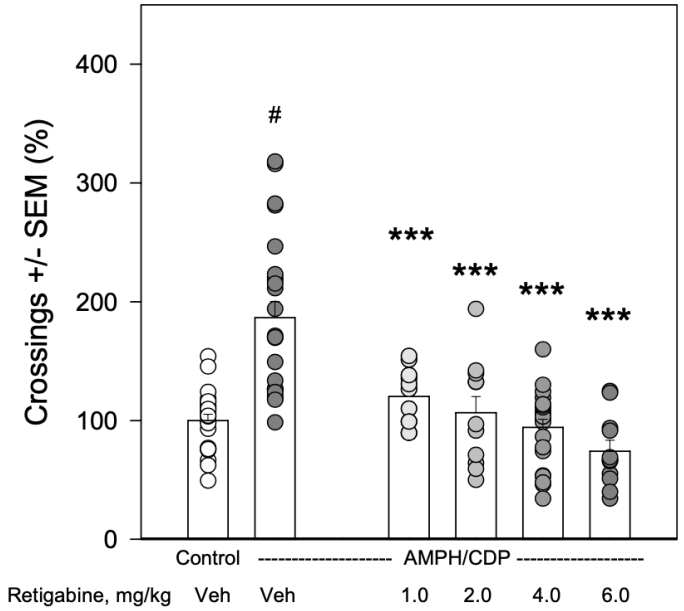
Kv7 activation demonstrates treatment benefits in preclinical models

1. Ferreira MA et al, Nat Genet. 2008 Sep;40(9):1056-8. 2. Psychiatric GWAS Consortium Bipolar Disorder Working Group. Nat. Genet. 2011. 3. Pan Z et al, J Neurosci. 2006 Mar 8;26(10):2599-613 . 4. Judy JT et al, Front Genet. 2013 May 17;4:87. 5. Koromina M et al, medRxiv [Preprint]. 2024 Feb 13:2024.02.12.24302716. 6. *Smolin et al. International Journal of Neuropsychopharmacology*, Volume 15, Issue 7, August 2012, Pages 869–882. 7. Kaminsky Z et al, Bipolar Disord. 2015 Mar;17(2):150-9.

BHV-7000: Ezogabine Improves Behavioral and Imaging Outcomes in Preclinical Mania Models

Amphetamine-chlordiazepoxide (AMPH/CDP) rodent mania model

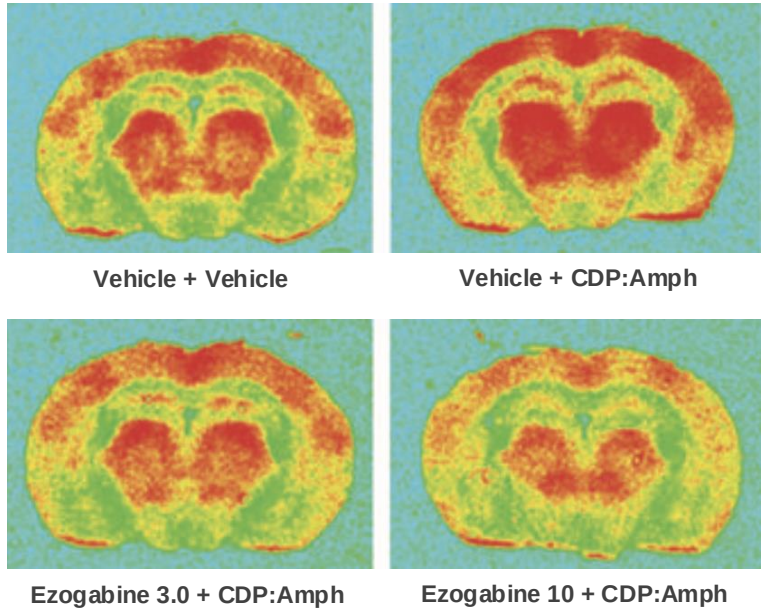
Ezogabine Reduces Hyperactive Locomotion



Kv7.2/7.3 activation results in dose-dependent decreases in AMPH/CDP induced hyperlocomotion without affecting basal locomotor activity at these doses

Dencker D, et al Epilepsy Behav. 2008 Jan;12(1):49-53 .

Ezogabine Reduces Brain Hypermetabolism



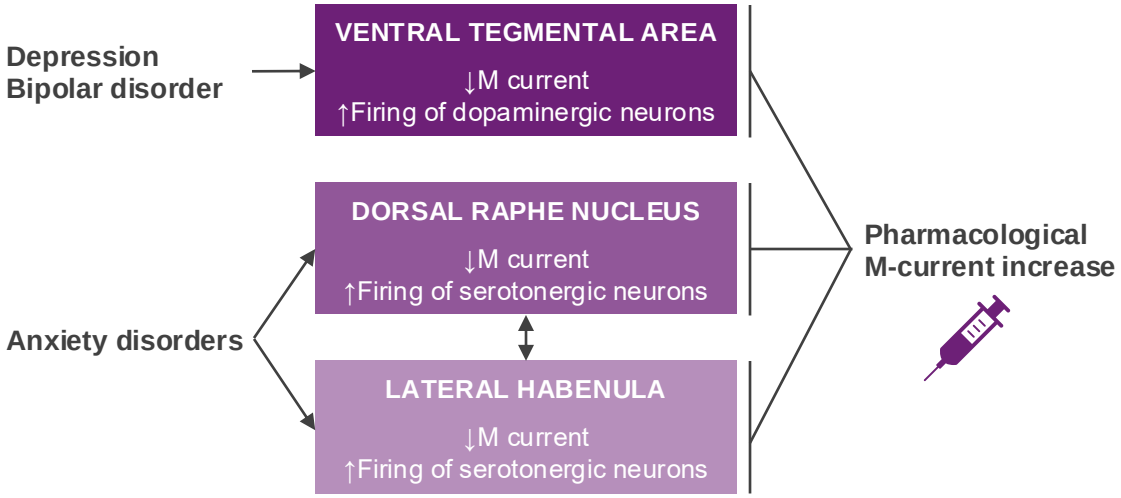
Kv7.2/7.3 activation results in dose-dependent decreases in brain hypermetabolism assessed via 2-deoxyglucose uptake

Kristensen LV et al , J Neurochem. 2012 May;121(3):373-82 .

BHV-7000: Demonstrates Positive Effects in Modulating Impulsive Behavior Consistent with M-current Activation

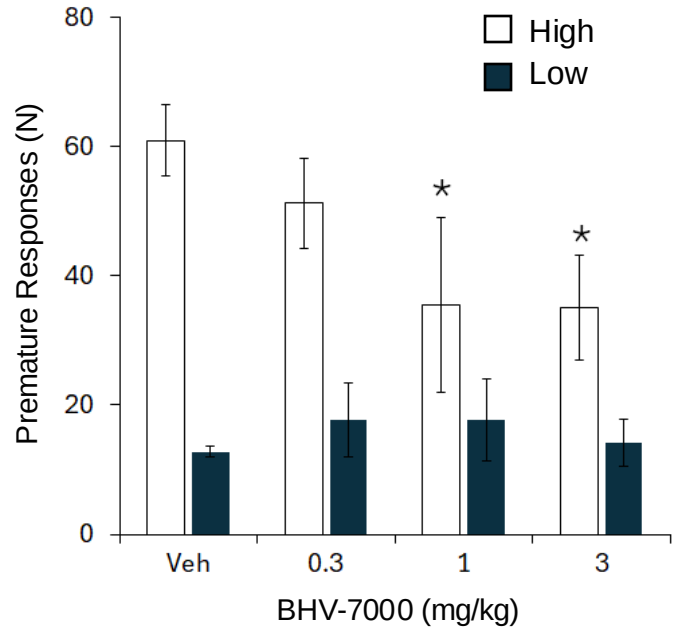
Operant model behavior and stratification in 5-choice serial reaction time task

Scientific rationale:

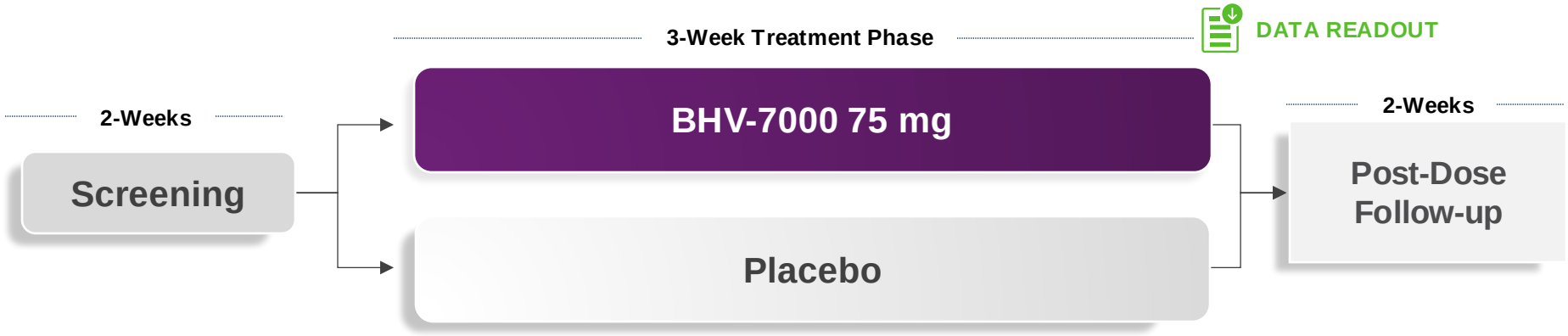


- BHV-7000 (1–3 mg/kg) shows evidence of reducing a measure of impulsiveness
- Effect seen in 2 task conditions: 5 and 10 sec inter trial intervals

Premature Responses
(High vs. Low Impulsive)



BHV-7000: Phase 2/3 Study in Bipolar Disorder (Acute Mania) Is Ongoing



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Subjects with Bipolar Disorder I with at least one prior mood episode who are currently experiencing a manic episode (YMRS ≥ 20)
SAMPLE SIZE	256 subjects (randomized 1:1)
TREATMENT	BHV-7000 vs. placebo
TREATMENT DURATION	3-weeks
ENDPOINTS	YMRS (primary), CGI-S

YMRS, Young Mania Rating Scale; **CGI-S**, clinical global impression, severity.

KEY POINT

Pivotal topline results expected in 1H 2025

First-in-Clinic TRPM3 Antagonist — Novel Mechanism for the Treatment of Migraine and 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 such as hyperthermia

Phase 1 Study Data Supports Evaluation in Pain

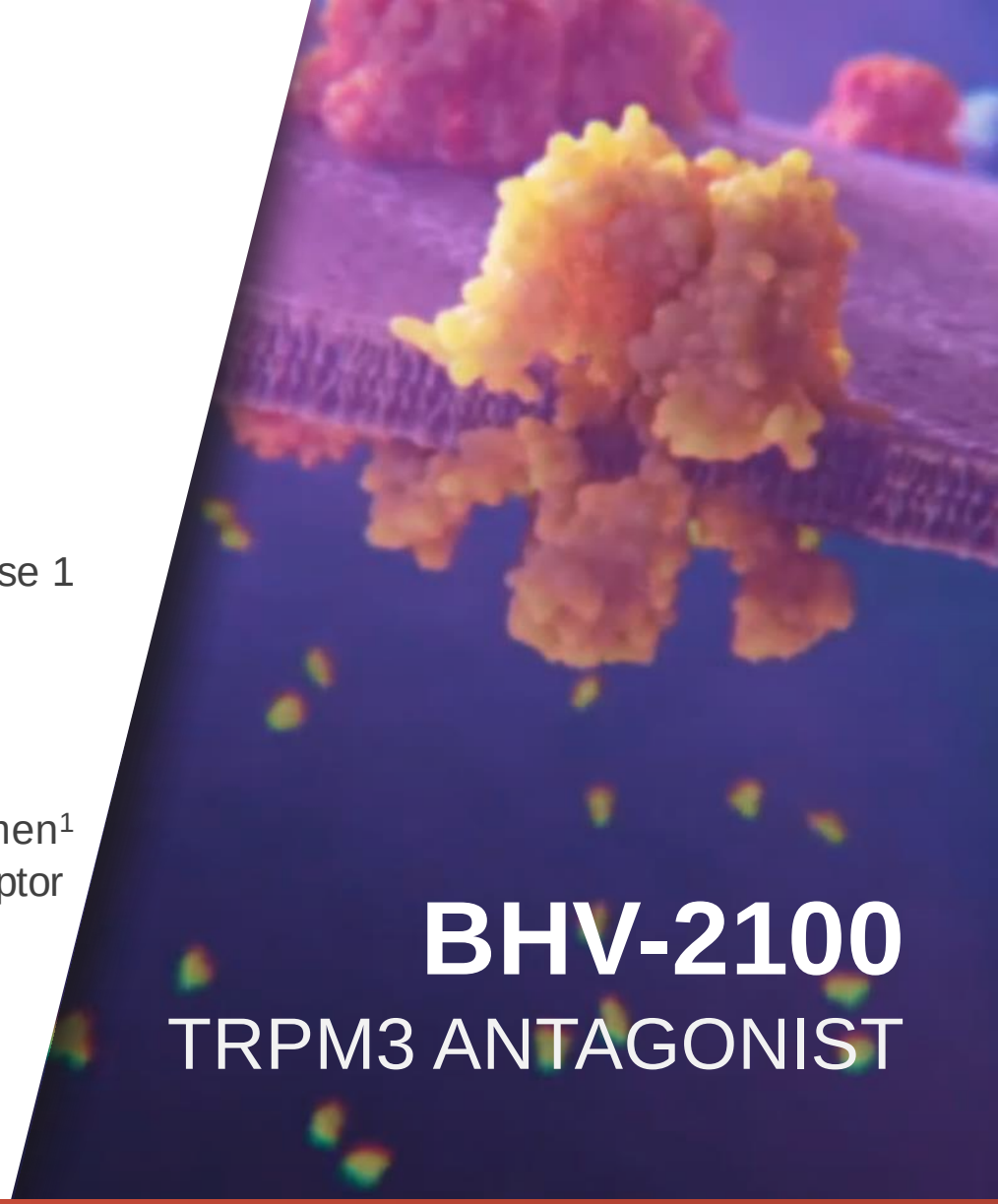
BHV-2100 demonstrated excellent safety/tolerability and favorable PK in Phase 1

Significant Unmet Need Remains

- The CDC estimates the prevalence of chronic pain to be 20%[2]
- The global opioid crisis highlights the unmet needs in pain management[3]
- Migraine is 2nd leading cause of disability worldwide, 1st among young women[1]
- 30–40% of patients do not respond to treatments that block CGRP or its receptor

Milestones Achieved

- Laser-evoked potential proof-of-concept trial for pain initiated in 2H 2024
- Proof of concept trial for acute treatment of migraine initiated in 2H 2024



1. Steiner TJ et al, J Headache Pain. 2020 Dec 2;21(1):137 2. Cohen SP, Vase L, Hooten WM. Lancet 2021;397(10289):2082-2097.
3. Volkow, N.D. and W.J. Koroshetz, Nat Rev Neurol, 2019. 15(5): p. 301-305.

BREAKING NEWS

Emerging data with BHV-2100 in laser heat-induced pain and brain evoked potentials validates the TRPM3 inhibitor class in the treatment of pain

BHV-2100: Targeting the Unmet Medical Need in Pain and Migraine

Biohaven's legacy of success

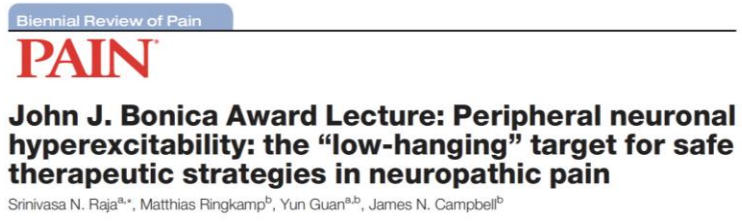

The NEW ENGLAND JOURNAL of MEDICINE

Rimegepant, an Oral Calcitonin Gene–Related Peptide Receptor Antagonist, for Migraine

Richard B. Lipton, M.D., Robert Croop, M.D., Elyse G. Stock, M.D., David A. Stock, Ph.D., Beth A. Morris, B.A., Marianne Frost, M.A., Gene M. Dubowchik, Ph.D., Charles M. Conway, Ph.D., Vladimir Coric, M.D., and Peter J. Goadsby, M.D., Ph.D.

MIGRAINE

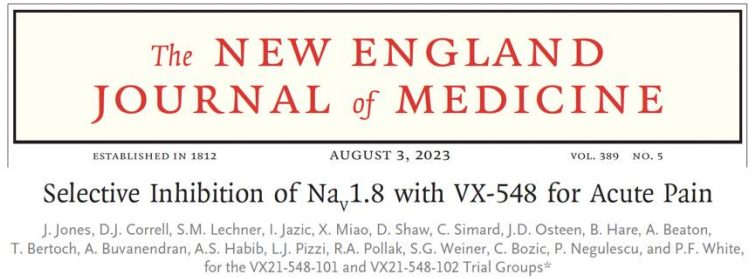
Emerging role of novel mechanisms: ion channels in the periphery


Biennial Review of Pain

PAIN

John J. Bonica Award Lecture: Peripheral neuronal hyperexcitability: the "low-hanging" target for safe therapeutic strategies in neuropathic pain

Srinivasa N. Raja[a,*], Matthias Ringkamp[b], Yun Guan[a,b], James N. Campbell[b]


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 3, 2023 VOL. 389 NO. 5

Selective Inhibition of $Na_V1.8$ with VX-548 for Acute Pain

J. Jones, D.J. Correll, S.M. Lechner, I. Jazic, X. Miao, D. Shaw, C. Simard, J.D. Osteen, B. Hare, A. Beaton, T. Bertoch, A. Buvanendran, A.S. Habib, L.J. Pizzi, R.A. Pollak, S.G. Weiner, C. Bozic, P. Negulescu, and P.F. White, for the VX21-548-101 and VX21-548-102 Trial Groups*

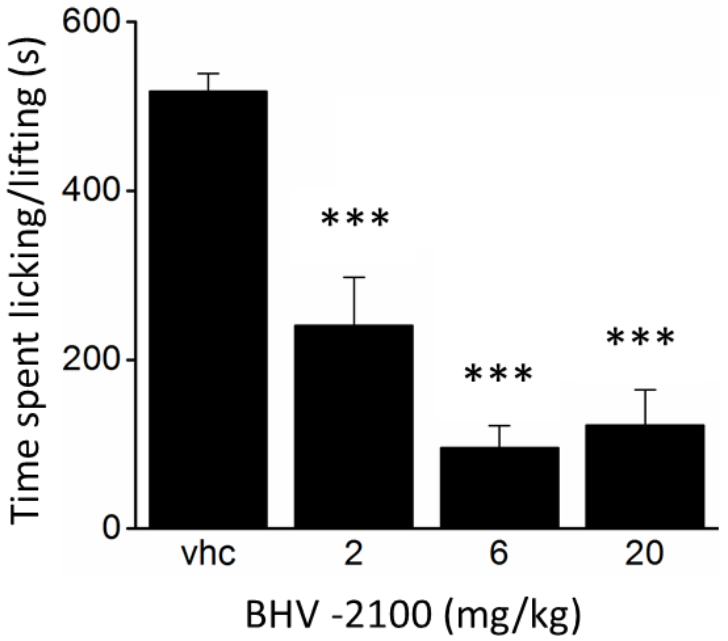
ACUTE PAIN & NEUROPATHIC PAIN

KEY POINT

BHV-2100 is a selective, peripherally-restricted TRPM3 antagonist that is a potentially highly-effective, non-sedating, non-opioid treatment for pain and migraine

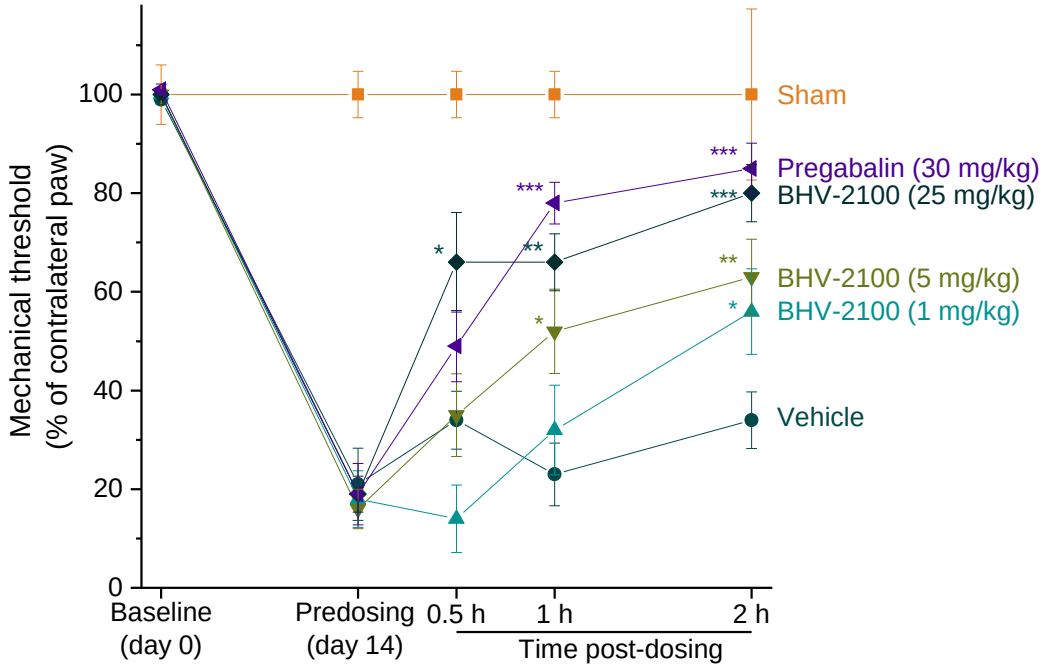
BHV-2100: Potently Reduces Acute Chemogenic Pain and Pain Following Nerve Injury

PS-Induced Acute Pain Model



Drug administered 30 minutes prior to TRPM3 agonist injection in a hind paw of rats

Partial Sciatic Nerve Ligation Model



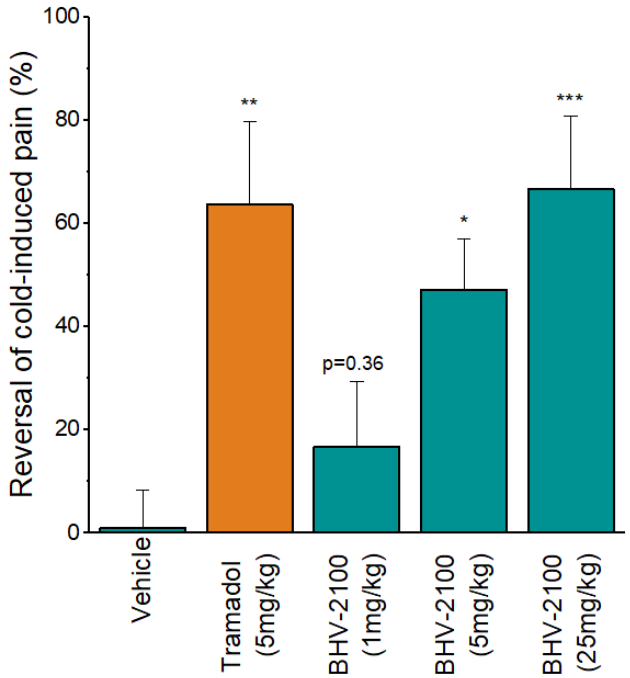
Drug administered 14 days after unilateral sciatic nerve injury in rats

Encouraging evidence of pain reduction without the sedation observed with high-dose pregabalin

*** p<0.001, ** p<0.01 , * p<0.05

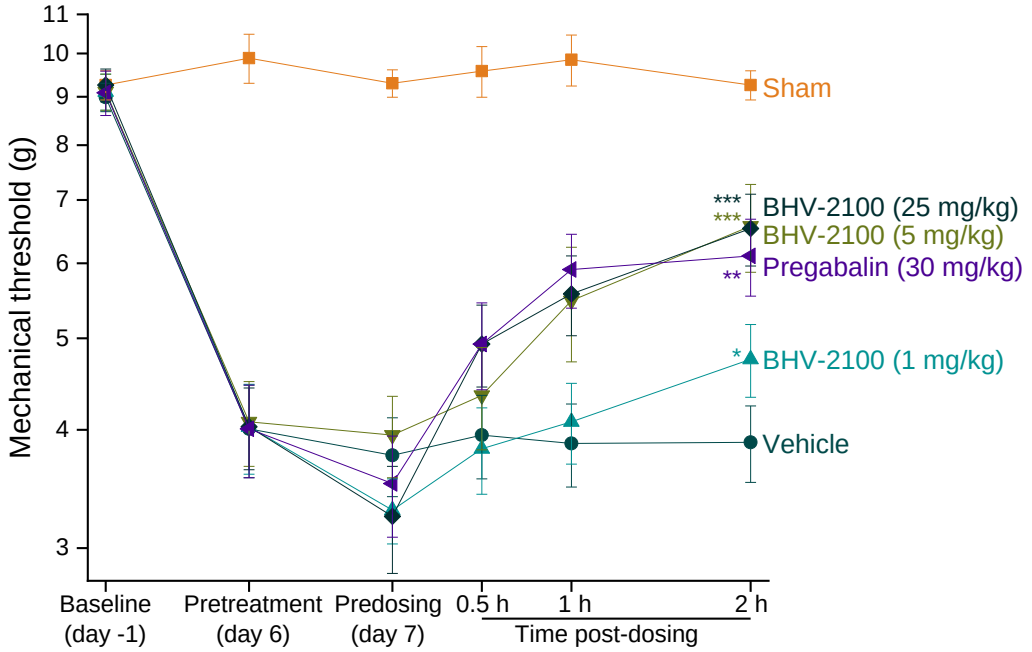
BHV-2100: Reverses Established Pain States in Peripheral Neuropathic Pain Models

Chemotherapy-Induced Neuropathic Pain Model



Drug administered 6 days after oxaliplatin treatment in mice

Diabetic Neuropathy Model



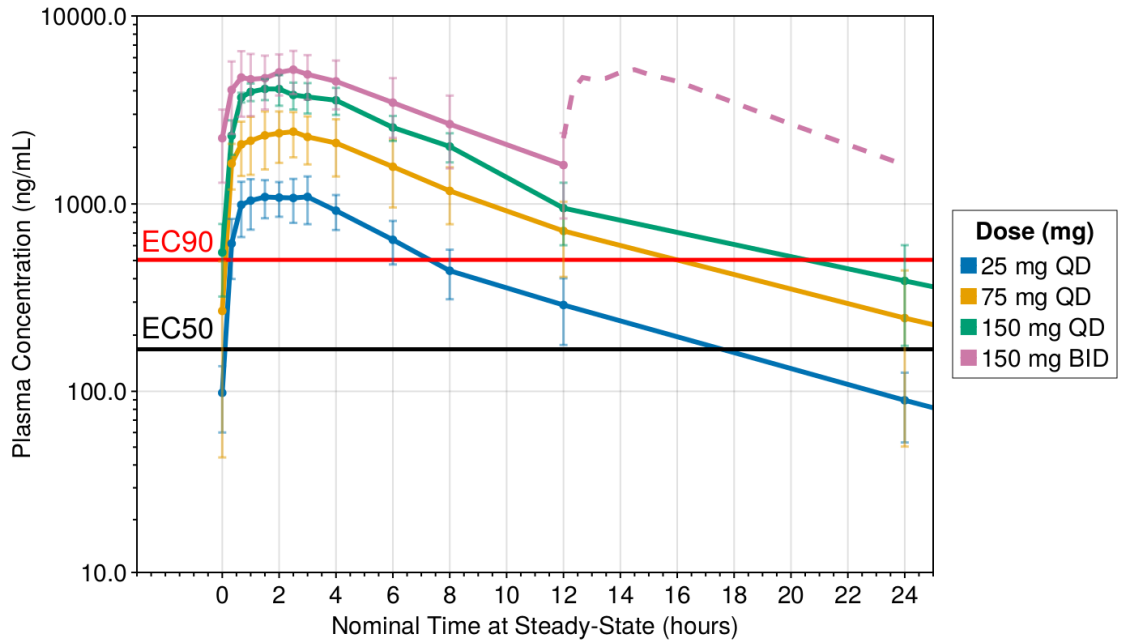
Drug administered 7 days after STZ treatment in rats

Encouraging evidence of pain reduction without the sedation observed with high-dose pregabalin/tramadol

*** p<0.001, ** p<0.01 , * p<0.05

BHV-2100: Ideal Pharmacokinetic Profile for Treating Pain

Mean Concentration vs. Time Profiles at Steady-State After Multiple Oral Doses of BHV-2100



EC90 represents the estimated plasma concentration threshold based on a preclinical model

KEY POINT

Phase 1 data in healthy subjects shows plasma PK exceeds EC90 by 20 min at all doses tested and is sustained above EC50 for 24 hours at doses > 25 mg QD

BHV-2100: Safe and Well-Tolerated in Healthy Subjects

SAFETY AND TOLERABILITY

- No dose limiting toxicities in studies
- No SAEs
- No severe TEAEs; most TEAEs were mild
- No clinically significant trends in vital signs (including body temperature), laboratory values, or ECGs

DOSING

- SAD: single doses up to 500 mg
- MAD: multiple doses up to 150 mg twice a day for 14 days

SAD Cohorts (pooled) TEAEs in ≥ 2 subjects	Placebo (N=9) n (%)	BHV-2100 (N=30) n (%)
Dizziness	0 (0)	2 (6.7)
Fatigue	0 (0)	2 (6.7)

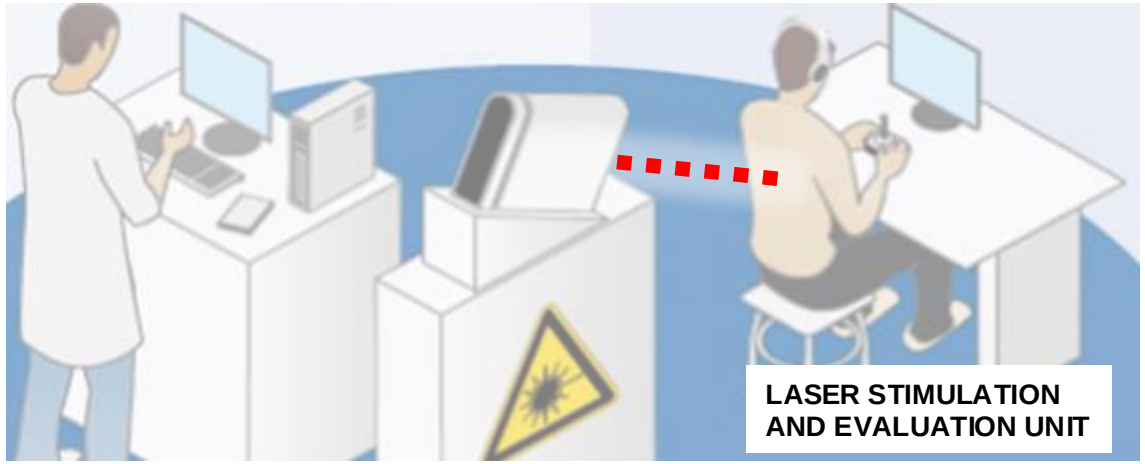
MAD Cohorts (pooled) TEAEs in ≥ 2 subjects	Placebo (N=8) n (%)	BHV-2100 (N=24) n (%)
	0 (0)	0 (0)

MAD, multiple ascending dose**; SAD**, single ascending dose; **SAE,** serious adverse events; **TEAE,** treatment emergent adverse events.
Pooled preliminary data.

KEY POINT

No TEAE occurred in > 1 participant across the MAD cohorts

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

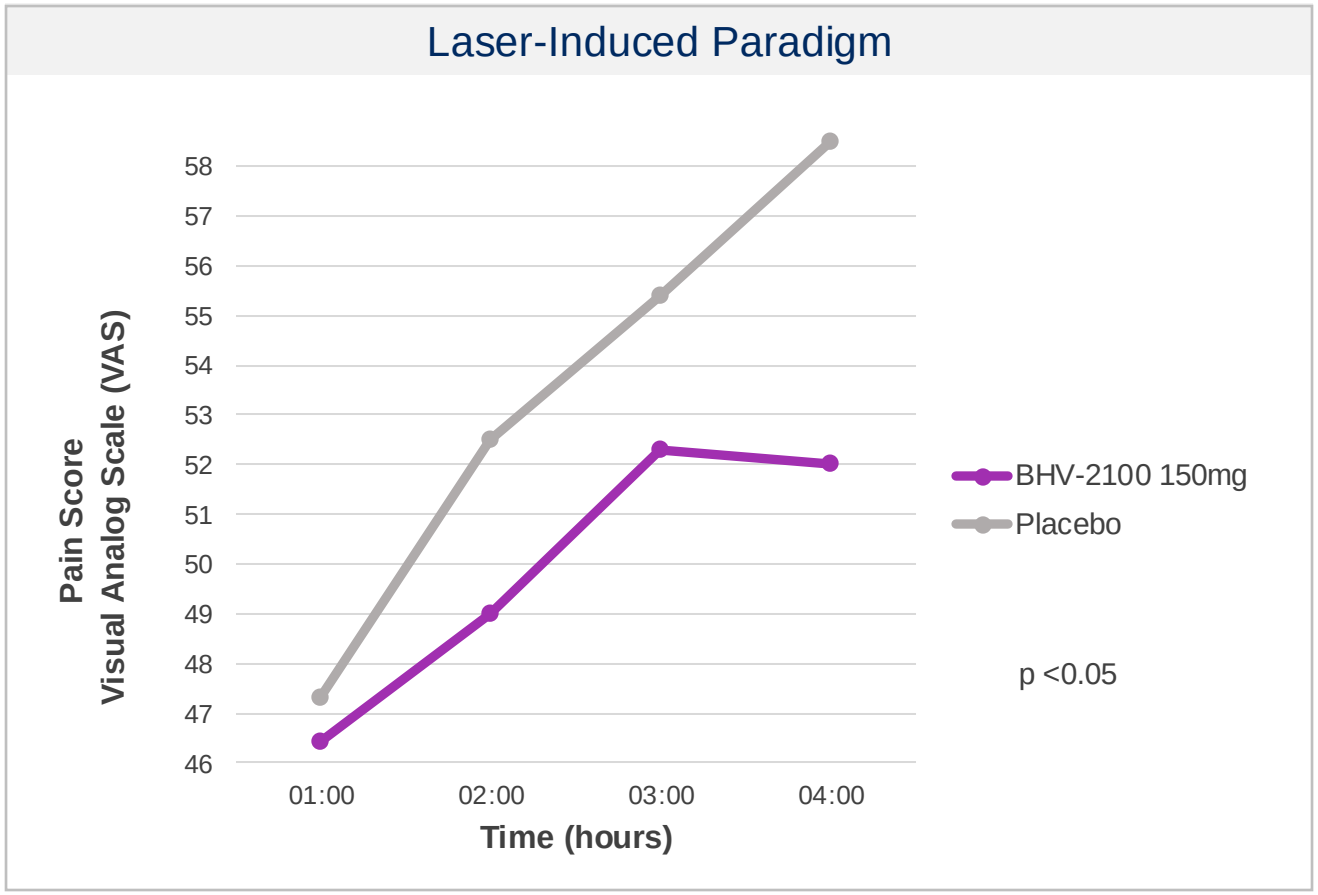


Efficacy

- Lowering in self-reported VAS pain rating scale
- Clinically meaningful reductions in laser-evoked potentials in normal and UVB-inflamed skin

Safety

- Well-tolerated
- No effects observed on core temperature
- No change on heat pain threshold

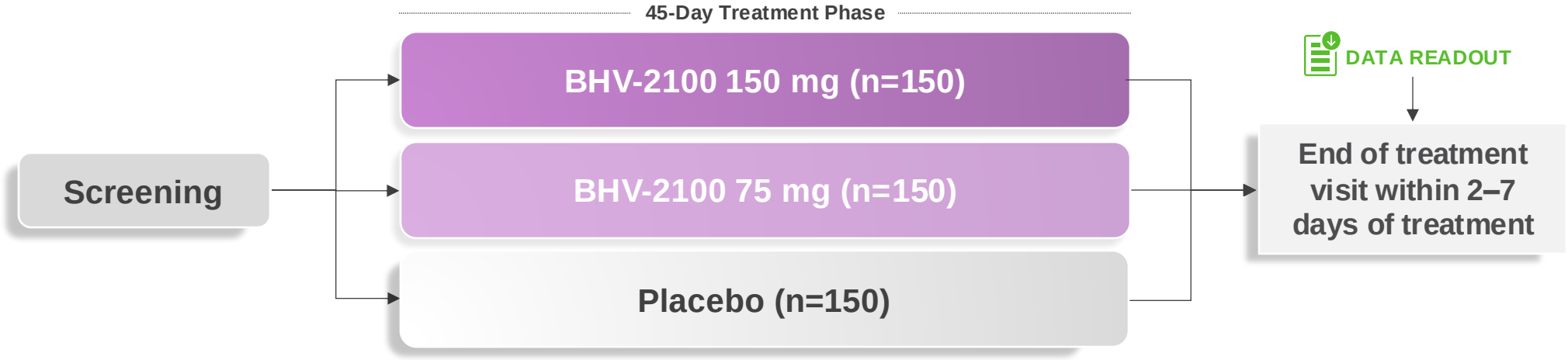


Preliminary Data up to Tmax; p-value out to 8 hour test period

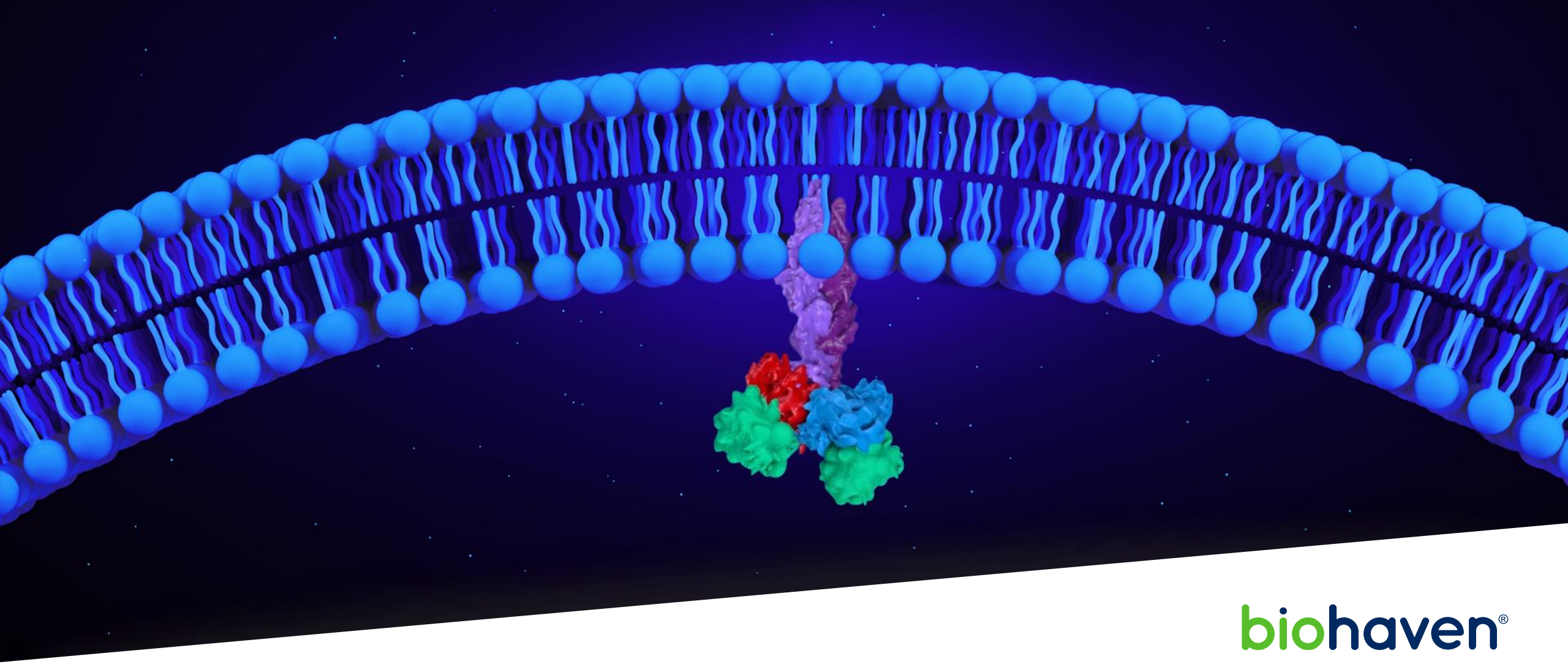
KEY POINT

First indication of potential clinical efficacy in pain with the novel TRPM3 mechanism

BHV-2100: Phase 2 Study in Acute Treatment of Migraine



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Participants with at least 1 year history of migraine (with or without aura)
SAMPLE SIZE	450 (randomized 1:1:1 across 2 doses and placebo)
TREATMENT	BHV-2100 (75/150 mg) vs. placebo
TREATMENT DURATION	Single dose, up to 45 days to treat eligible migraine
COPRIMARY ENDPOINTS	Pain freedom at 2 hours, Freedom from most bothersome symptom at 2 hours



biohaven®

Neurodegenerative Disorders

First-in-Clinic, Oral, Selective, Brain-Penetrant TYK2/JAK1 Inhibitor

- Uniquely potent, TYK2/JAK1 selective, brain-penetrant inhibitor
- Selectivity profile avoids class risks associated with JAK2/3 inhibition

Breaks the Cycle of Neuroinflammation

- Reduces inflammatory impacts of microglia, astrocytes and infiltrating T-lymphocytes

Potential to Treat Multiple Neuroinflammatory Disorders

- Supported by a broad range of clinical, translational, and epidemiological evidence
- Indications include Parkinson's disease, anti-amyloid therapy induced ARIA, Alzheimer's disease, and multiple sclerosis

Encouraging Results from Completed Phase 1 Trial

- Safe and well-tolerated
- Evidence of target engagement
- Robust brain penetration

Milestone Achieved

FDA meetings successfully completed enabling registrational programs for Parkinson's disease and prevention of ARIA

BHV-8000

TYK2/JAK1 INHIBITOR
(brain-penetrant)

ARIA, Amyloid-related imaging abnormalities; **SAD**, single ascending dose; **MAD**, multiple ascending dose; **TYK**, tyrosine kinase; **JAK**, Janus kinase.

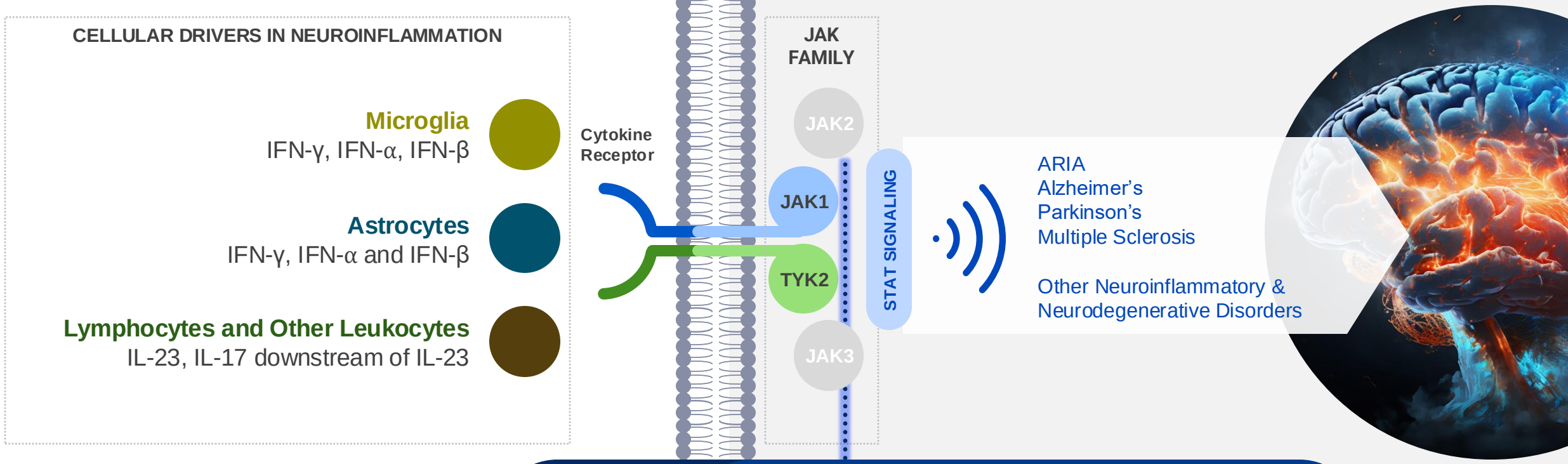
BREAKING NEWS

Pivotal study in Parkinson's disease planned to initiate in 1H 2025

BHV-8000 Is a Brain-Penetrant TYK2/JAK1 Inhibitor With Potential to Treat Neuroinflammatory & Neurodegenerative Disorders

Inflammation plays a key role in the pathogenesis of neurodegenerative diseases

Nonclinical, clinical, genetic, and epidemiological data show that interrupting chronic inflammation may slow disease progression



BHV-8000 Dual, brain-penetrant inhibitor of TYK2 and JAK1 that effectively blocks Th17 cell generation, Type I IFN signaling, and inflammation

Selectivity of BHV-8000 Predicts Improved Safety With Targeted Efficacy

Approved JAK Inhibitors — Significant Safety Risks Associated with JAK2 and/or JAK3 Inhibition						
		IC_{50} in nM				
Inhibitor	Status	JAK1 (autoimmune)	JAK2 (hematology)	JAK3 (leucocyte)	TYK2 (inflammation)	Safety
Tofacitinib[1]	Approved	15	77	55	489	Boxed Warning (MACE, malignancy, thrombosis, serious infections)
Baricitinib[1]	Approved	4	7	787	61	Boxed Warning
Upadacitinib[1]	Approved	47	120	2304	4690	Boxed Warning
Abrocitinib[1] (selective JAK1)	Approved	29	803	>15,000	1250	Boxed Warning* (*Development program suggests no increased clinical risk for these events)
Deucravacitinib[1] (selective TYK2)	Approved	>10,000	>10,000	>10,000	0.2	NO Boxed Warning

BHV-8000 Expected to Have a Favorable Safety Profile (avoids JAK2 and JAK3 inhibition)						
		IC_{50} in nM				
Inhibitor	Status	JAK1 (autoimmune)	JAK2 (hematology)	JAK3 (leucocyte)	TYK2 (inflammation)	Safety
BHV-8000	Phase 2 ready	4	118	>500	4	No expected risk of JAK2 and JAK3-related safety issues

IC_{50}, half maximal inhibitory concentration; **JAK**, Janus kinase; **MACE**, major adverse cardiac event; **TYK**, tyrosine kinase.

1. Wrobleski et al. *J Med Chem*. 2019;62(20):8973-8995.

BHV-8000: Demonstrates a Promising Phase 1 Profile

STUDY COMPLETED: 3 SAD cohorts and 3 MAD cohorts

- SAD dose cohorts (10, 20 and 30 mg); MAD dose cohorts (6, 10 and 20 mg)
- 8 healthy subjects per cohort (6 active: 2 placebo)

SAFETY PROFILE: Safe and well-tolerated to date

- No SAEs or severe AEs; only mild AEs observed that resolved spontaneously
- No adverse laboratory trends related to study drug

PHARMACODYNAMIC EFFECTS

hs-CRP, IFN-beta, and IP-10 showed drug-related changes in plasma

PHARMACOKINETICS

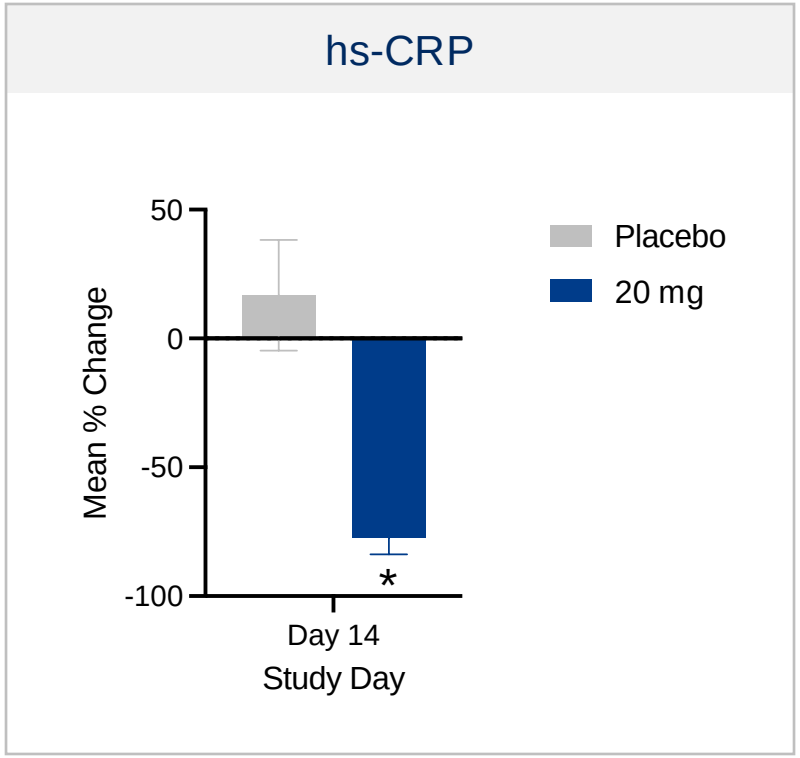
Approximately 50% CNS penetration in humans

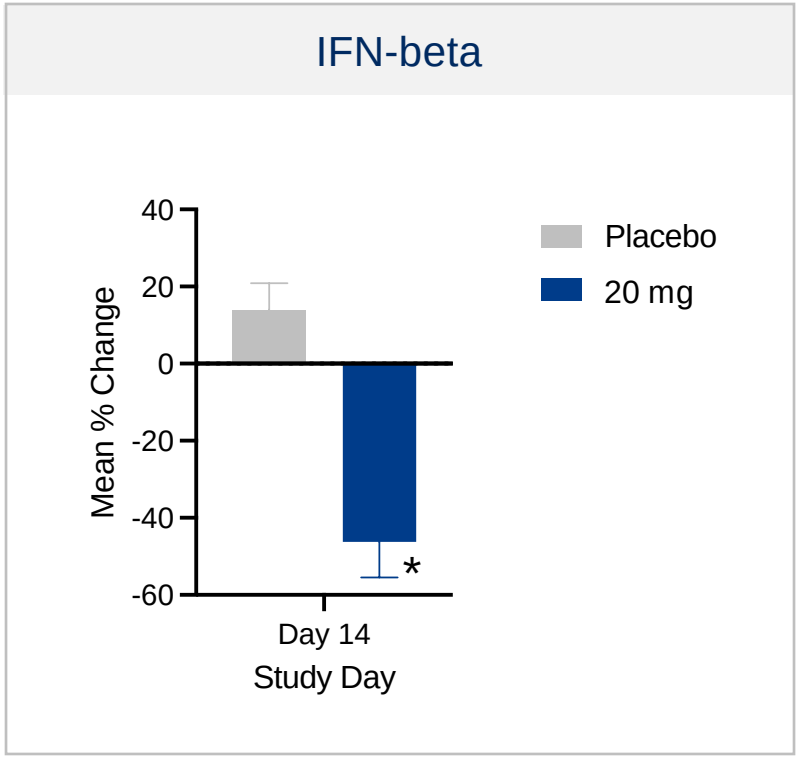
AE, adverse event; **hs-CRP**, high-sensitivity C-reactive protein; **IFN-beta**, Interferon beta; **MAD**, multiple ascending dose; **SAD**, single ascending dose; **SAE**, serious adverse event.

KEY POINT

BHV-8000 is safe and well-tolerated at doses showing evidence of CSF penetration and target engagement

BHV-8000: Shows Evidence of Pharmacodynamic Effects





* p<0.05

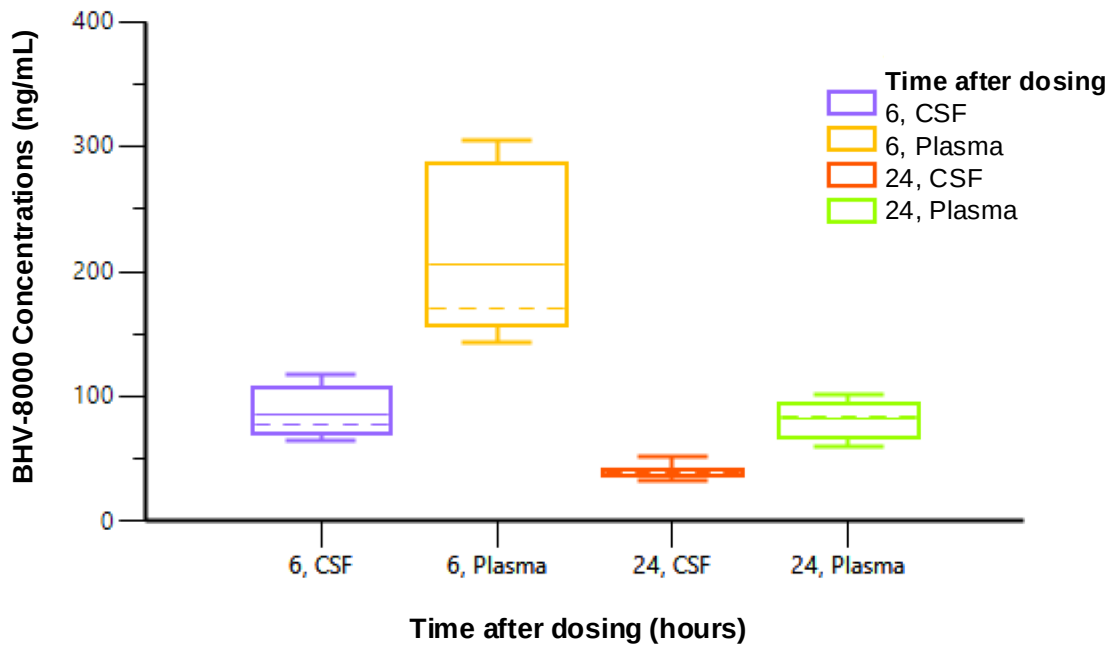
Preliminary Phase 1 data. **hs-CRP**, high-sensitivity C-reactive protein; **IFN-beta**, Interferon beta.

KEY POINT

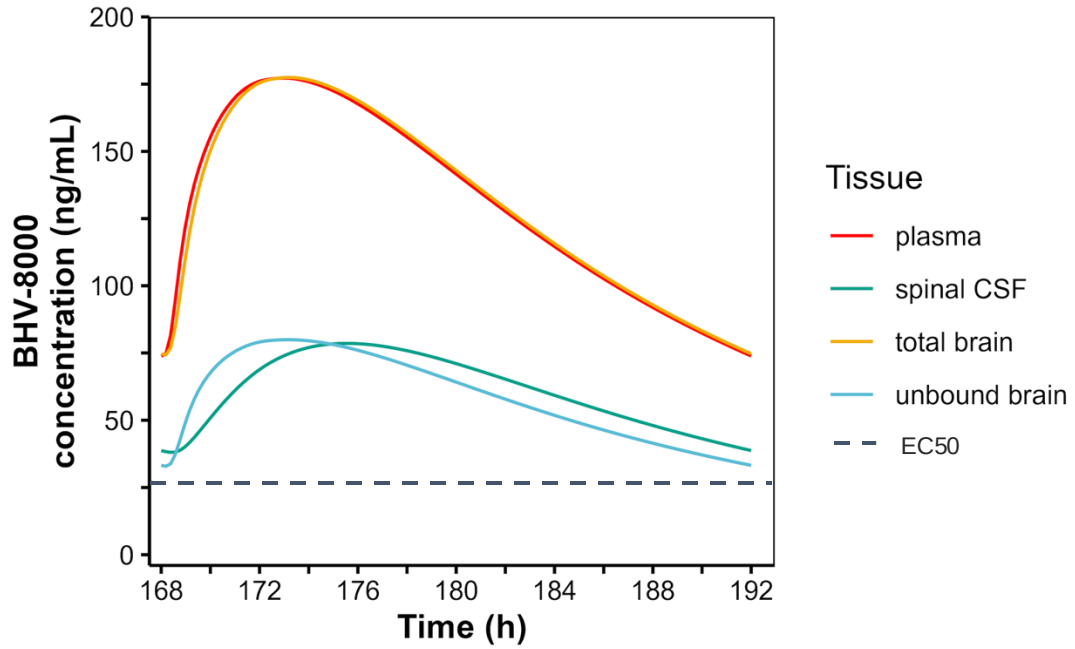
Pharmacodynamic data is indicative of target engagement in healthy subjects

BHV-8000: Demonstrates CNS Exposure

CSF and Plasma Concentrations (20 mg QD)



Brain PK sustained above EC50 for 24 hours at 20 mg QD



Modelling data

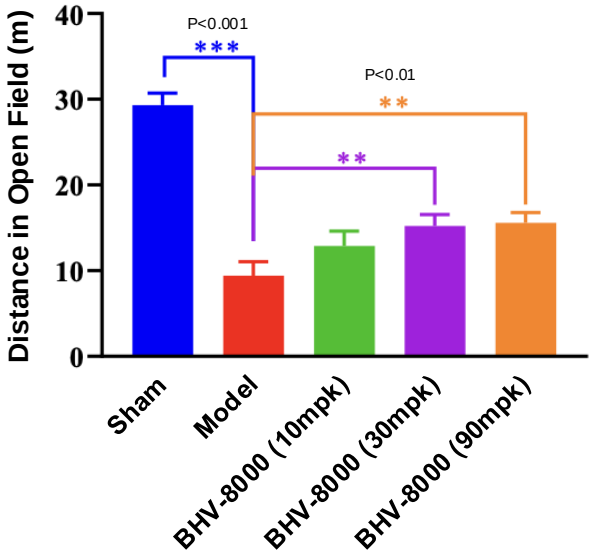
CSF, Cerebro Spinal Fluid

KEY POINT

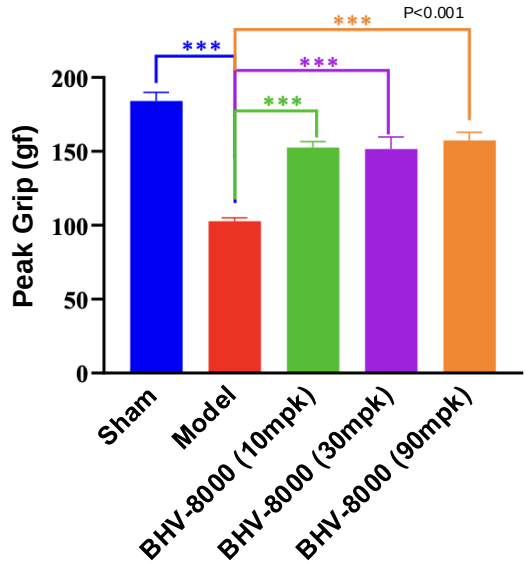
BHV-8000 expected to have sustained brain exposures above EC50 (target engagement)

BHV-8000: Efficacious in an AAV-α-synuclein Mouse Model of Parkinson's

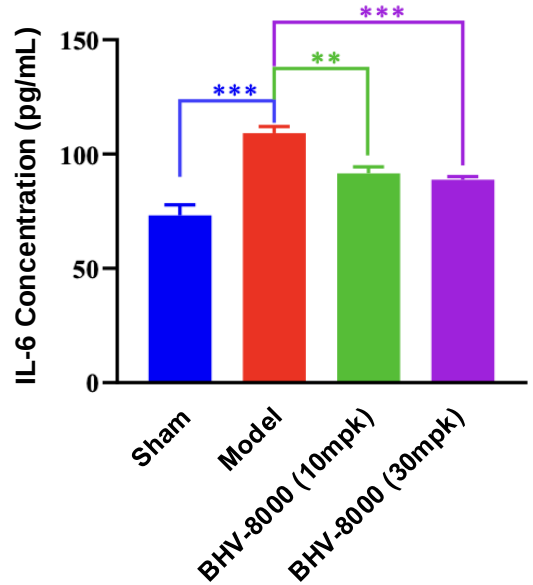
BHV-8000 Shows Dose Proportional Increase in Total And Corner Movement in an Open Field



BHV-8000 Shows an Increase in Grip Strength



BHV-8000 Treatment Significantly Decreased IL-6 Level in Str and SN Tissues of Mice



Note: IL-6 levels are elevated in PD patients

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-IL17 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

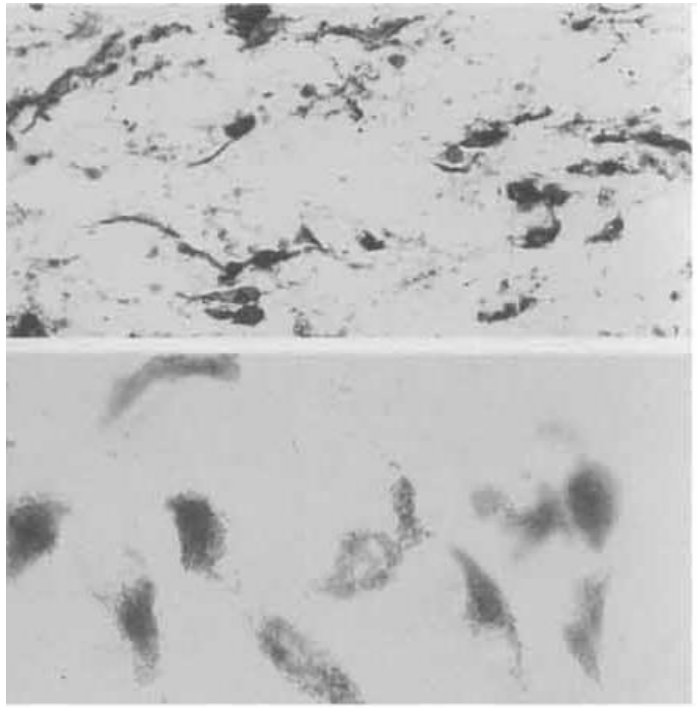
Treatment	PD Events	Person-years	Rate (per 100 person-years)	Adjusted IRR (95% CI)	P-value
Anti-TNF or Anti-IL-17 exposure	2,957	393,114	**0.66**	0.77 (0.74 – 0.80)	<0.0001
No Treatment	50,562	5,328,307	0.95		
Anti-TNF exposure	2,471	371,867	**0.66**	0.64 (0.52 – 0.80)	<0.0001
No Treatment	50,562	5,328,307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

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

BHV-8000: Clinical Data Supports Targeting Neuroinflammation in Parkinson's Disease

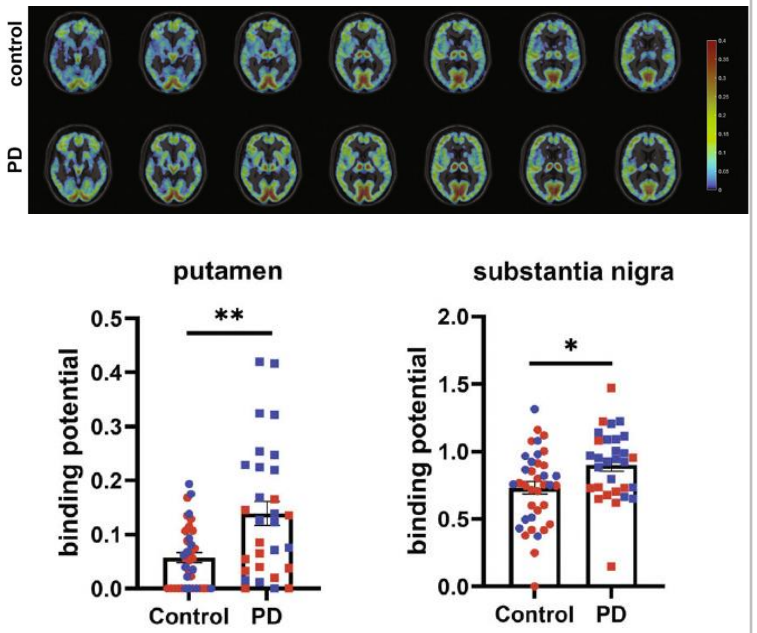
Post-Mortem Data[1]

PD patient brains express high levels of HLA-DR+ reactive microglia



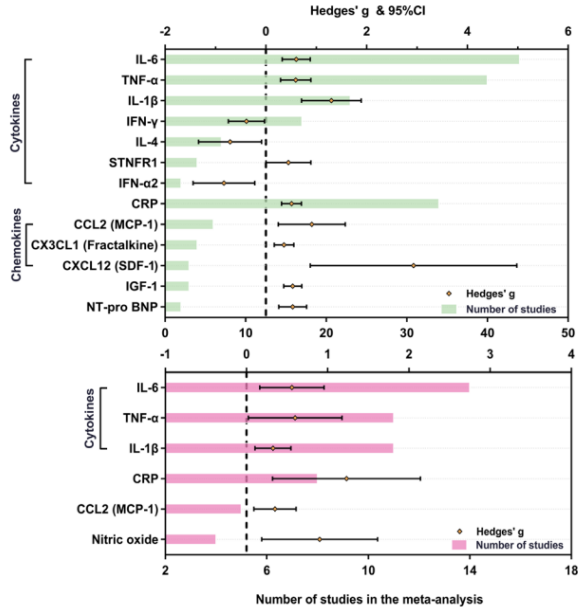
In Vivo Imaging[2]

^{18}F-DPA-714 TSPO imaging increased in early PD relative to healthy controls



In Vivo Cytokine Levels[3]

Elevated levels of pro-inflammatory cytokines (e.g., IL-1β, IL-6, TNF-α, IFN-ɣ) found in the CSF and blood of PD patients



1. McGeer PL, et al. *Neurology*. 1988 Aug;38(8):1285-91. 2. Yacoubian TA, et al. *Mov Disord*. 2023 May;38(5):743-754. 3. Qu Y, et al. *NPJ Parkinsons Dis*. 2023 Feb 4;9(1):18.

BHV-8000: Unique Phase 2/3 Study Design for Parkinson's Disease

Novel Primary Efficacy Endpoint

Time-to-event (≥ 2-point worsening on MDS-UPDRS-Part II)

- Addresses FDA requirement for a functional endpoint in PD trials
  - MDS-UPDRS-Part II recommended, but declines very slowly in early PD
- 300 fewer patients per trial versus a mean change on MDS-UPDRS-Part II
- Based on comprehensive analyses of PPMI and placebo-arm clinical trial data (C-Path)

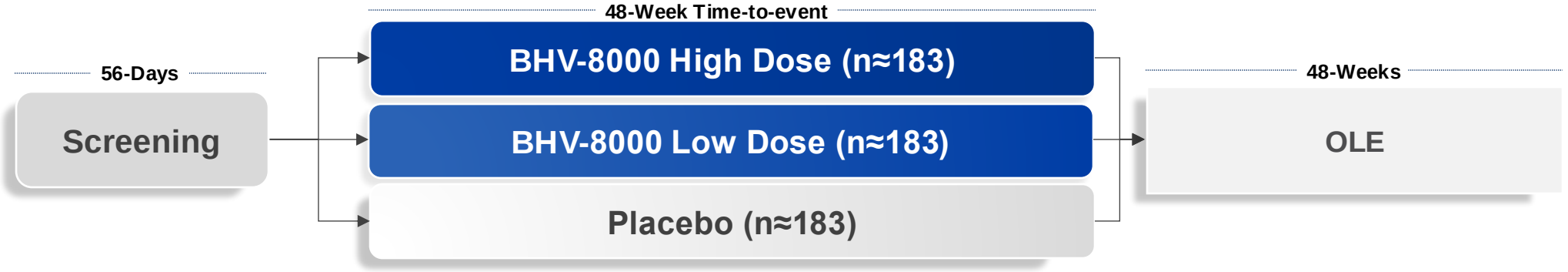
Provides a meaningful efficacy endpoint with a smaller sample size

Novel Composite Endpoint

Parkinson's Disease Composite Score (PARCOMS)

- Based on established methodology (i.e., Alzheimer's Disease Composite Score [ADCOMS])
- Leverages PPMI and placebo-arm clinical trial data (C-Path)
- Comprises the most responsive items from common endpoints in early PD trials

Provides a highly-sensitive supportive secondary efficacy endpoint



PPMI, Parkinson's Progression Markers Initiative; **MDS-UPDRS**, Movement Disorder Society – Unified Parkinson's Disease Rating Scale.

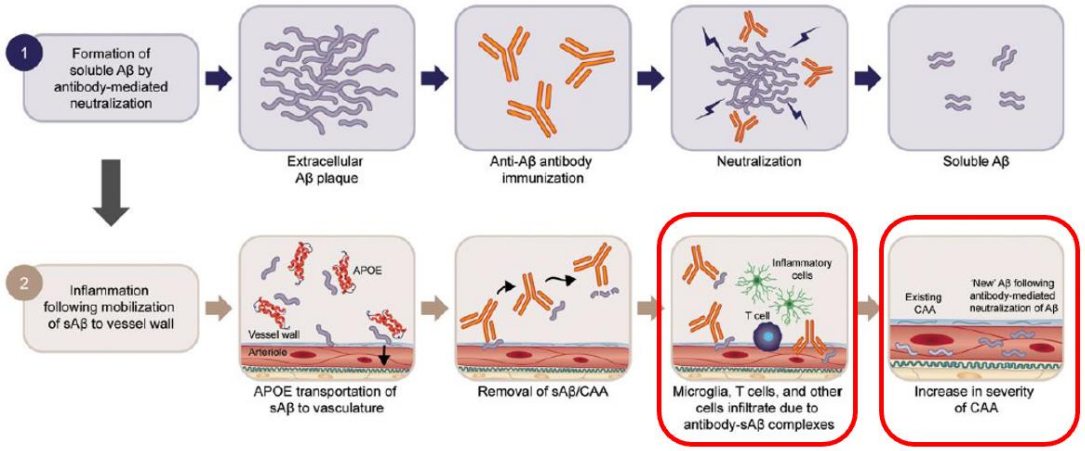
BREAKING NEWS

Pivotal study planned to initiate in 1H 2025

BHV-8000: ARIA—A Potential Therapeutic Target for TYK2/JAK1 Inhibition

- ARIA events typically occur early after initiation of anti-amyloid mAb therapy.[1] The occurrence of ARIA can complicate the benefit-risk assessment in certain patient groups
- Reduction or elimination of ARIA should improve the uptake of anti-amyloid mAb therapies
- **Therapeutic hypothesis:**
  - TYK2/JAK1 inhibition reverses activated glial- and T-cell mediated pathology and general inflammation
  - Corticosteroids and other immunosuppressive drugs show benefit in treatment and reduce the risk for ARIA.[1,2,3] Generally, TYK2/JAK1 inhibition has a favorable benefit-risk profile over corticosteroids and other immunosuppressive drugs

Proposed Pathogenesis of ARIA[2]



- Antibody-dependent complement-mediated vascular injury, secondary to amyloid deposition in blood vessels[4]
- Loss of vascular integrity, impaired clearance and CAAri lead to vasculitis[2]
- Leakage of proteinaceous fluid and blood, results in ARIA-E or ARIA-H, respectively[2]
- Activated glial- and T-cell infiltration[2]
- Overexpression of C3 induces signaling through the JAK/STAT3 pathway[5]

[1]Cummings et al, *J Prev Alz Dis.* 2023;3(10):362-77; [2]Hampel e al, *Brain.* 2023 146;4414-24; [3]Regenhardt et al, *JAMA Neurol.* 2020 Oct;77(10)1-10; [4]Alzforum, 2023 https://www.alzforum.org/news/conference-coverage/aria-inflammatory-reaction-vascular-amyloid; [5]Yuan et al, *J Exp Clin Cancer Res.* 2020 V39;PMC6956509

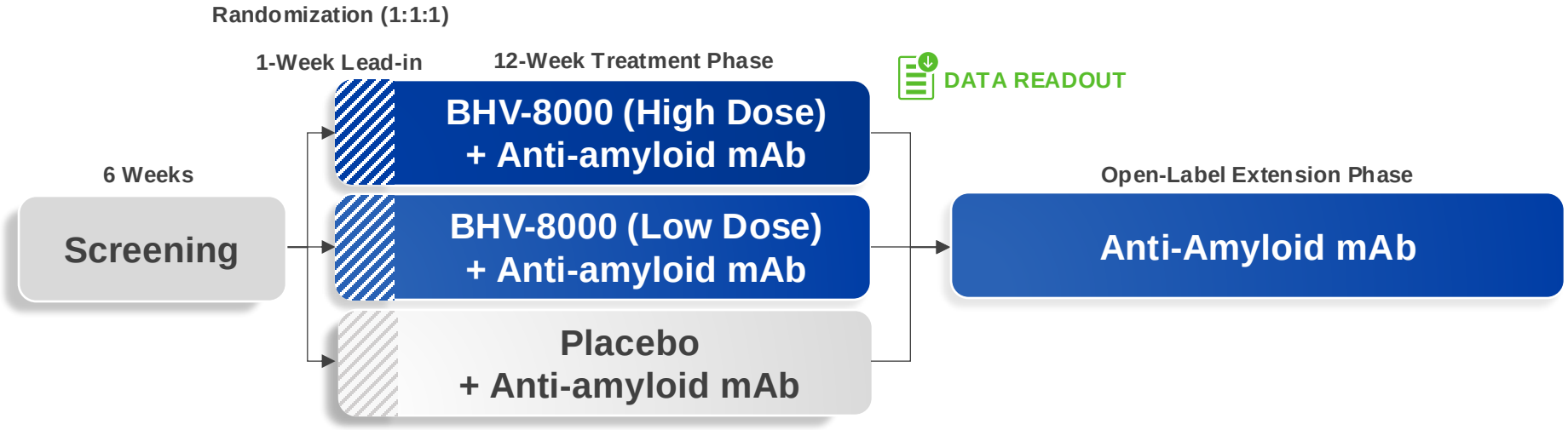
BHV-8000: Incidence of ARIA-E with Anti-Amyloid Therapy

Anti-Amyloid mAb, (n)	Overall, % (n)	APOE4/4, % (n)	APOE4/-, % (n)	Non-carriers, % (n)
EMERGE & ENGAGE TRIALS[1]				
Aducanumab[2] (1,029)	35.2 (362)	43.0[3] (290/674)		20.3 (72/355)
Placebo (1,076)	2.7 (29)	2.2[3] (16/742)		3.9 (13/334)
CLARITY-AD[4]				
Lecanemab (898)	12.6 (113)	32.6 (46/141)	10.9 (52/479)	5.4 (15/278)
Placebo (897)	1.7 (15)	3.8 (5/133)	1.9 (9/478)	0.3 (1/286)
TRAILBLAZER-ALZ2[5]				
Donanemab (853)	24.0 (205)	40.6 (58/143)	22.8 (103/452)	15.7 (40/255)
Placebo (874)	18 (2.1)	3.4 (5/146)	1.9 (9/474)	0.8 (2/250

- APOE4 carriers at increased risk for ARIA and accelerated progression of AD[6,7]
- Risk of ARIA can complicate the benefit-risk assessment of anti-amyloid mAbs, the only approved disease-modifying treatment for AD[8]

1. Salloway S., et al., JAMA Neurol. 2022;79(1):13-21. doi:10.1001/jamaneurol.2021.4161. 2. Results represent ARIA rates with aducanumab 10 mg/kg. 3. Represents ARIA-E rates with aducanumab (10 mg/kg) in APOE4 carriers (both hetero- and homo-zygotes); 4. van Dyck CH., et al., Lecanemab in early Alzheimer's disease. N Engl J Med. 2023;388(1):9-21. doi:10.1056/NEJMoa2212948. 5. Sims JR., et al., Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA. 2023;330(6):512-27. doi:10.1001/jama.2023.13239. 6. Doran SJ., et al., Risk factors in developing amyloid related imaging abnormalities (ARIA) and clinical implications. Front Neurosci. 2024;18:1326784. doi: 10.3389/fnins.2024.1326784. 7. Hunsberger HC., The role of APOE4 in Alzheimer's disease: strategies for future therapeutic interventions. Neuronal Signal. 2019;3(2):NS201180203. doi: 10.1042/NS20180203. 8. Doran SJ., et al., Risk factors in developing amyloid related imaging abnormalities (ARIA) and clinical implications. Front Neurosci. 2024;18:1326784. doi: 10.3389/fnins.2024.1326784.

BHV-8000: Phase 2/3 Prevention of ARIA Study Design



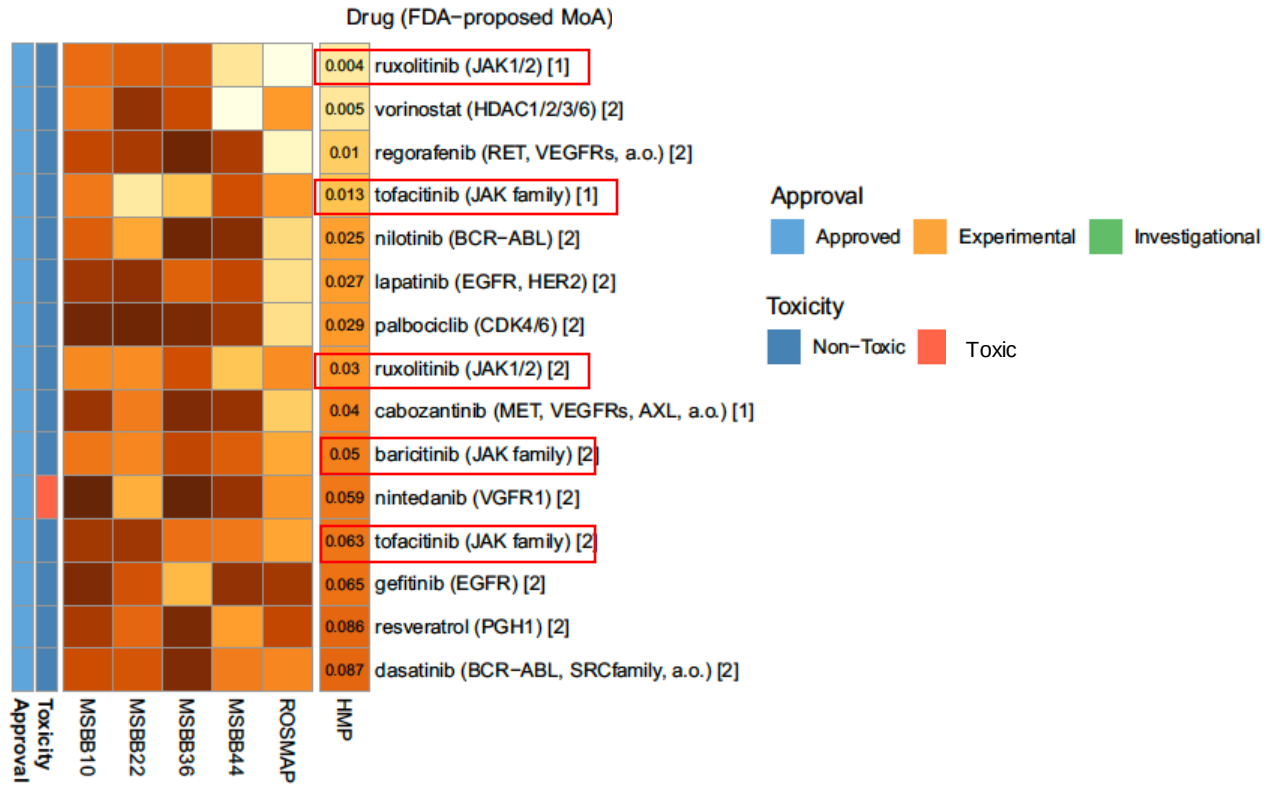
DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Male and female adults with early Alzheimer's disease who are APOE4 gene carriers
SAMPLE SIZE	450 participants (randomized 1:1:1 across 2 active and 1 placebo arm)
TREATMENT	BHV-8000 (high/low dose) vs. Placebo + anti-amyloid mAb
TREATMENT DURATION	1-week lead-in with BHV-8000 or Placebo; 12-week treatment period with BHV-8000 + anti-amyloid mAb; OLE with anti-amyloid mAb only
ENDPOINTS	Incidence of ARIA-E at Week 13; PK/PD; change in inflammatory and AD biomarkers, including brain amyloid

KEY POINT

Positive FDA feedback on novel prevention of ARIA indication, and on study design and clinical development plan

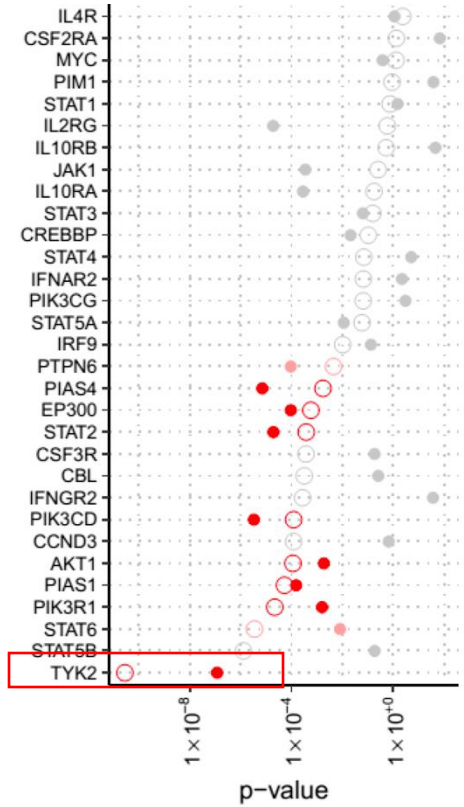
BHV-8000: Patient-Derived Evidence of TYK2/JAK1 Signaling in AD

Transcriptional Profiling Study of AD Patient Brains With Drug Mechanism Reveals Strongest Association For JAK Family Kinases



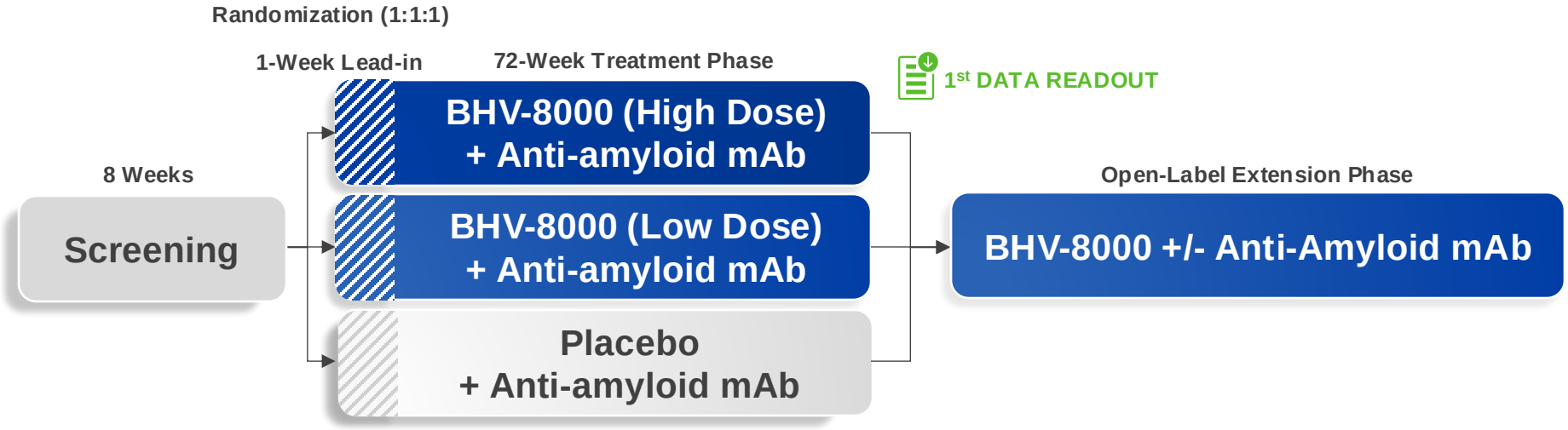
Rodriguez et al, *Nature Communications.* 2021 12:1033

TYK2 Is The Most Prominent Blood Leukocyte Gene In AD Patients



Nevado-Holgado et al, *Cells.* 2019 May 8;8(5):425

BHV-8000:
Phase 2/3 Disease-Modifying Therapy Study in Early AD

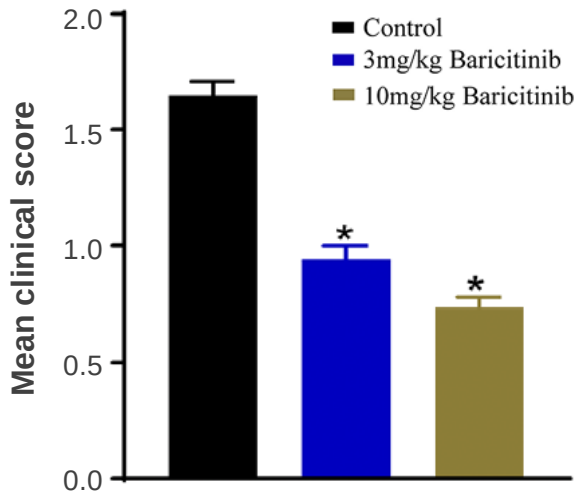


DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Male and female adults with early symptomatic Alzheimer's disease
SAMPLE SIZE	2,000 participants (randomized 1:1:1 across 2 active and 1 placebo arm)
TREATMENT	DBT Phase: BHV-8000 (high/low dose) vs. PBO + anti-amyloid mAb; OLE Phase: BHV-8000 +/- anti-amyloid mAb (IF amyloid PET "negative" can stop anti-amyloid mAb)
TREATMENT DURATION	1W lead-in with BHV-8000 or PBO; 72W DBT Phase; OLE Phase
ENDPOINTS	**Primary:** iADRS at W73; **Secondary:** CDR-SB, ADAS-Cog, MMSE, ADCS-iADL; **Exploratory:** Rates of ARIA, Change in inflammatory and AD biomarkers including brain amyloid / tau

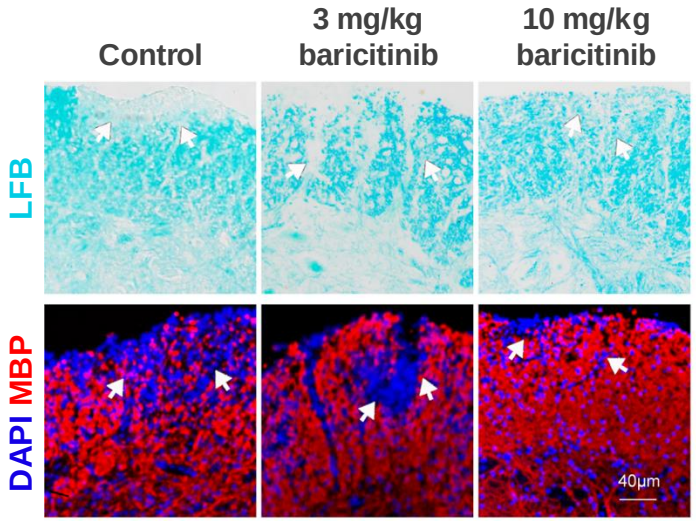
BHV-8000:
TYK2/JAK1 Inhibition Is a Potential Treatment for Multiple Sclerosis

- **Genetic evidence:** Recent study found a protective genetic variation in the TYK2 gene that decreased signaling capacity in response to IL-12 and IL-23, reducing the function of TYK2, resulting in reduction in risk for developing MS[1]
- **Nonclinical data:** Suggests JAK/STAT pathway regulates differentiation and function of Th1 and Th17 cells which are essential for development of experimental autoimmune encephalomyelitis (EAE)[2]
- **Clinical data:** Supports the presence of abnormal immune activation in MS patients[3]

Baricitinib (JAK1/2 Inhibitor) Improved Mean Clinical Scores in Mice With EAE[2]

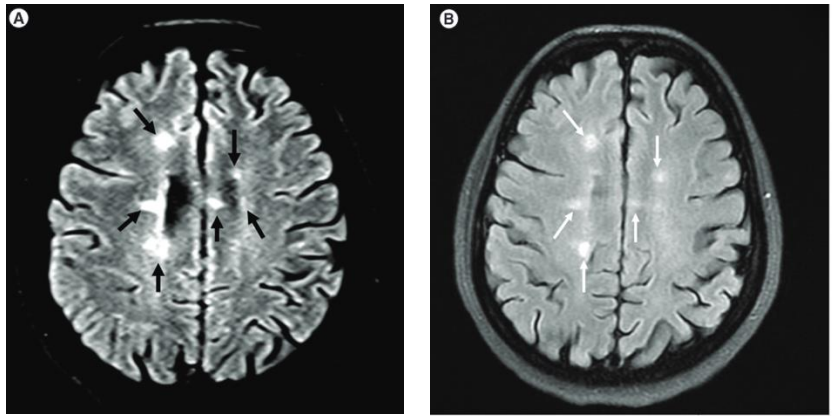


Baricitinib (JAK1/2 Inhibitor) Reduces Pathological Tissue Injuries In EAE Mice[2]

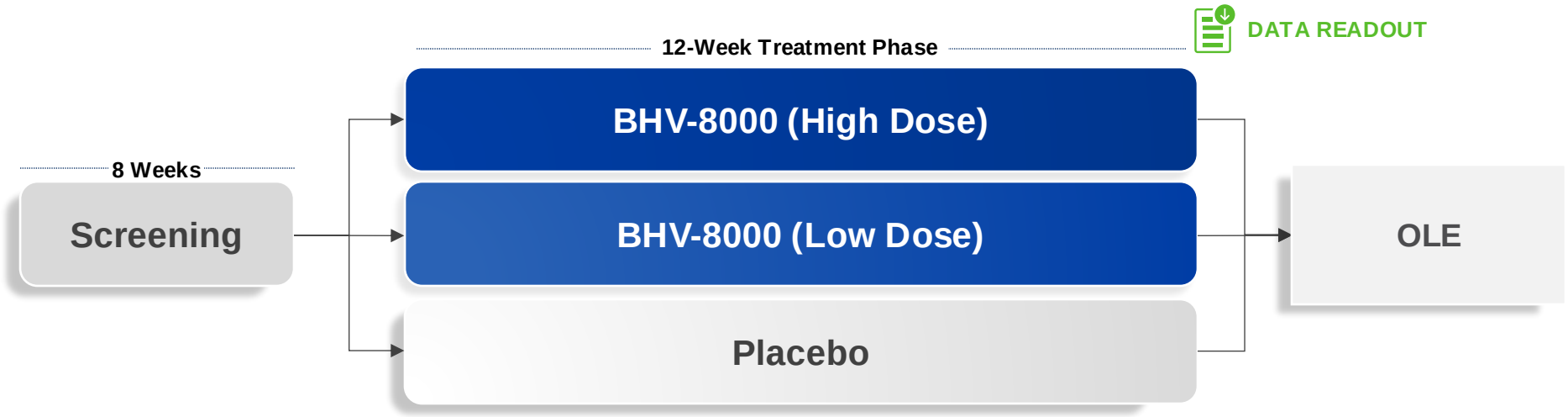


Secukinumab (IL-17A) Demonstrates an Effect in Relapsing Remitting MS[3]

Lesions regressed in MS patients 5 months of secukinumab treatment

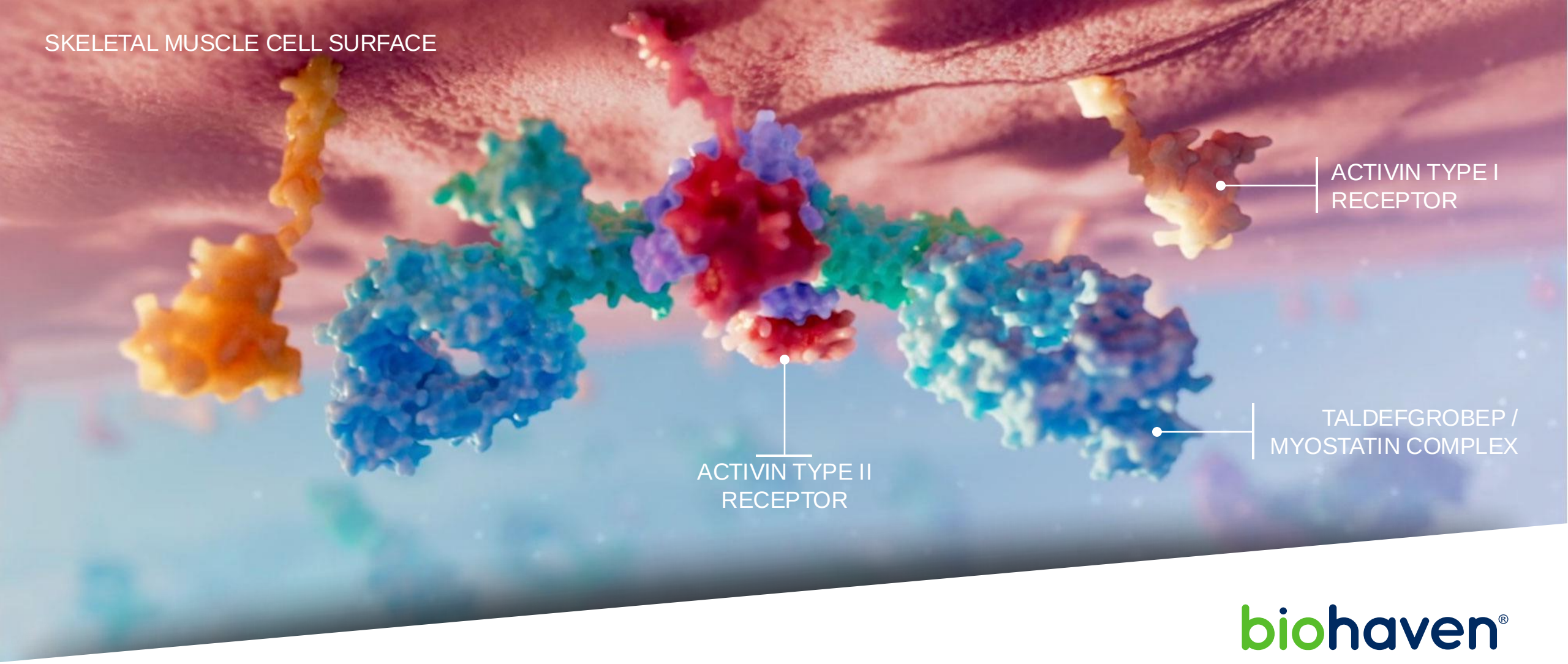


BHV-8000: Phase 2 Imaging POC Study in Relapsing Multiple Sclerosis



DESIGN	Randomized, double-blind, placebo-controlled Phase 2 imaging proof-of-concept study
POPULATION	Adults with relapsing multiple sclerosis (RMS)
SAMPLE SIZE	140 participants (randomized 2:2:1)
TREATMENT	BHV-8000 low dose or high dose versus placebo
TREATMENT DURATION	12-week double-blind phase followed by open label study
ENDPOINTS	Cumulative number of new gadolinium (Gd)-enhancing T1 lesions, total number of Gd-enhancing T1 lesions, number of new or enlarging T2 lesions, change in phase rim lesions, PK/PD

Preliminary clinical trial design



biohaven®

Myostatin — SMA and Obesity

Differentiated Pharmacology Balancing Both Efficacy and Safety

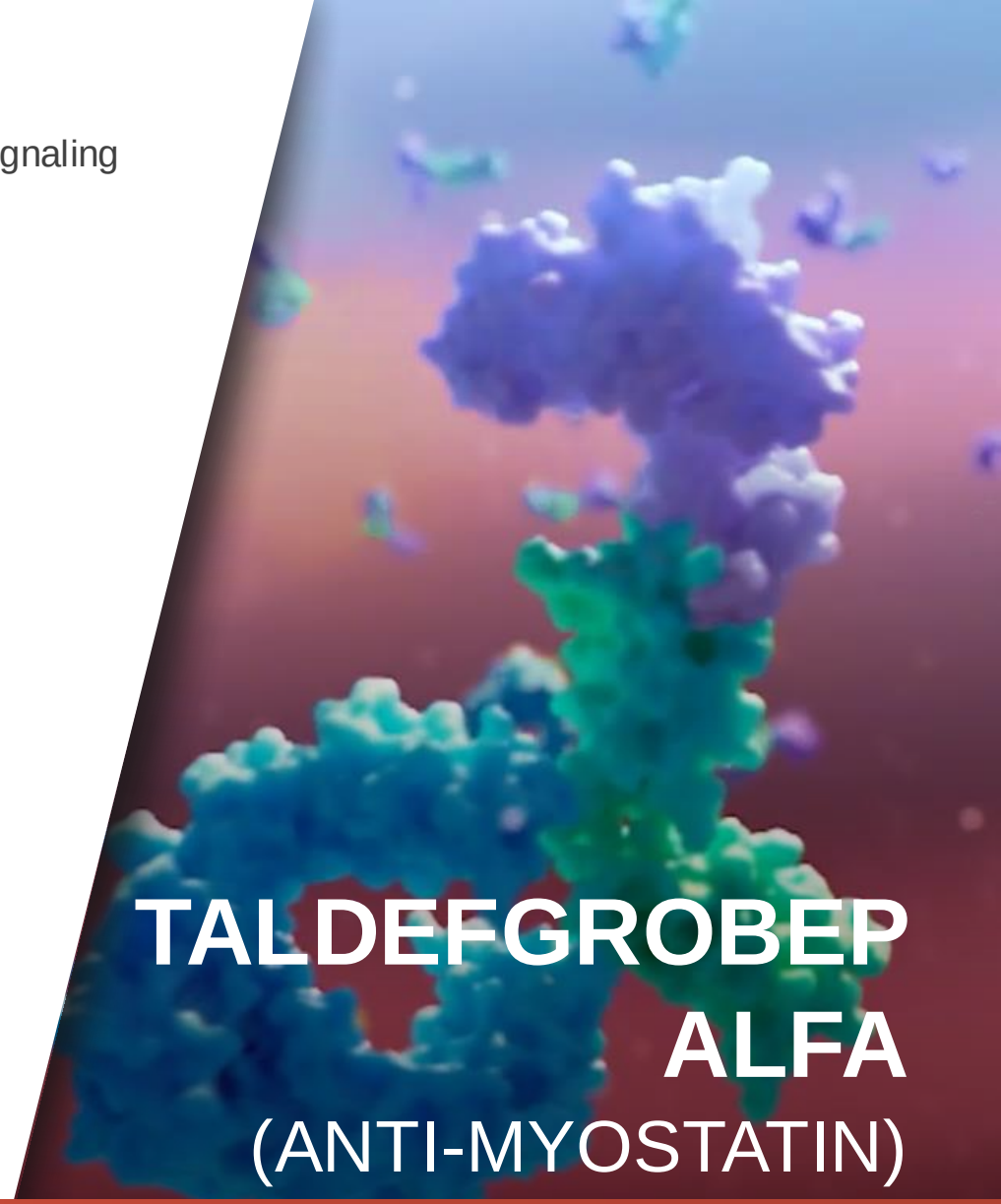
- Taldefgrobep binds myostatin and the taldefgrobep-myostatin competitively inhibits signaling through the ActRII receptor of several key ligands
- Leads to beneficial effects on both muscle and adipose tissues
- Favorable safety profile established in diverse clinical populations (N >700)

Phase 3 Data in Spinal Muscular Atrophy

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

Potential Paradigm Shift in the Treatment of Obesity

- Improve quality of weight loss
- Lower total body weight by specifically reducing fat mass while also preserving or increasing lean muscle mass
- Use as monotherapy or in combination with incretin mimetics
- Weekly SC administration via off-the-shelf autoinjector, with potential for extended dosing intervals



TALDEFGROBEP ALFA
(ANTI-MYOSTATIN)

BREAKING NEWS

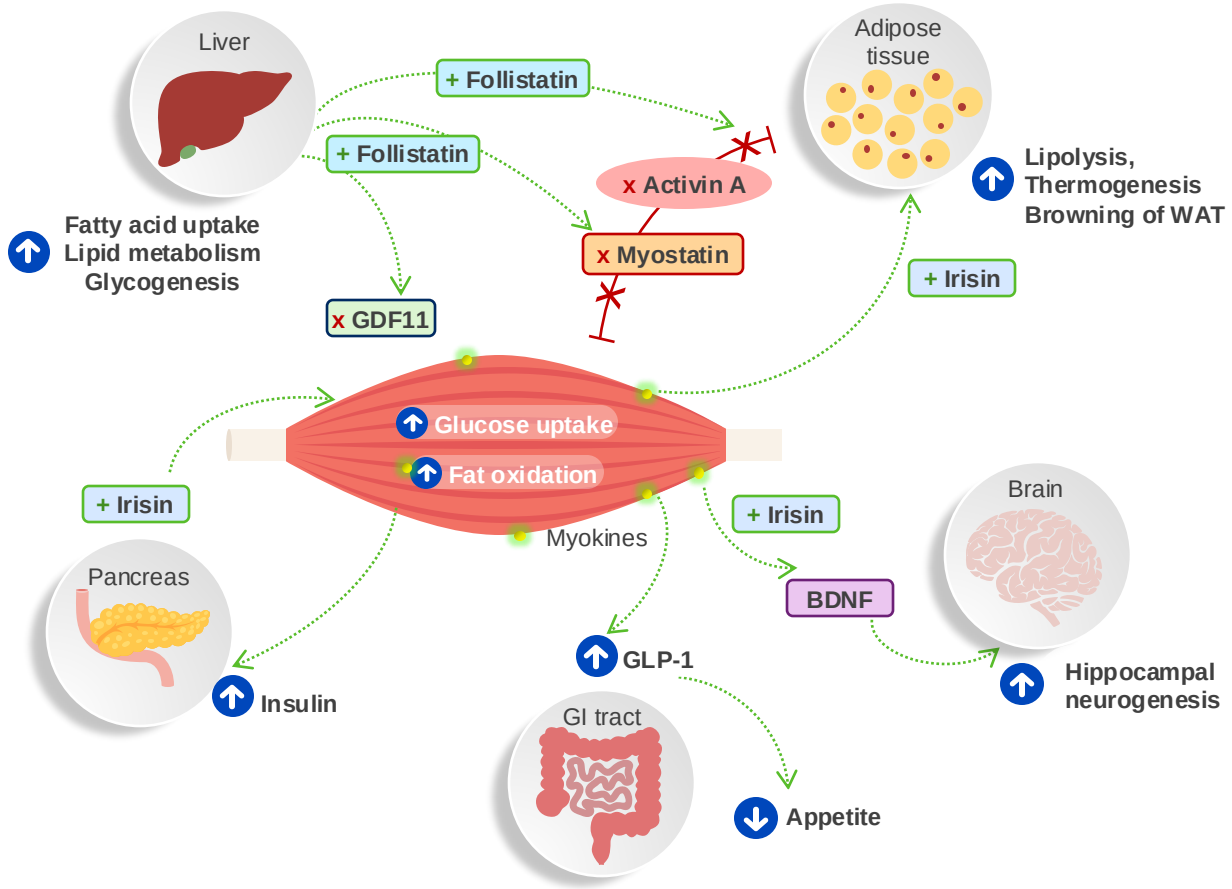
- Phase 2 study in obesity planned to initiate in 1H 2025
- FDA meeting planned to discuss SMA registrational path in 1H 2025

Taldefgrobep's Novel MOA Optimizes Metabolic and Body Composition Change Important to those with Obesity

LOW MUSCLE MASS is associated with age-related cognitive decline[2] and increase in all-cause mortality[3]

HIGH MUSCLE MASS is associated with improvements in overall health and wellness

MYOKINES are important in the regulation of fat metabolism, inflammation, appetite, glucose control, bone density, and basal metabolic rate[1]



HIGH ADIPOSE MASS increases TGF-β ligands, leads to insulin resistance, and is a multifactorial driver of the morbidity of obesity

TALDEFGROBEP ALFA targets TGF-β ligands that signal through Activin II receptors including myostatin, GDF-11, and Activin A.[3-4] Inhibition of 3 ligands and ActRIIB optimizes muscle growth.[5]

1. Illustration adapted from Severinsen et al. Endocr Rev. 2020 Aug 1;41(4):594–609. 2. Daghlas et al. BMJ Med. 2023;2(1):e000354. 3 Lee et al. Exp Biol Med. 2018;243:1275-85. 4. Chen et al. Life Metabolism, 2024. 5. Latres, E., Mastaitis, J., Fury, W. *et al. Nat Comm* 8, 15153 (2017). **MSTN,** myostatin; **GDF11,** growth differentiation factor 11; **BDNF,** brain-derived neurotrophic factor.

KEY POINT

Taldefgrobep alfa inhibits negative regulators of skeletal muscle and adipose tissue improving body composition and resulting in metabolic changes important to overall health and wellness

Taldefgrobep Alfa Has Differentiated Pharmacology that Balances Efficacy and Safety

Apitegromab/GYM329
Scholar Rock/Roche

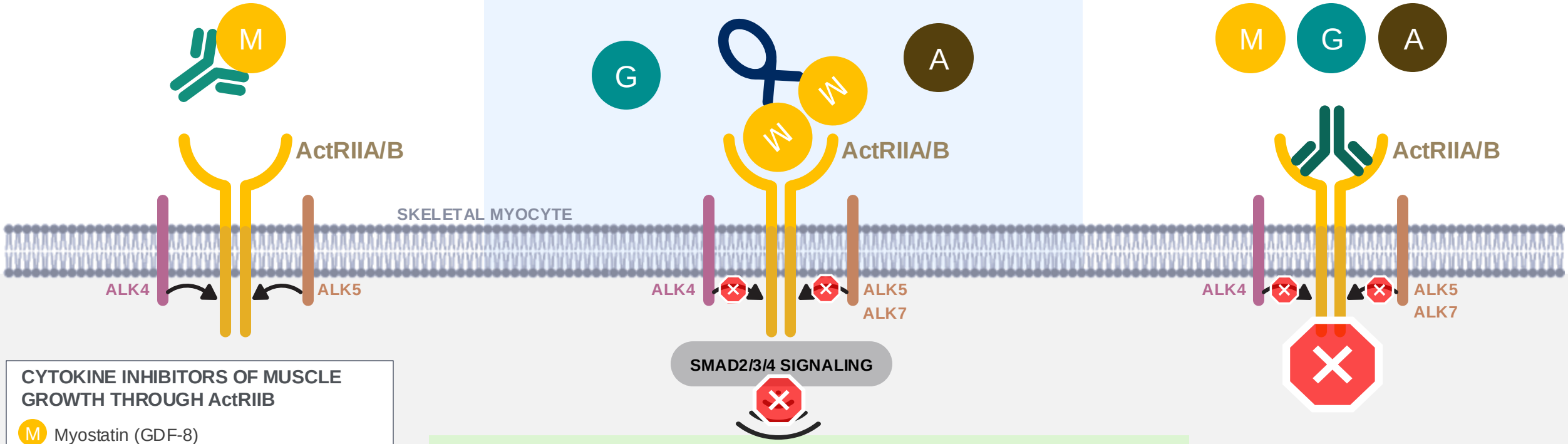
TARGETS pro- and latent myostatin

Taldefgrobep alfa
Biohaven

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

Bimagrumab
Versanis-Lilly

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



CYTOKINE INHIBITORS OF MUSCLE GROWTH THROUGH ActRIIB

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

Inhibiting signal transduction in muscle leads to hypertrophy

Inhibition in adipocytes leads to lipolysis

Increased brown fat enhanced mitochondria activity and increased thermogenesis

Taldefgrobep Alfa Offers a Highly Favorable and Differentiated Profile Within the "Myostatin Pharmacologic Class"

Apitegromab/GYM329
Scholar Rock/Roche

Pure Myostatin Agent

- Inhibits latent myostatin
- No direct ActRIIB receptor effects, so activity limited to PK of drug (limited PK/PD)
- Claims better safety due to selectivity
- Likely associated with decreased efficacy in muscle and adipose
- Requires IV infusion

Taldefgrobep alfa
Biohaven

Dual Myostatin Clearance and Activin Receptor Inhibition

- Binds active myostatin (pM), GDF-11 (pM) and Activin A (nM)
- Superior muscle growth to myostatin inhibition alone
- Accesses Activin A pharmacology
- Long lived T-alfa/myostatin complex reversibly binds ActRIIA/B inhibiting receptor signal transduction
- Low rates of AEs
- Favorable SC dosing

Bimagrumab
Versanis-Lilly

Activin Receptor Inhibitor

- Tight binding to and inhibition of ActRIIB receptors
- Superior muscle growth to myostatin inhibition alone
- Accesses Activin A pharmacology
- Long off-rate and tight binding results in **muscle spasms, fatigue, and diarrhea**
- Potent receptor inhibition results in lower FSH
- Requires IV infusion

AE, adverse event; **FSH**, follicle stimulating hormone; **SC**, subcutaneous; **IV**, intravenous; **PK**, pharmacokinetics; **PD**, pharmacodynamics.

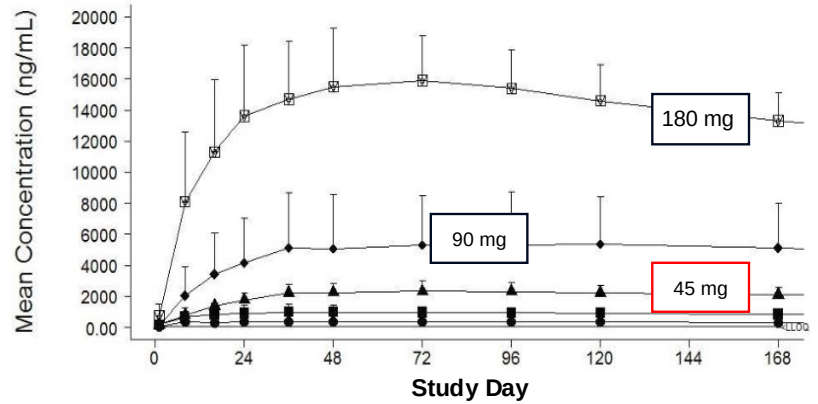
KEY POINT

Taldefgrobep alfa potentially offers optimized efficacy, safety, and ease of use

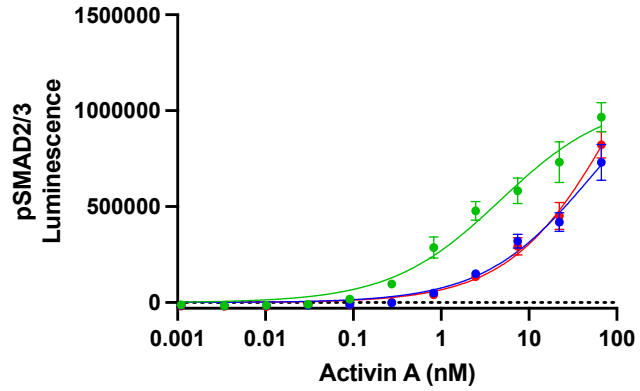
Taldefgrobep Alfa Complexes Extend Favorable Effects

- Myostatin and GDF-11 exhibit low pM binding affinity to T-alfa and low nM to Activin A
- After a single 45 mg dose, T-alfa/myostatin complex is ~20nM in plasma, in excess over ligands
- T-alfa/myostatin complex interaction with ActRIIB receptor effectively competes with Activin A and GDF8/11
- Inhibition of SMAD2/3 signaling directly impacts muscle and adipose tissues

Stable T-alfa-ligand complexes in human plasma remain elevated



Stable T-alfa-ligand complexes inhibit Activin A mediated signal transduction through ActRIIA/B



Ligand	EC_{50} (nM)
Activin A only	4.687
GDF-8 complex	50.58
GDF-11 complex	100.4

KEY POINTS

- T-alfa complexes have longer serum half lives than T-alfa, extending T-alfa PK, PD, and breadth of pharmacology
- T-alfa complexes inhibit signal transduction at ActRIIB, improving both muscle growth and fat metabolism

Current Treatment Options for SMA Are Inadequate

SMA is characterized by muscle atrophy and weakness

- SMA is a rare, inherited neuromuscular disease characterized by muscle atrophy and severe muscle weakness[1]
- Despite available treatments, SMA remains a progressive and debilitating condition[2–5]

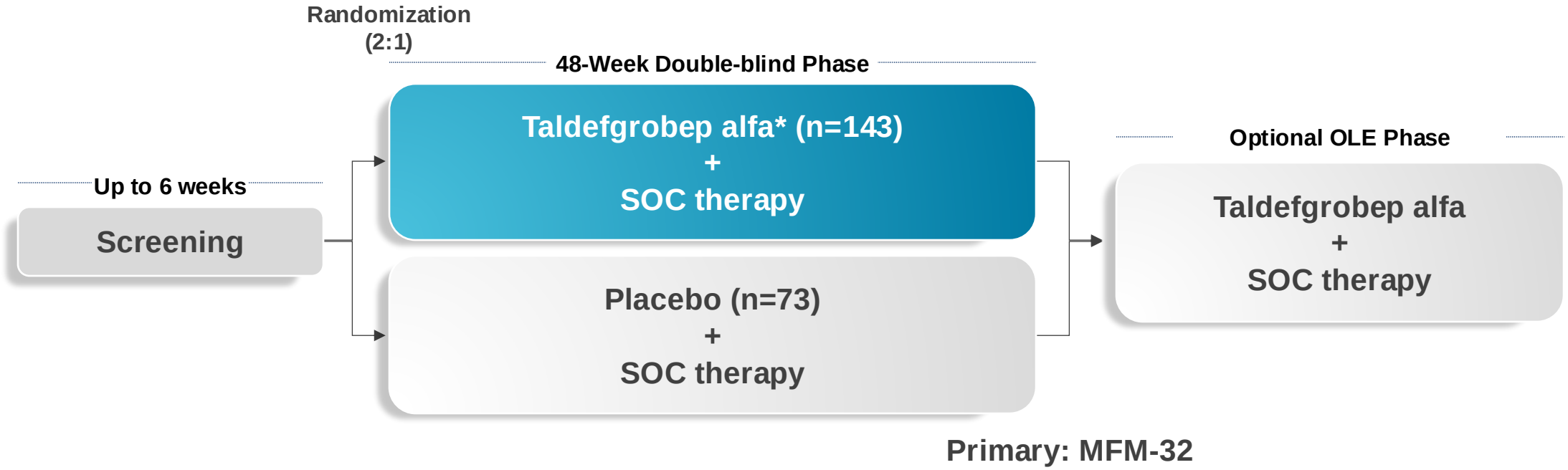
Standard of care treatments target neurons, not muscle, and SMA patients still experience weakness and reduced functioning

- Available SMN (Survival Motor Neuron) upregulating treatments target motor neurons[2]
- Despite these treatments, SMA patients still experience significant muscle weakness, reduced levels of functioning, and impairment in quality-of-life[5-7]
- No treatment that specifically targets muscle in SMA is currently available

Significant opportunity exists in SMA for novel treatments that target muscle to improve functioning and quality-of-life

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; ENDEAR Study Group. N Engl J Med. 2017;377(18):1723-1732 5. 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; ENDEAR Study Group. N Engl J Med. 2017;377(18):1723-1732.

Taldefgrobep Phase 3 Study in SMA



STRATIFICATION FACTORS

Age: 4–12 or 13–21 years old

Ambulatory status: Ambulatory or non-ambulatory

SOC therapy: Nusinersen, risdiplam, and/or onasemnogene

*Weight-based 35 mg or 50 mg weekly, SC
MFM-32, 32 item Motor Function Measure

RESILIENT: Broad Population Selected Based on Unmet Need and Potential for Benefit on Validated Clinical Endpoints

	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.

KEY POINT

RESILIENT population overlaps Scholar Rock and Roche populations but is uniquely suited to demonstrate benefit on MFM-32 primary endpoint

Baseline Characteristics

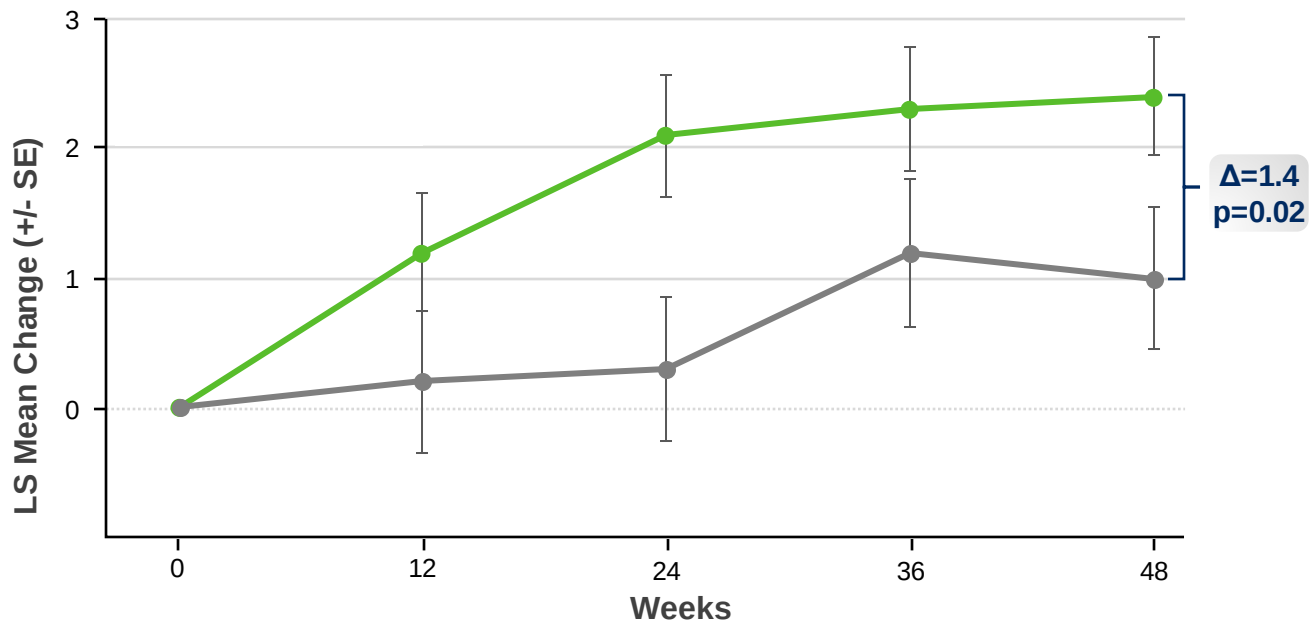
	Placebo (N = 73)	Taldefgrobep (N=143)
Female Sex, n (%)/ Male, n (%)	35 (47.9) / 38 (52.1)	65 (45.5%) / 78 (54.5%)
Age at Screening – years, mean (SD)	9.2 (4.4)	9.0 (4.3)
4–12, n (%) / 13–21, n (%)	57 (78.1%) / 16 (21.9%)	116 (81.1%) / 27 (18.9%)
Ambulatory Status: Non-ambulatory/Ambulatory	51 (69.9%) / 22 (30.1%)	100 (69.9%) / 43 (30.1%)
SOC Therapy, n (%)		
Risdiplam	17 (23.3%)	35 (24.5%)
Nusinersen	43 (58.9%)	78 (54.5%)
Onasemnogene	29 (20.3%)	13 (17.8%)
SMN Therapy Initiation Age, <6 (%)	53 (72.6%)	98 (68.5%)
SMN2 Copy Number, 2 / 3 / 4 (%)	13 (17.8%) 50 (68.5%) 10 (13.7%)	37 (25.9%) 90 (62.9%) 15 (10.5%)
Baseline MFM-32 Score, mean (SD)	58.3 (15.8)	54.9 (17.3)

KEY POINTS

- Large proportion of young and non-ambulatory subjects (similar to other anti-myostatin SMA studies)
- Imbalances in SMN2 copy number

Efficacy Results: Clinically Meaningful Improvements Enhanced In Myostatin-Positive Caucasian Participants

MFM-32 Total Score Change from Baseline



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

LS, least squares; **MFM-32**, 32-Item Motor Function Measure; **SE**, standard error
* response defined as ≥ 3-point change from baseline improvement on MFM-32 at Week 48 **Preliminary data

ADDITIONAL SUPPORTIVE DATA

- *Responder Analysis**
  50% of taldefgrobep-treated participants responded vs. 30% on placebo
- *Open-label Extension***
  Motor function continues to improve

Taldefgrobep Significantly Reduced Fat Mass Gain in SMA Participants While Increasing Lean Muscle Mass and Bone Density (vs. Placebo)

DXA prespecified outcome measures in overall study population at Week 48 demonstrated:

- Greater reduction in percent change in total body **fat mass** (p=0.008)
- Numerically larger increases in **lean muscle mass**
- Numerically larger increases in **bone density**

KEY POINT

Placebo adjusted difference similar to what was seen with other SMA therapy (risdiplam) in registrational SUNFISH trial; magnitude of effect appears addictive since added to SOC

Efficacy Results: Clinically Meaningful Improvements In Motor Function

- Clinically meaningful improvements in motor function on MFM-32 at all study timepoints
- Efficacy signals observed in clinically relevant and biomarker-defined subgroups
- Largest study population (87% Caucasian; n=180) showed 2.2-point (taldefgrobep) vs. 1.1-point (placebo) improvement on MFM-32 at Week 48 ($p < 0.039$)
- Taldefgrobep demonstrated target engagement, reducing myostatin levels below detection in treated participants
- Confounded by imbalances in treatment arms (SMN2 copy number, race), low baseline myostatin levels, and placebo response

Taldefgrobep Was Well-Tolerated Across Multiple Studies

Well-tolerated in SMA

- 97% of participants continued into optional OLE
- No taldefgrobep treatment-related serious adverse events (SAEs)
- Upper respiratory tract infection: taldefgrobep 26% vs placebo 29%

Favorable safety profile consistent with other clinical studies

- Safety and tolerability profile established across diverse population (N >700) of pediatric and adult participants in multiple clinical trials (n=6)

KEY POINT

Taldefgrobep was well-tolerated during the 48-week SMA study and in the ongoing OLE

Taldefgrobep: The Path Forward

SMA

- Evaluation of SMA clinical, biomarker and genetic data ongoing
- Engagement with the FDA planned in 1H 2025
  - Largest prespecified population is deriving functional benefit
  - Achieved target engagement
  - Objective physical improvements observed on DXA in lean body mass, fat mass, and bone density

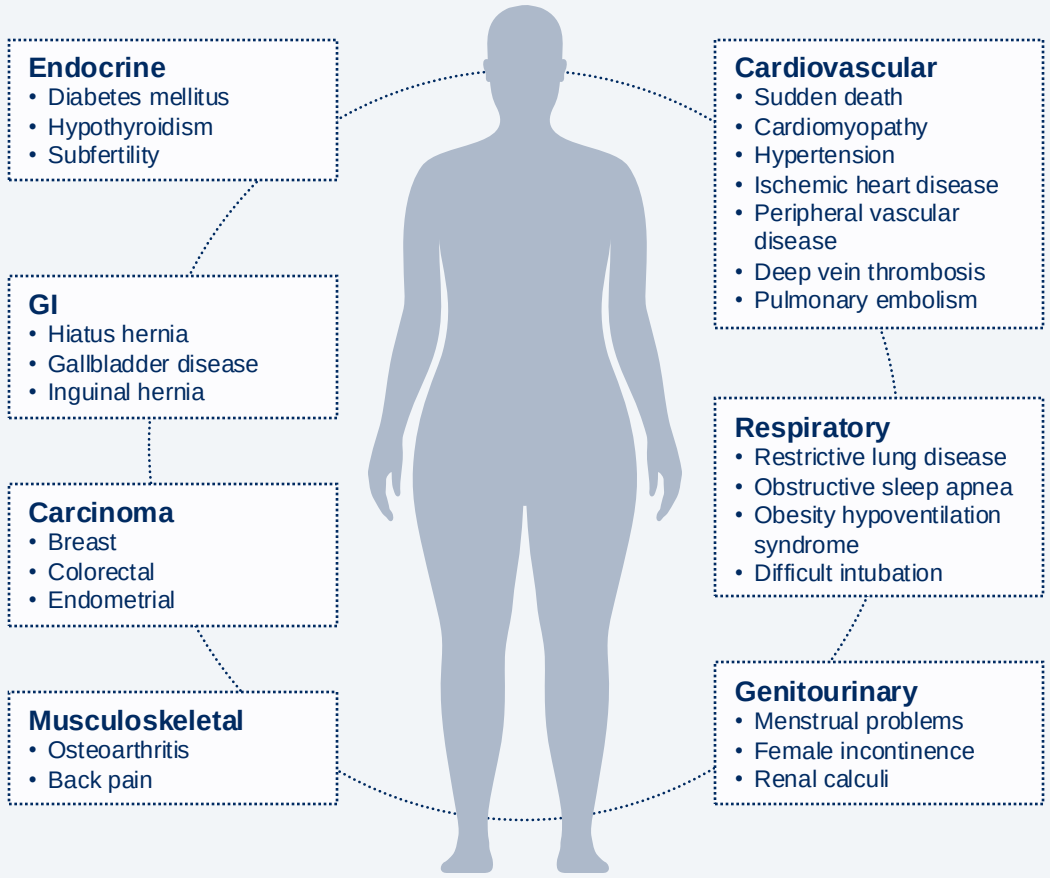
Obesity

- Strength and consistency of taldefgrobep's effects on body composition in nonclinical studies and clinical trials, including SMA, provide confidence to advance into obesity and metabolic disease
- Phase 2 study in obesity planned to initiate in 1H 2025

Optimal Management of Obesity Remains a Critical Unmet Medical Need

- By 2030, 1 billion people worldwide will be living with obesity, including 50% of American adults[1]
- Obesity is a disease of excess and/or abnormal adipose tissue, not excess mass
- Incretin mimetics have revolutionized management of obesity, but present liabilities
  - Up to 40% of total body weight loss is lean mass[2]
  - Gastrointestinal side effects[3]
  - Reduced bone mass[4]
  - Two-thirds stop GLP-1 therapy within 1 year[5]
  - Two-thirds of lost body weight returns within 1 year of stopping GLP-1 therapy[5,6]

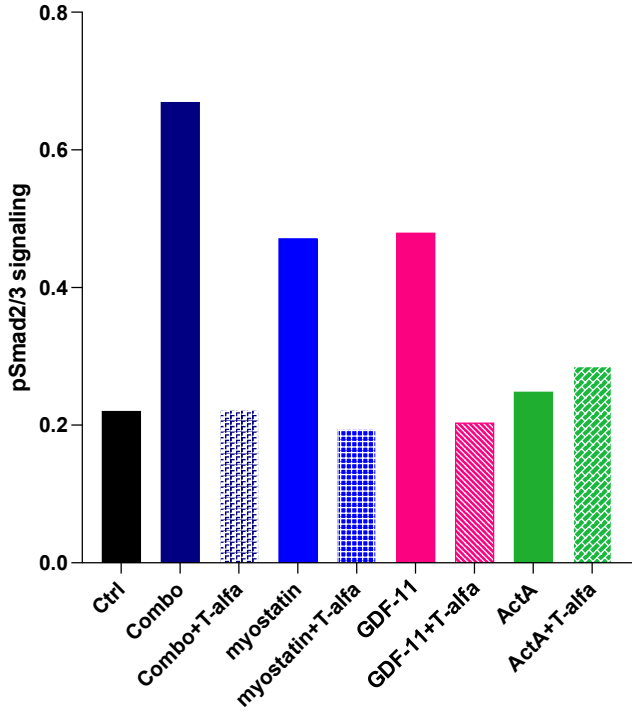
Complications of Obesity[7]



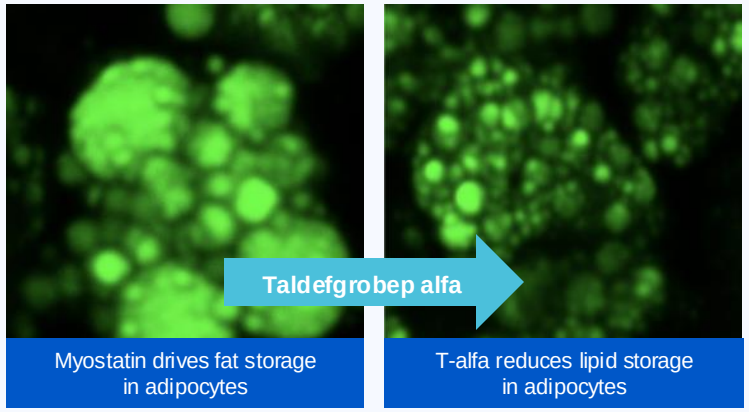
1 https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2022; Accessed 9-JAN-2025. 2. Wilding JPH et al, *N Engl J Med*. 2021;384(11):989-1002. 3. Wilding, et. al., Diabetes Obes Metab. 2022; 24(8):1553-64. doi: 10.1111/dom.14725 4. Hansen MS, et al., eClinicalMedicine. 2024;72:102624 5. Scientific American. What happens when you quit Ozempic or Wegovy? APR 2024. https://www.scientificamerican.com/article/you-quit-ozempic-or-wegovy-what-happens-next/ Accessed 9-JAN-2025. 6. Sikirica MV. Et al., Diabetes Metab Syndr Obes. 2017;10:403-12. 7. UpToDate. Overweight and obesity in adults: health consequences. https://www.uptodate.com/contents/overweight-and-obesity-in-adults-health-consequences. Accessed 9-JAN-2025.

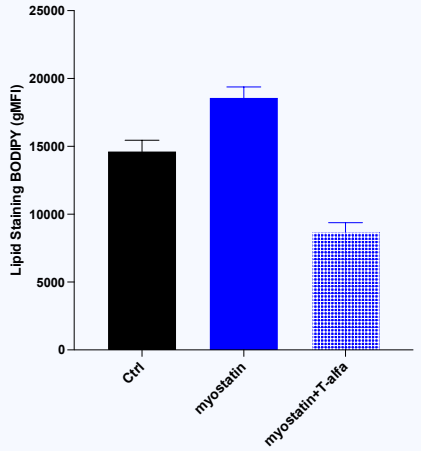
Taldefgrobep Alfa Reduces Adipocyte Lipids and Increases Mitochondrial Content

T-alfa Decreases pSmad2/3 Signaling, Directly Regulating Lipid Storage in Adipocytes

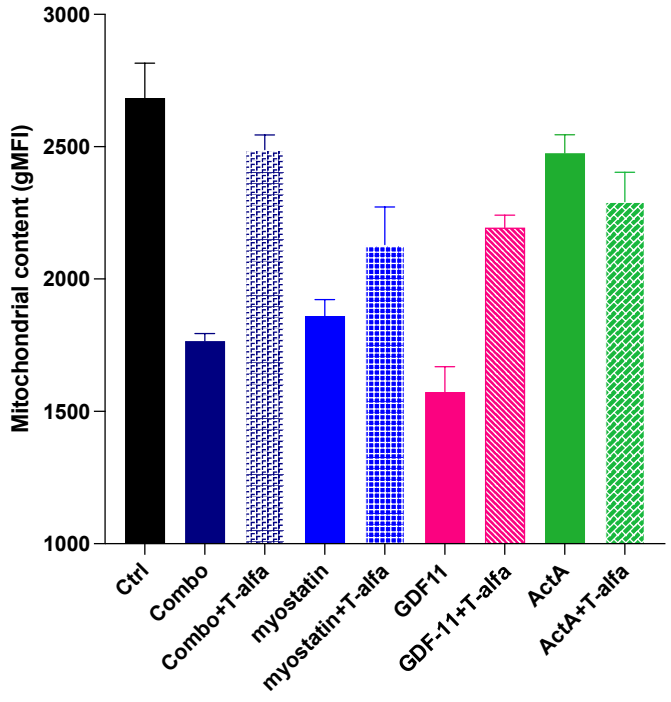


*combo—myostatin, GDF-11, activin





T-alfa Increases Mitochondrial Content in Adipocytes



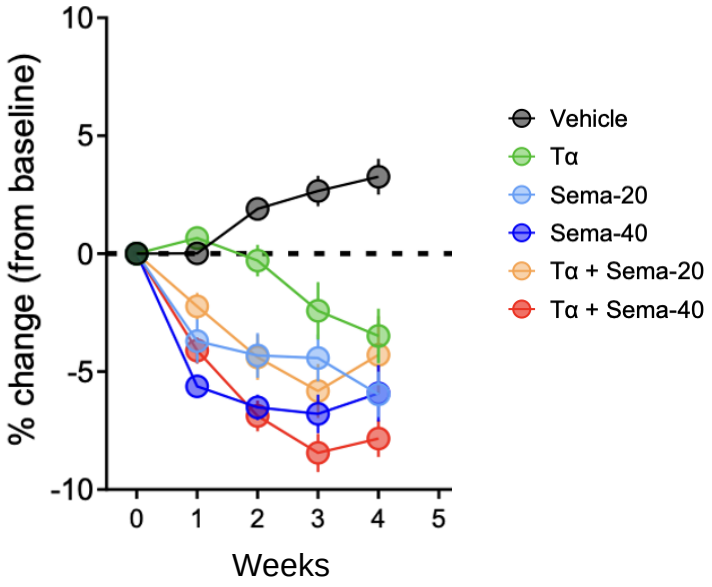
*combo—myostatin, GDF-11, activin

KEY POINT

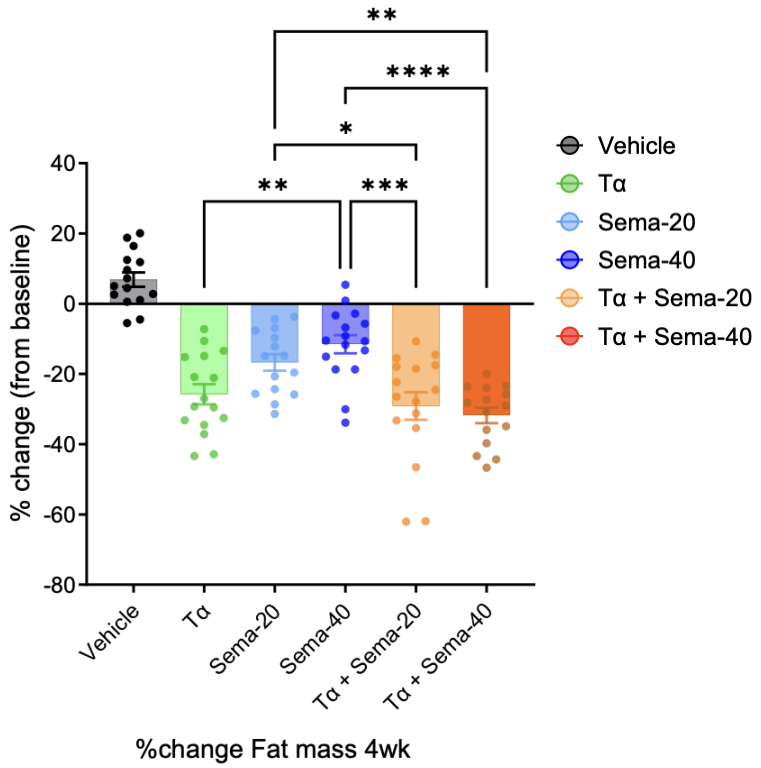
Taldefgrobep alfa directly reduces adipose tissue storage of fat

Taldefgrobep Alfa Shows Greater Effect in Combination With Semaglutide than Semaglutide Alone in DIO Mice

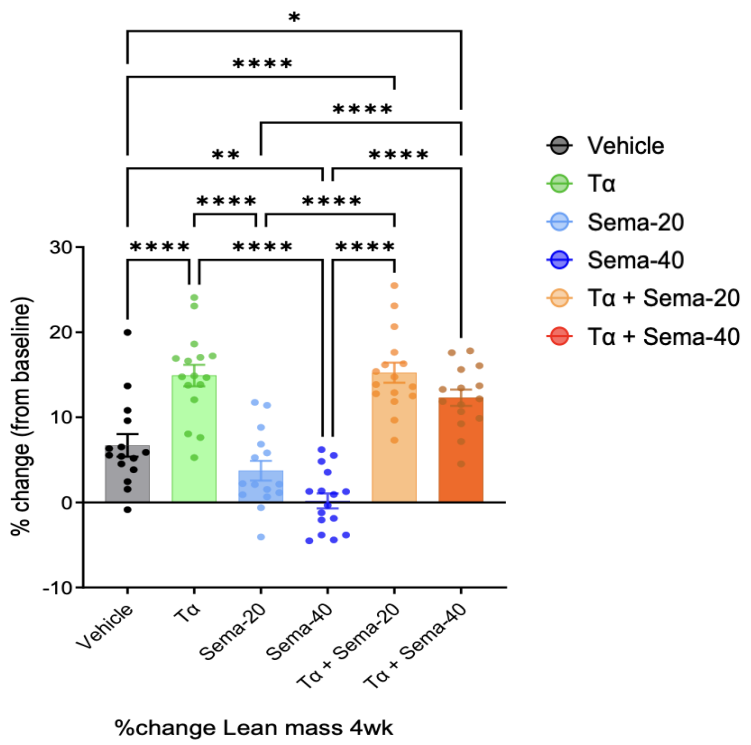
T-alfa Shows Weight Loss, and Combination with Semaglutide Shows **Higher Reduction in Body Weight** Than Semaglutide Alone



T-alfa and Combination Show **Greater Reduction in Fat Mass** Than Semaglutide Alone



T-alfa and Combination Show **Greater Increases in Lean Mass** Than Semaglutide Alone

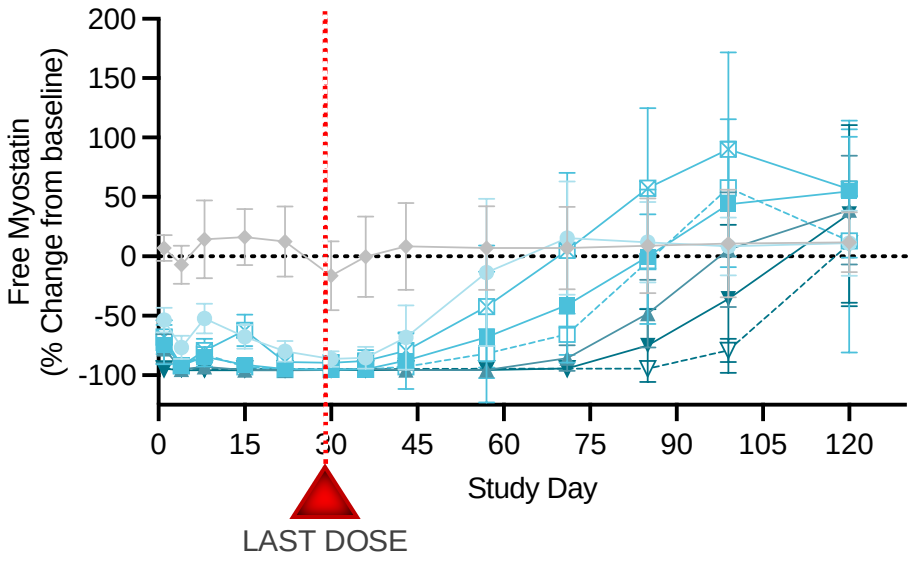


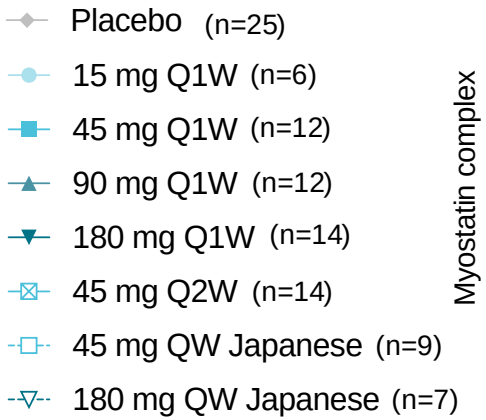
Tα, taldefgrobep alfa; **DIO**, diet induced obesity.
* <= 0.05, ** <= 0.01, *** < 0.001 and **** <0.0001.

Taldefgrobep Alfa Effectively Suppresses Free Myostatin in Healthy Adults and Has Prolonged Pharmacodynamic Effects

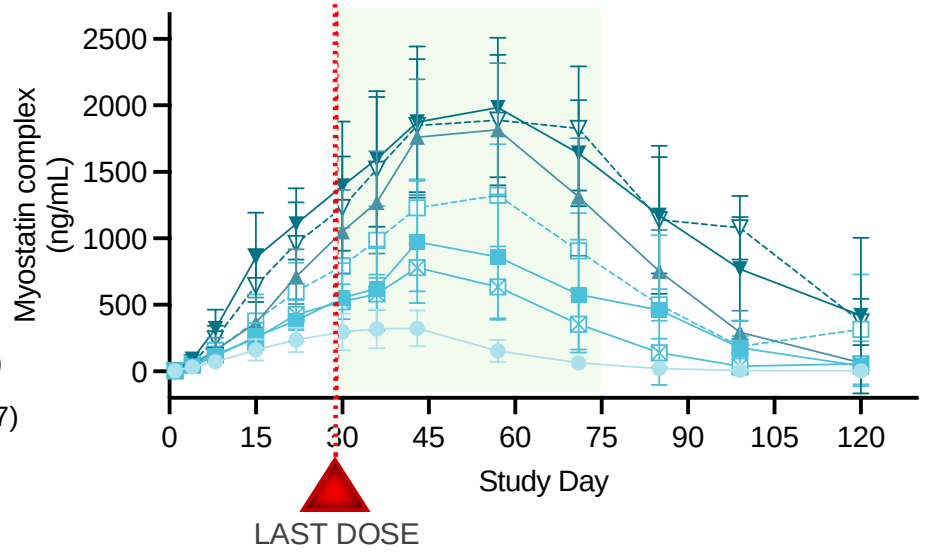
Taldefgrobep alfa activity is sustained by circulating taldefgrobep alfa-myostatin complex

Free Myostatin Levels





Drug-Myostatin Complex Sustains Activity

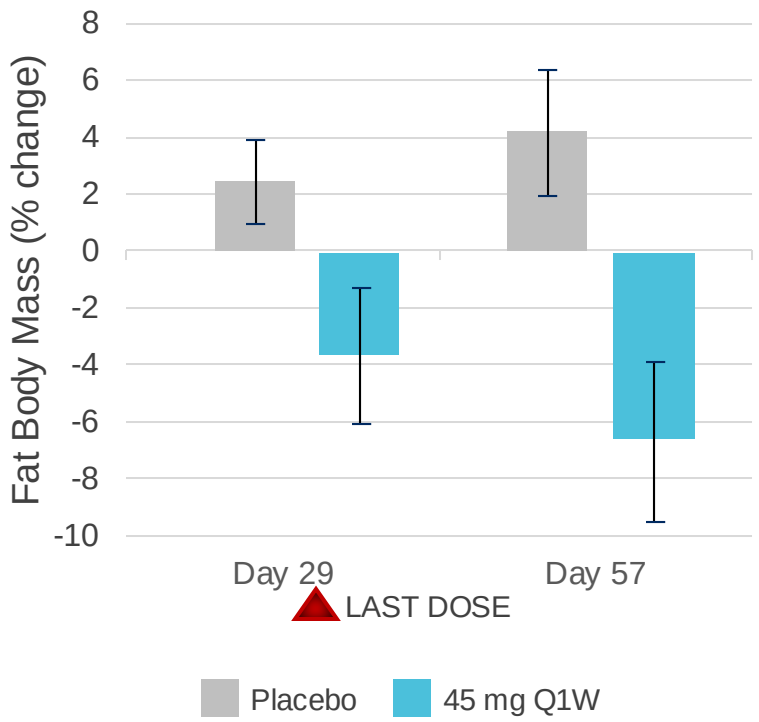


KEY POINTS

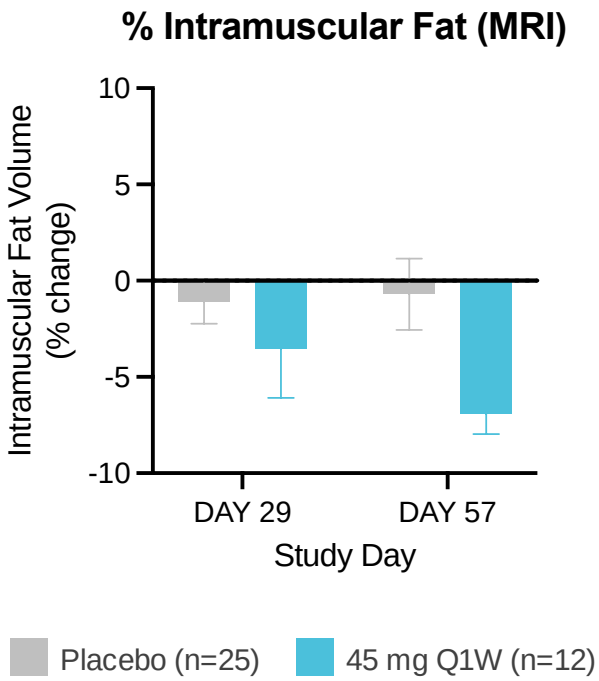
- Robust lowering of free myostatin after administration of taldefgrobep alfa 45 mg Q1W
- Taldefgrobep-myostatin complex continues to exert activity for weeks after dosing stops

Taldefgrobep Alfa Improves Body Composition in Non-Obese Adults

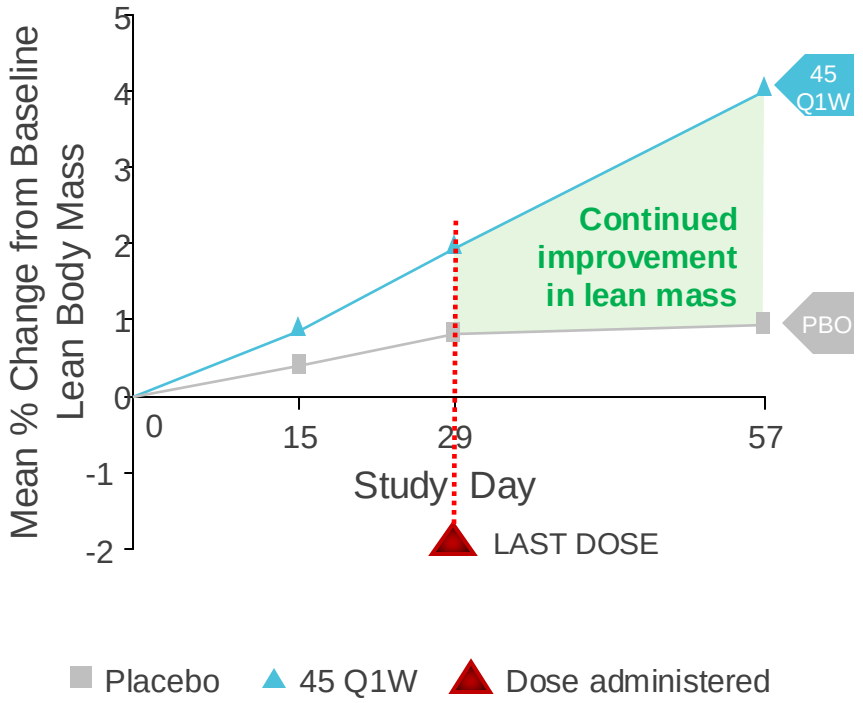
Taldefgrobep Alfa Continued to Decrease **Total Fat Mass** Beyond the Dosing Period



Effect of Taldefgrobep Alfa on **Intramuscular Fat** After 1 Month of Dosing — Healthy Adults

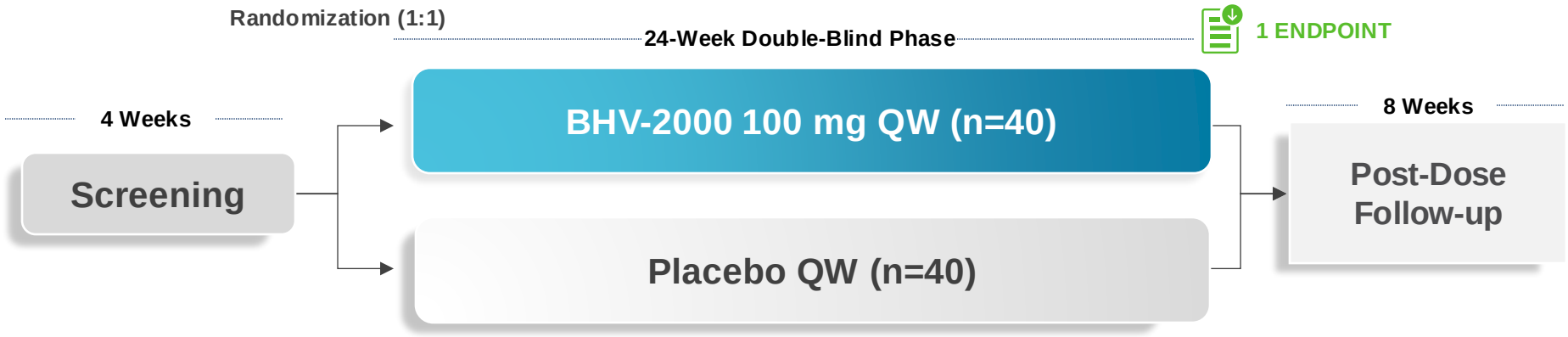


Taldefgrobep Alfa Demonstrates Continued Improvement in **Lean Mass** in Healthy Adults at 30 Days Post-dosing



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

Taldefgrobep Phase 2 Study in Obesity

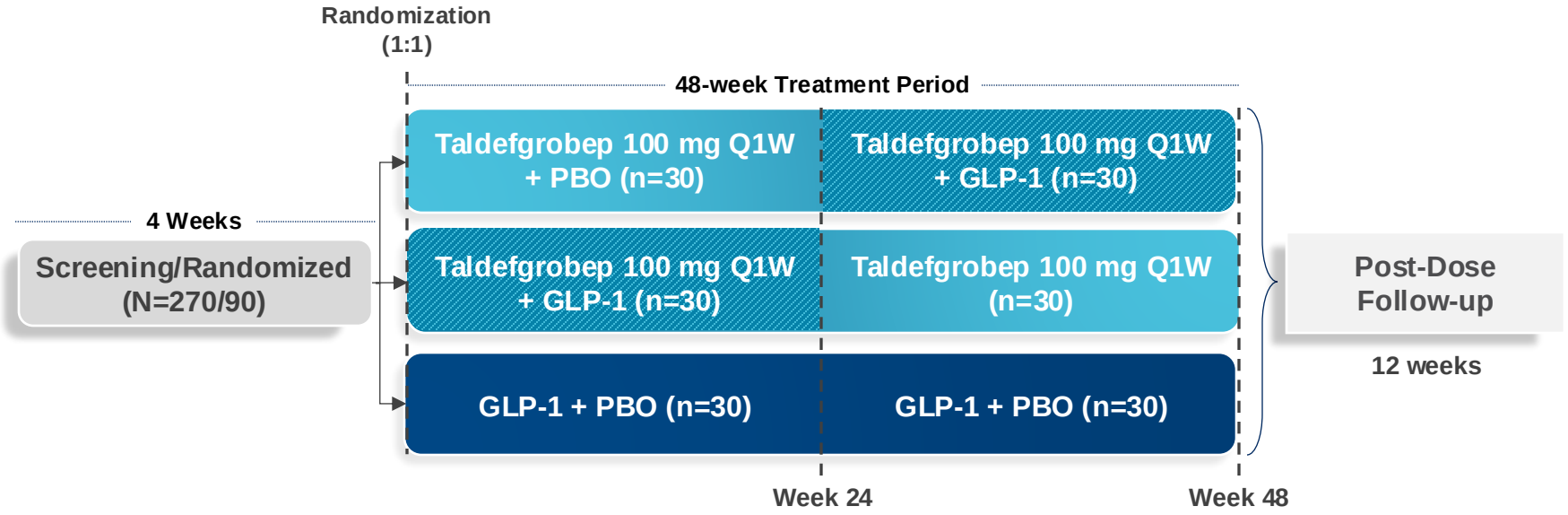


DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Male and female adults living with overweight or obesity (BMI 27 - 40) without comorbid diabetes mellitus
SAMPLE SIZE	80 participants randomized 1:1 (Sex [M/F] and BMI [<35, ≥35-40])
TREATMENT	Taldefgrobep 100 mg SC QW via autoinjector vs. Placebo SC QW
TREATMENT DURATION	24-week treatment period, 8-week post-dose follow-up
KEY ENDPOINTS	Change in lean mass, fat mass, bone density, total body weight, and insulin sensitivity; PK/PD; safety/tolerability

KEY POINT

Phase 2 study planned to initiate in 1H 2025

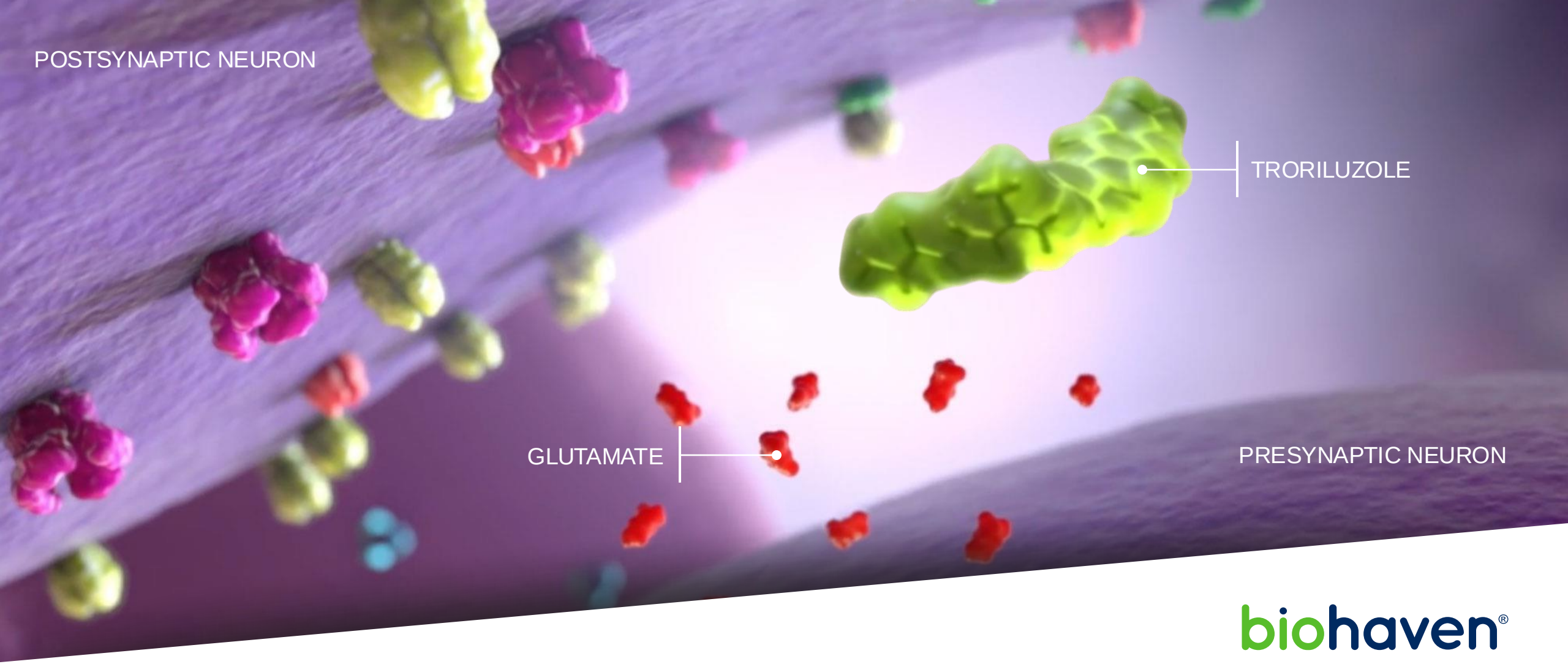
Taldefgrobep +/- GLP-1 Phase 2 Study in Overweight and Obesity



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Male and female adults living with overweight or obesity (BMI 27 - 40) without comorbid diabetes mellitus
SAMPLE SIZE	90 participants randomized 1:1:1 (Sex [M/F] and BMI [<35, ≥35-40])
TREATMENT	Taldefgrobep 100mg SC QW via autoinjector vs. Placebo SC QW
TREATMENT DURATION	48-week double-blind treatment period, pre-specified switch in therapy after Week 24. 12-week post-dose follow-up
KEY ENDPOINTS	Change in lean mass, fat mass, bone density, total body weight, and insulin sensitivity; PK/PD; safety/tolerability

Innovative study design allows for early insight into key clinical questions

- Impact of taldefgrobep alfa monotherapy on changes in body composition, total body weight, and metabolic parameters
- Ability of taldefgrobep alfa to augment total body weight and fat mass loss when used as adjunct to anti-obesity standard of care (GLP-1 agonist)
- Potential for taldefgrobep alfa to prevent against GLP-1-induced lean muscle loss
- Influence of taldefgrobep alfa on weight regain following discontinuation of GLP-1 agonist



biohaven®

Troriluzole — SCA

Troriluzole Is First Treatment to Slow SCA Disease Progression

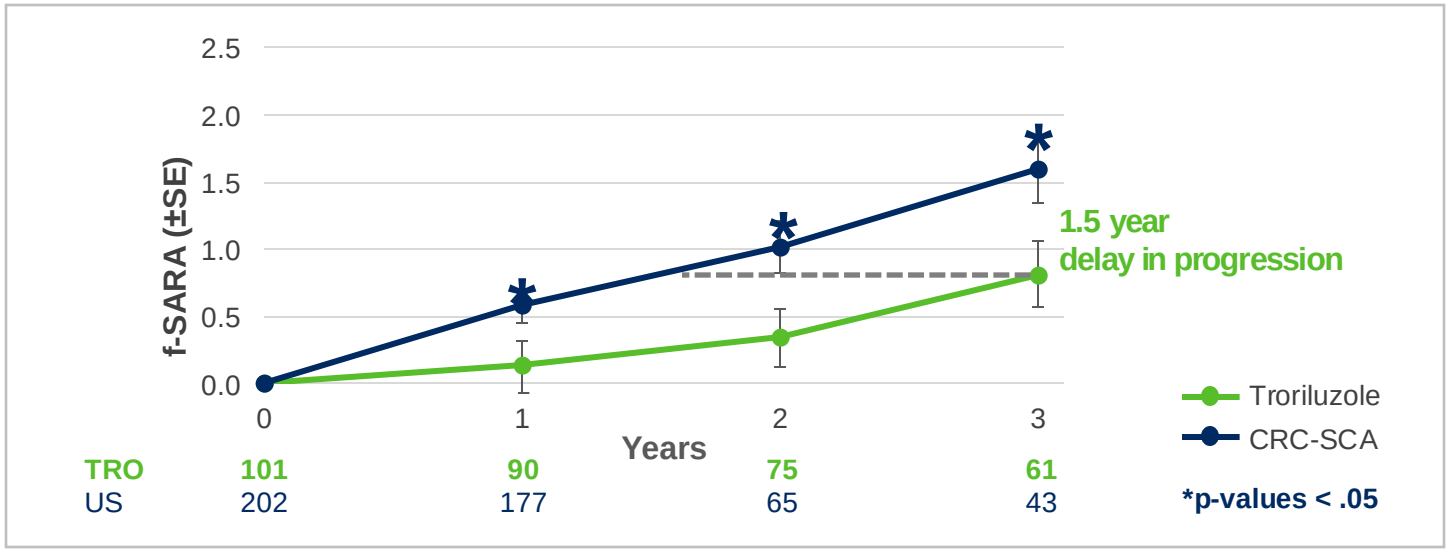
- Long-term RWE study confirmed benefit over 3 years in all SCA genotypes

SCA Represents Significant Commercial Opportunity

- Est. 15,000 patients in the US and 24,000 in UK and EU
- No currently approved SCA treatments

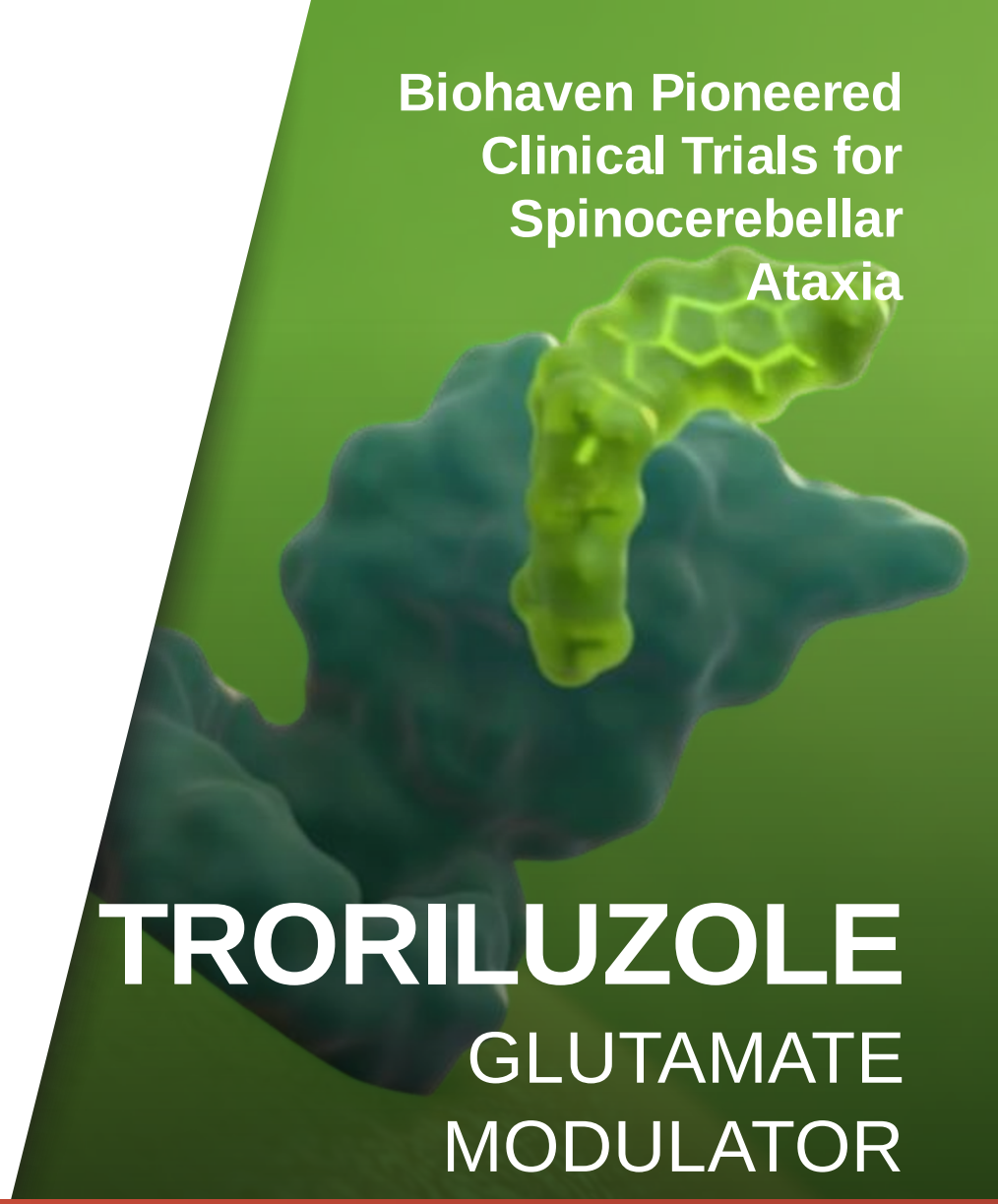
Milestones Achieved

- Submitted NDA after pre-NDA meeting in 4Q 2024 (potential Priority Review)
- EMA MAA for all SCA genotypes under review



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

Biohaven Pioneered Clinical Trials for Spinocerebellar Ataxia



TRORILUZOLE

GLUTAMATE MODULATOR

BREAKING NEWS

- Submitted NDA for treatment of all SCA genotypes (potential Priority Review)
- Preparing for commercial launch in 2025

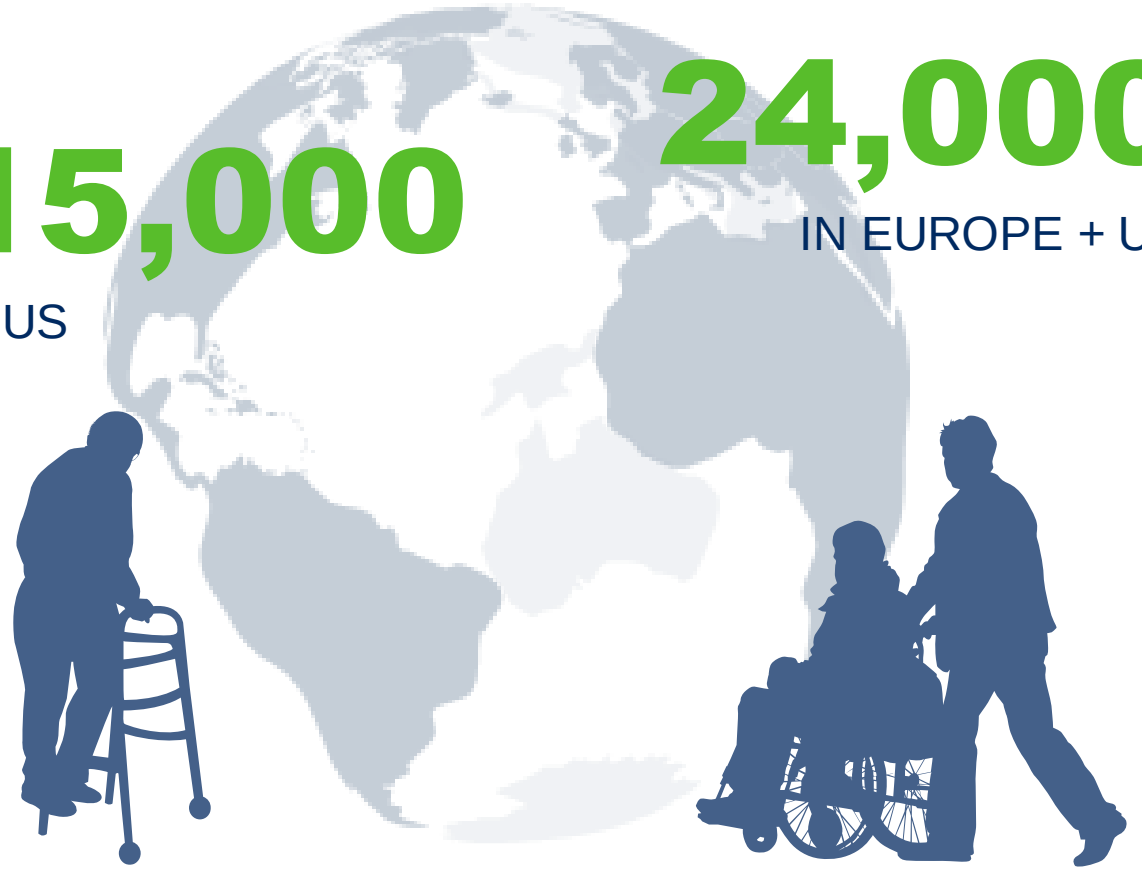
SCA: Rare Progressively Debilitating and Fatal Neurodegenerative Disorder with No Approved Treatment

- Autosomal dominant, progressive, neurodegenerative disease with multiple genotypes[1–3]
- Onset in early adulthood with symptoms leading to severe disability and premature death[3]
- High unmet need and no approved therapies[1,2]

SCA Prevalence[4]

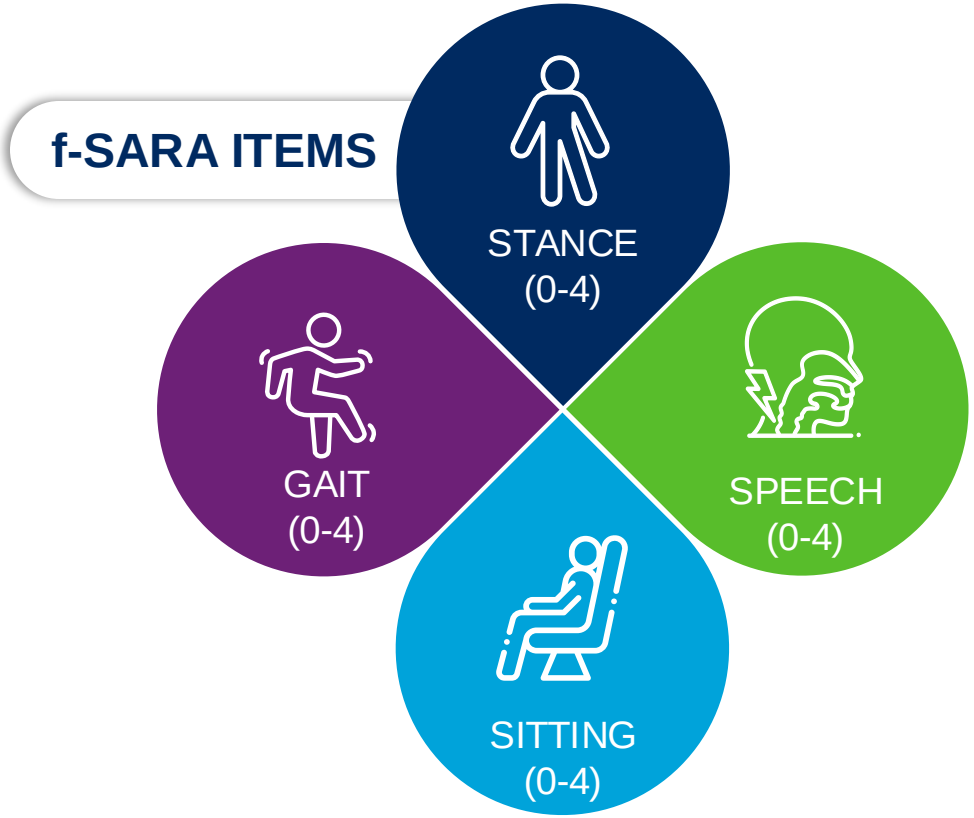
15,000
IN US

24,000
IN EUROPE + UK



f-SARA: Neurologist-Assessed Scale that Tracks SCA Disease Progression

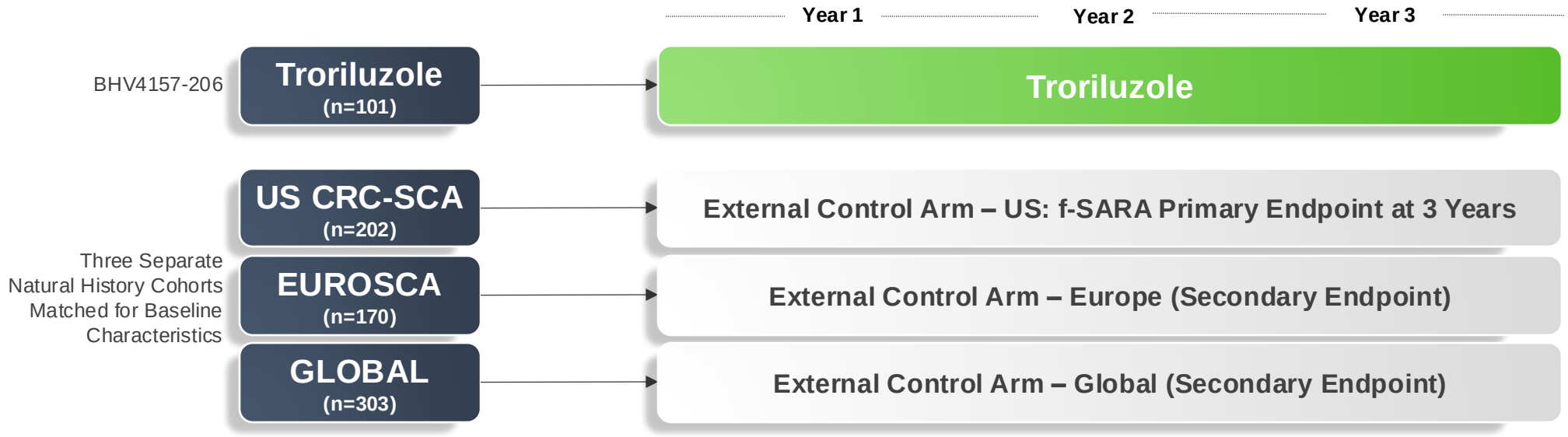
- Measures 4 core functional items that are clinically meaningful and reflect hallmark symptoms of SCA5
- Individual items rated 0–4 with total score range 0–16
- Generally increases (worsens) 0.5 points annually
- Developed with FDA input
- Psychometric and qualitative validation performed according to FDA guidance[5,6]



KEY POINT

f-SARA is an approvable endpoint in SCA

Troriluzole Long-term Real-World Evidence Study



DESIGN	3-Year Real-World Evidence Protocol with external control using Propensity Score Matching (PSM)
PRIMARY ENDPOINT	**Total f-SARA Scale** Change from baseline at 3 years in troriluzole-treated subjects vs untreated subjects from US Natural History control (CRC-SCA)
SECONDARY ENDPOINTS INCLUDE	• f-SARA change from baseline at 1 and 2 years vs US Natural History external control (CRC-SCA) • f-SARA change from baseline at 1, 2 and 3 years vs EU Natural History external control (EUROSCA) • f-SARA change from baseline at 1, 2, and 3 years vs Global US and EU Natural History external control (CRC-SCA and EUROSCA)

206-RWE Study Designed With FDA Feedback to Reduce Bias

Biohaven Proposal	FDA Feedback	BHV4157-206-RWE Protocol
Analyze new data from subjects completing 3-years of treatment	**Follow Industry Guidance for RWE***	Regulatory precedent for NDA approval based on RWE and external control for analysis of 3-year endpoint. Inclusion of new 3-year completers nearly doubles the sample size and thus increases power and precision as these data were not previously available
Submit SAP for FDA review	**Submit both Protocol and SAP for FDA review prior to database lock**	Submitted Protocol and SAP to FDA with prespecified endpoints and analysis plan based on FDA input ahead of database lock; **Biohaven adopted all feedback proposed by the FDA**
Use composite scale as primary outcome measure	**Use f-SARA as primary outcome measure**	f-SARA used as primary outcome measure; a reliable and validated scale to measure clinically meaningful change in function in SCA; designed with FDA input that is objective and minimizes effort dependence
Use global SCA Natural History cohorts as external control	**Use US SCA Natural History cohort as external control for primary analysis**	Minimizes potential for bias by ensuring the Biohaven trial & US SCA Natural History study conducted by same sites/investigators, evaluating similar scales, over similar time period, with same population, on same standard of care treatment
Use MAIC analysis as primary	**Use Propensity Score Matching (PSM) for primary analysis**	Minimizes potential for confounding bias by balancing baseline characteristics between treatment group and external control; Used in other NDAs leveraging RWE**
Genetic risk factors not included in matching	**Match populations based on trinucleotide repeat length for primary analysis**	Minimizes potential for bias by further matching treatment group and external control based on additional genetic factors associated with disease burden

*Guidance for Industry Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision Making for Drug and Biological Products https://www.fda.gov/media/171667/download
**Lynch DR, et. al. Propensity matched comparison of omaveloxolone treatment to Friedreich ataxia natural history data. Ann Clin Transl Neurol. 2024 Jan;11(1):4-16

Demographic and Baseline Characteristics

	BHV4157-206	CRC-SCA	EUROSCA
n	105	446	358
Age (years), n	105	434	358
mean (SD)	47.6 (13.1)	51.6 (13.8)	47.3 (12.7)
median (range)	49.0 (18, 73)	52.0 (0, 89)	47 (18, 84)
Sex, n	105	446	358
Male (%)	47 (45)	200 (45)	171 (48)
Female (%)	58 (55)	246 (55)	187 (52)
Age at symptom onset (years)			
mean (SD)	37.7 (12.4)	41.2 (13.9)	36.7 (11.8)
median (range)	38 (10, 71)	41 (0, 76)	37 (7, 76)
Genotype (%)			
SCA1	15 (14)	66 (15)	102 (29)
SCA2	31 (30)	94 (21)	141 (39)
SCA3	41 (39)	153 (34)	115 (32)
SCA6	6 (6)	95 (21)	0
SCA7	5 (5)	5 (1)	0
SCA8	3 (3)	19 (4)	0
SCA10	3 (3)	6 (1)	0
Multiple	1 (1)	3 (1)	0
f-SARA			
mean (SD)	4.95 (1.6)	3.97 (3.5)	5.03 (4.1)
median (range)	4.00 (2,10)	3.00 (0,16)	4.00 (0,16)

Full Analysis Set

Troriluzole vs Matched US Natural History External Control Shows Slowing of Disease Progression out to Year 3

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

KEY POINT

Troriluzole reduced SCA disease progression by 50%

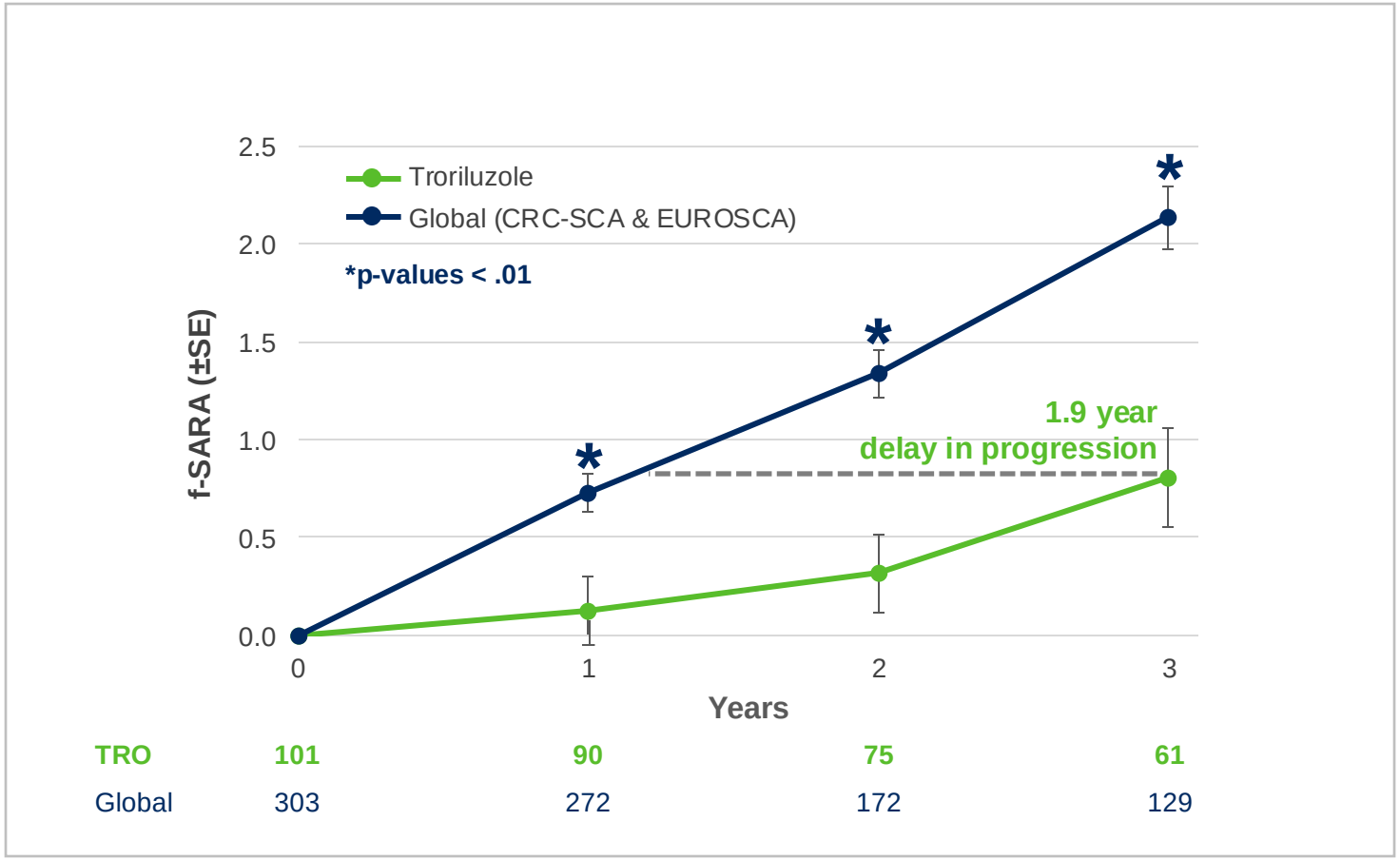
Troriluzole vs Independent Matched EU Natural History External Control Shows Slowing of Disease Progression out to Year 3

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

KEY POINT

Troriluzole reduced SCA disease progression by 70%

Troriluzole vs Matched Global Natural History External Control Shows Slowing of Disease Progression out to Year 3



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

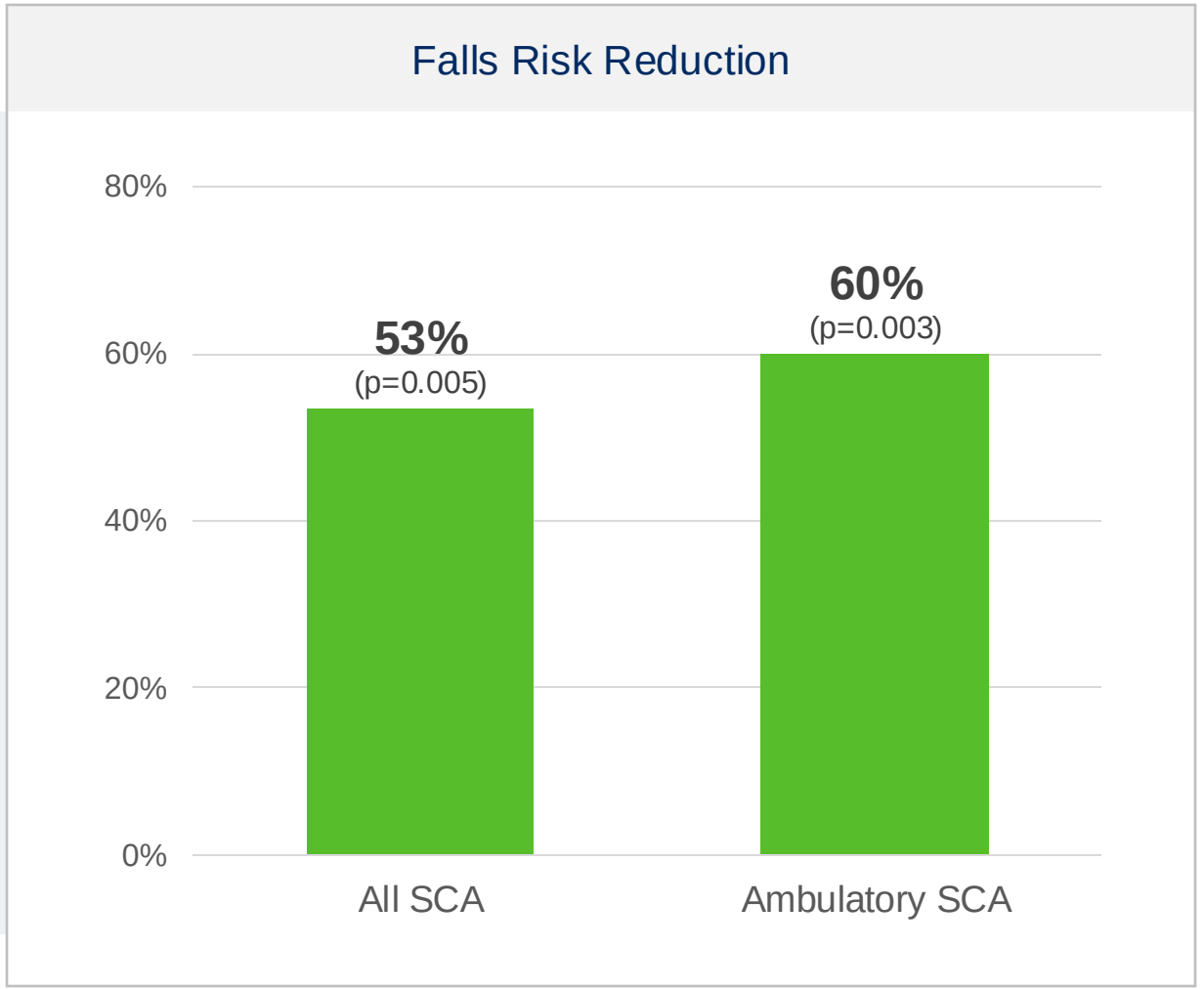
KEY POINT

Troriluzole reduced SCA disease progression by 60%

Troriluzole Substantially Reduced Fall Risk in Double-Blind Phase

Burden of Falls in SCA[9–10]

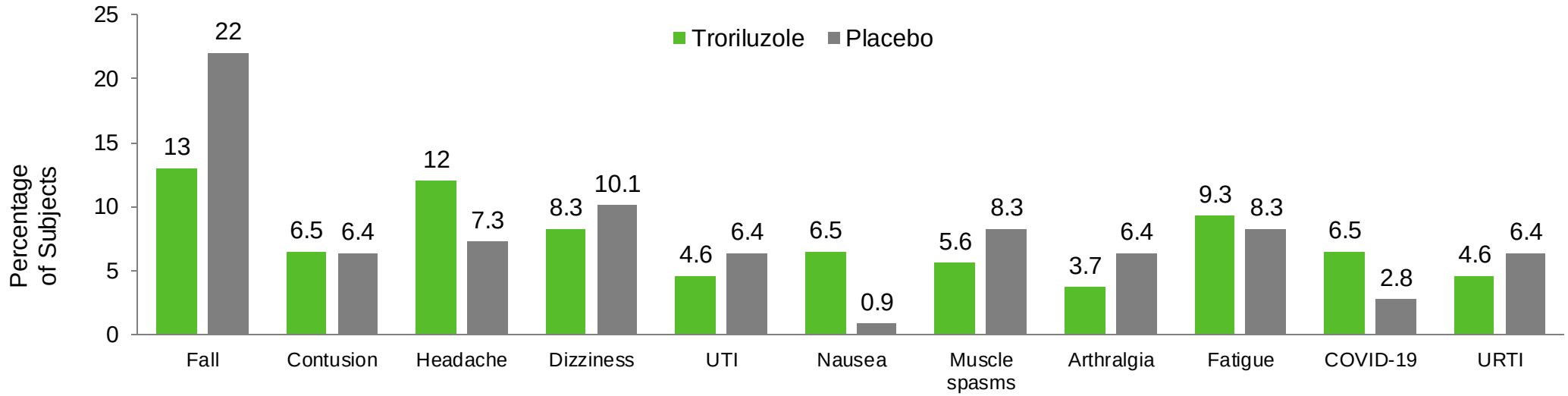
- Most SCA patients (74–84%) report falling in the preceding 12 months
- Falling is associated with a high rate of injury (74%)
- Frequent fallers report more fall-related injuries
- Fall frequency decreases when patients become wheelchair dependent or immobile



* Study BHV4157-206 double-blind phase results; Falls were captured in Study BHV4157-206 as adverse events if reported as "worsening falls" or if the fall resulted in an injury. For the analysis, a generalized linear model was fit using a Poisson family model with a log link function.
** Ambulatory SCA is defined as All SCA subjects who could ambulate without constant assistance (scoring 1 or 2 on the gait item of the f-SARA) at baseline

Troriluzole was Well-Tolerated in Clinical Trials

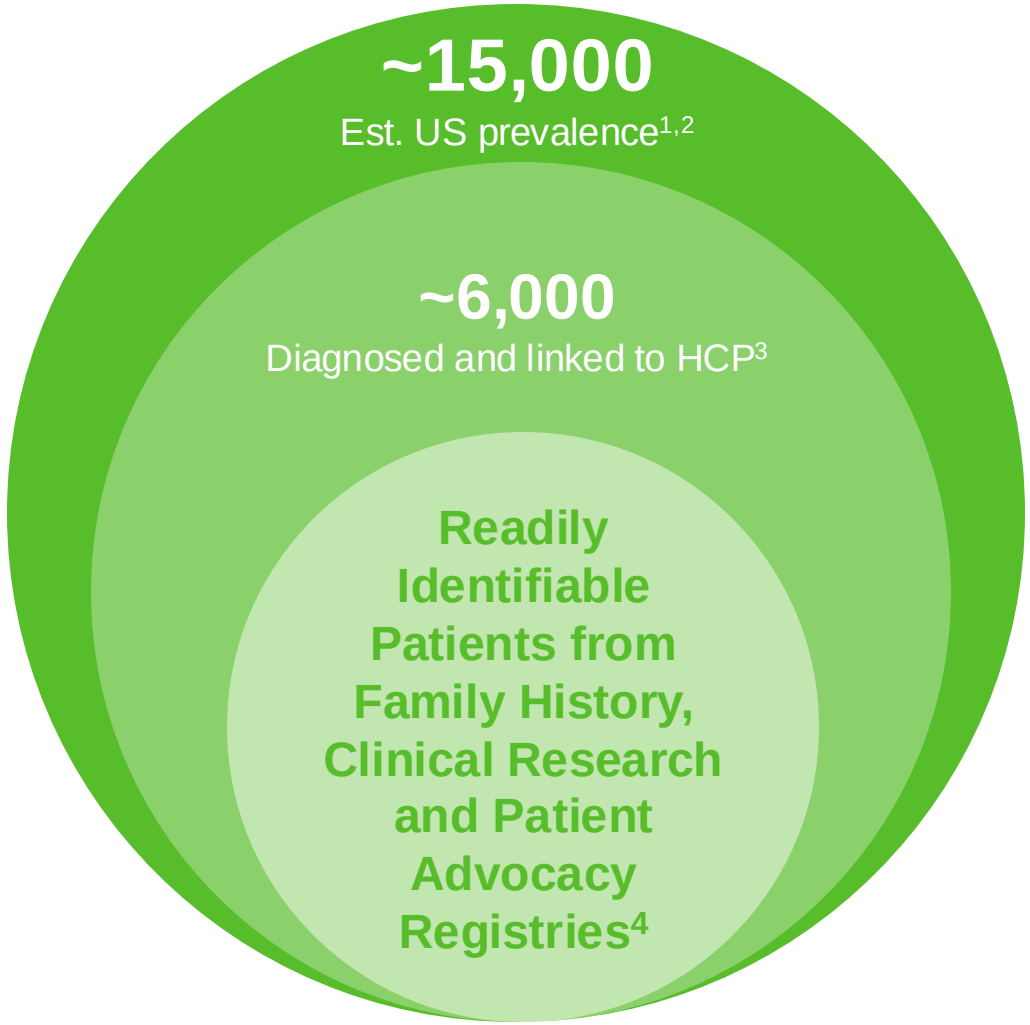
	Troriluzole N=108	Placebo N=109
Serious TEAE	**6 (5.6)**	8 (7.3)
Severe TEAE	**3 (2.8)**	8 (7.3)
TEAE Leading to Discontinuation	**5 (4.6)**	5 (4.6)



TEAEs occurring in ≥5% of subjects

Study BHV4157-206 double-blind phase results; falls were captured as adverse events if reported as "worsening falls" or if the fall resulted in an injury.

SCA Represents a Significant Commercial Opportunity



- 6,000 diagnosed US patients
- No currently approved SCA treatments
- Availability of genetic testing and advent of approved treatment will facilitate diagnosis
- Engaged, connected SCA patient community
- Strong patient advocacy support
- KOLs, HCPs and key centers treating SCA have been identified

1. Ruano L, Melo C, Silva MC, Coutinho P. The global epidemiology of hereditary ataxia and spastic paraplegia: a systematic review of prevalence studies. Neuroepidemiology. 2014;42(3):174-83. 2. National Ataxia Foundation Website: https://www.ataxia.org/what-is-ataxia/, https://www.ataxia.org/neurologists-and-specialty-clinics/ , https://www.ataxia.org/crc-sca/. 3. Source: Patients filtered from LAAD claims data between April 2016 – Mar. 2021 purchased from IQVIA. 4. Data on File based on claims data purchased from IQVIA.

TRORILUZOLE
OCD

3M+ OCD Patients in US with High Unmet Medical Need

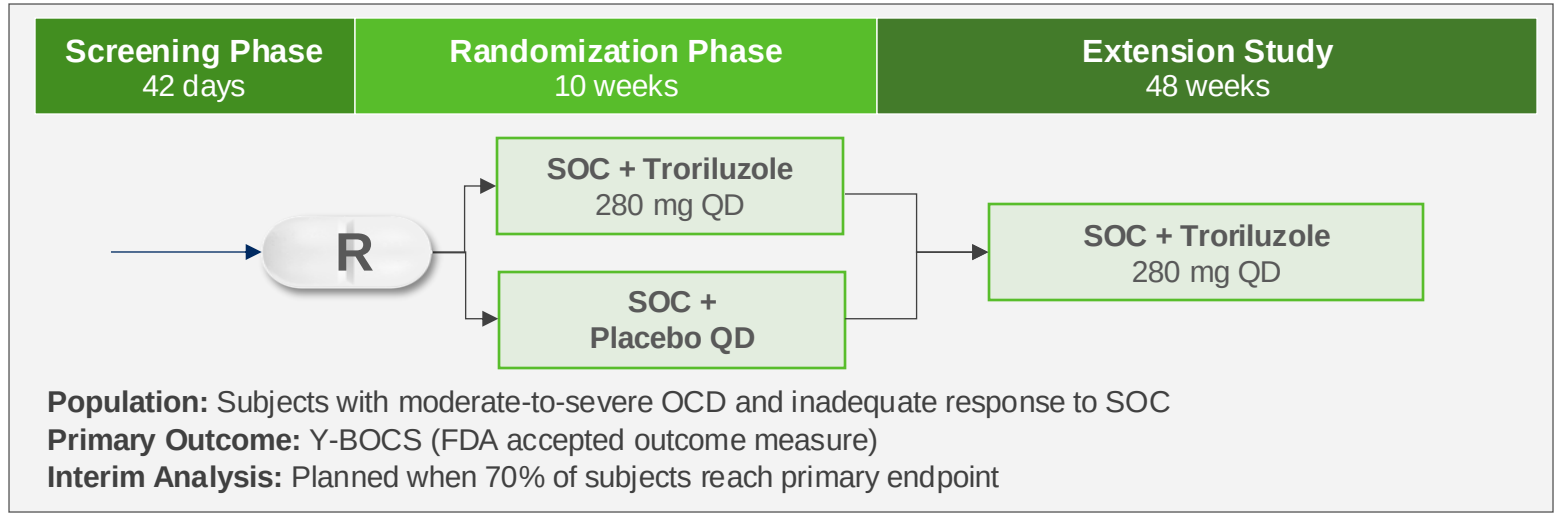
- 40–60% do not respond to first line treatment
- 10–40% are treatment refractory potentially requiring ablative neurosurgery or deep brain stimulation
- First novel mechanism in OCD in over 20 years and a potential breakthrough

Phase 2 Troriluzole Trial in OCD Demonstrated Efficacy Signal

- Consistent numerical benefits vs. placebo on Y-BOCS (primary endpoint) at all timepoints (weeks 4 to 12); $p < 0.05$ at week 8 and $p = 0.22$ at week 12

Global Phase 3 Program (2 Identical Studies) Currently Ongoing

Design informed by Phase 2 study



Population: Subjects with moderate-to-severe OCD and inadequate response to SOC
Primary Outcome: Y-BOCS (FDA accepted outcome measure)
Interim Analysis: Planned when 70% of subjects reach primary endpoint

OCD, obsessive-compulsive disorder; **R**, randomization; **SOC**, standard of care; **Y-BOCS**, Yale-Brown Obsessive-Compulsive Scale.

KEY POINT

- Top-line data from 1st Phase 3 OCD trial expected in 1H 2025
- Top-line data from 2nd Phase 3 OCD trial expected in 2H 2025

BHV-4157 Troriluzole Treated OCD Patients: Strong Signal Observed in Phase 2 POC Supports Advancement to Phase 3

STUDY BHV-4157-202

Patients with moderate-to-severe OCD (Y-BOCS score ≥ 19) and inadequate response to standard of care

SAMPLE SIZE

226 subjects

RANDOMIZATION

1:1

DOSE

Troriluzole 200 mg QD vs Placebo QD (in patients on standard of care)

PRIMARY OUTCOME

Y-BOCS, precedented outcome measure accepted by FDA

Table 1: Troriluzole Effect on OCD in Phase 2/3 Trial[1]

Y-BOCS Total Change from Baseline	Week 4 (N=115[a], 111[b])	Week 8 (N=108[a], 96[b])	Week 12 (N=102[a], 99[b])
a. Placebo[a]	-2.9	-3.6	-4.9
b. Troriluzole[b]	**-3.4**	**-5.1***	**-5.9**
p-value	0.451	0.041	0.220

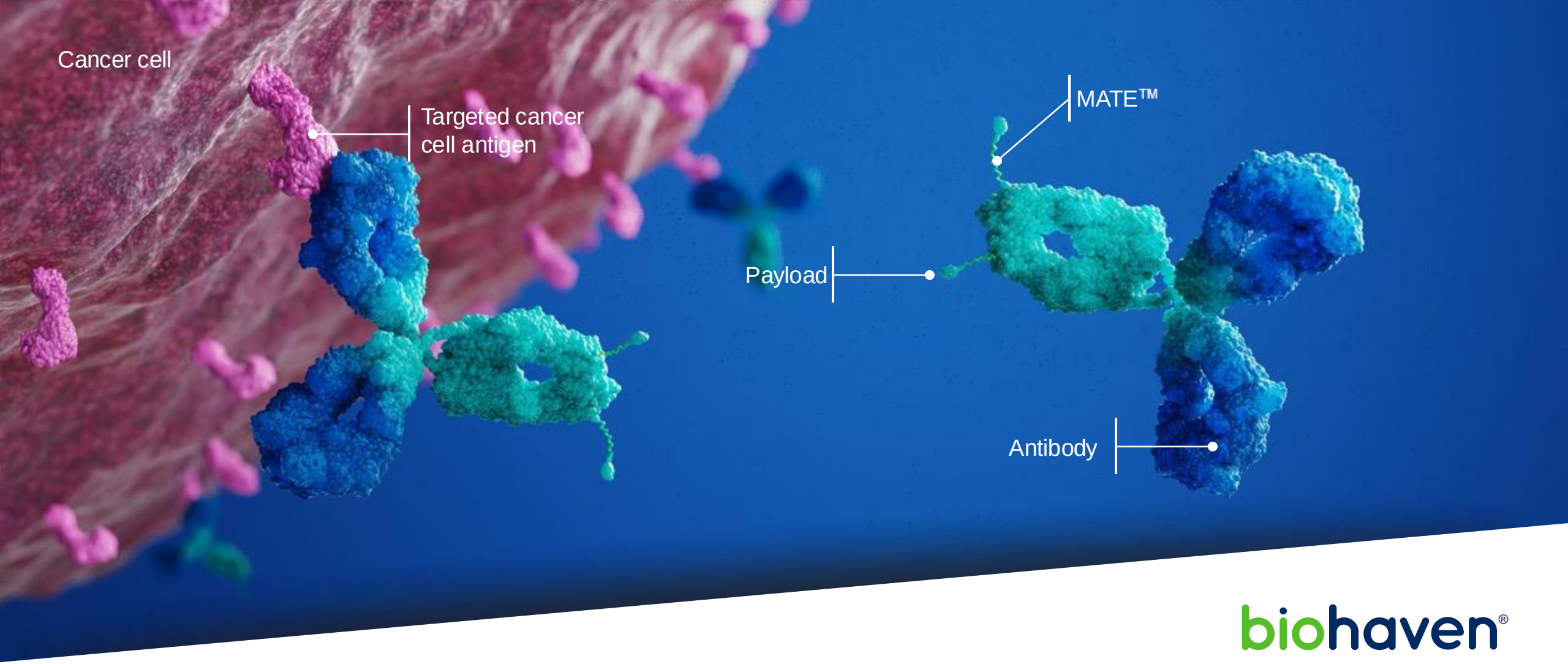
1. BHV-4157-202 Final Unblinded Analysis YBOCS Total Change from Baseline by Week LSMeans from MMRM Model MITT Data Set

Table 2: Troriluzole Effect on Patients with Severe OCD[1]

Y-BOCS Total Change from Baseline	Week 4 (N=47[c], 49[d])	Week 8 (N=45[c], 42[d])	Week 12 (N=43[c], 44[d])
a. Placebo[c]	-3.5	-3.1	-4.6
b. Troriluzole[d]	**-4.1**	**-6.0***	**-7.0**
p-value	0.584	0.035	0.084

1. Patients at baseline with median Y-BOCS total scores > 26 (severe OCD symptoms).
* $p < 0.05$ versus placebo

Y-BOCS, Yale-Brown Obsessive Compulsive Scale (FDA accepted outcome measure)



biohaven®

Oncology: Next-Generation ADCs

Biohaven's Novel ADC Conjugation Technology and Strategic Collaborations Driving Next-Generation Cancer Therapies

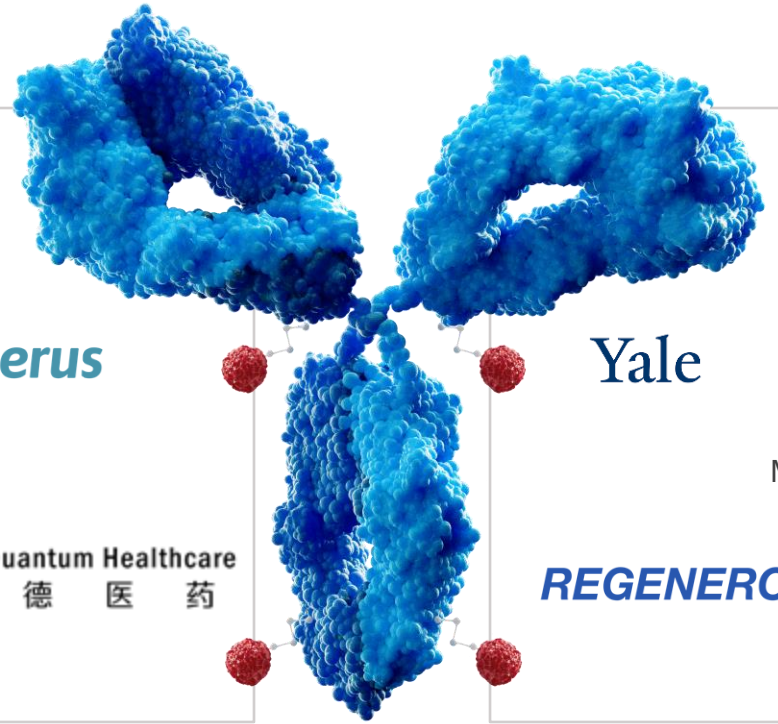
Collaborate to generate highly differentiated ADCs

Novel mAbs

- Validated and emerging targets
- Merus collaboration leverages differentiated dual-targeting antibody platform

Exclusivity to TopoIx payload

- Superior preclinical anti-PD/L1 synergy and immunogenic cell death
- GeneQuantum collaboration provides broad target exclusivity to the payload for 18 oncology targets



Broad and flexible platform applicability

Single-step chemistry, native mAbs

Modular, efficient, and scalable MATE® technology developed from Yale University Spiegel Lab

Irreversible, Site-Specific Conjugation

Minimize payload-associated tox, DAR homogeneity

Combination I/O Therapies

Supply agreement: BHV-1510 with Libtayo®

BHV-1510 (Trop2 TopoIx) in Phase 1 (mono and anti-PD1 combination)

BHV-1530 (FGFR3 TopoIx) in Phase 1 startup — FPI early 2025

BHV-1500 (CD30 MMAE) IND planned 2025

Novel ADCs and De-Risked Fast-Followers in Clinic

STRATEGIC COLLABORATIONS AND CLINICAL SUPPLY AGREEMENTS

MULTIPLE DC/INDs planned 2025–2026

BHV-1510 is a Highly Differentiated Trop2 ADC

- Ideally positioned for fast-to-market strategy with anti-PD-1 combo

Novel TopoIx Payload Synergy with Anti-PD-1 *In Vivo*

- Induces immunogenic cell death and complete tumor regressions
- Superior to datopotamab deruxtecan (DS-1062) plus anti-PD-1

Fully Optimized Next-generation ADC

- Novel and highly stable linker-payload (DAR4)

Differentiated Pre-clinical Safety Profile

- Datopotamab deruxtecan (DS-1062): interstitial lung disease (ILD)
- Sacituzumab tirumotecan (MK2870/SKB264): hematological toxicities
- TRODELVY®: neutropenia, diarrhea

Milestones Achieved

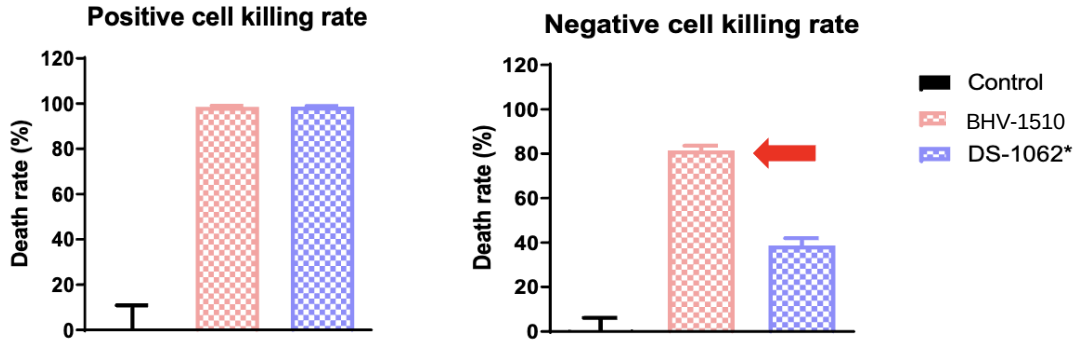
- First-in-human trial initiated April 2024
- Anti-PD-1 combo cohorts with Libtayo® initiated 4Q 2024

BREAKING NEWS

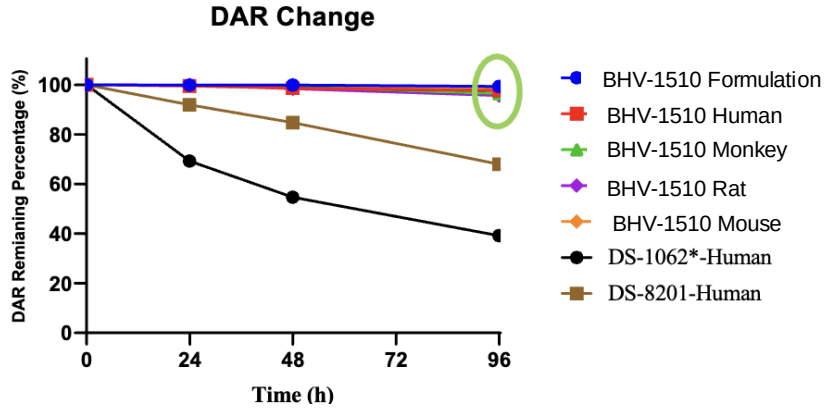
- Clinical activity and no ILD with TopoIx observed in early cohorts
- Target exclusivity expanded for up to 18 ADC targets incorporating TopoIx payload

BHV-1510 Improves Bystander Killing and Immunogenic Cell Death vs. DS-1062

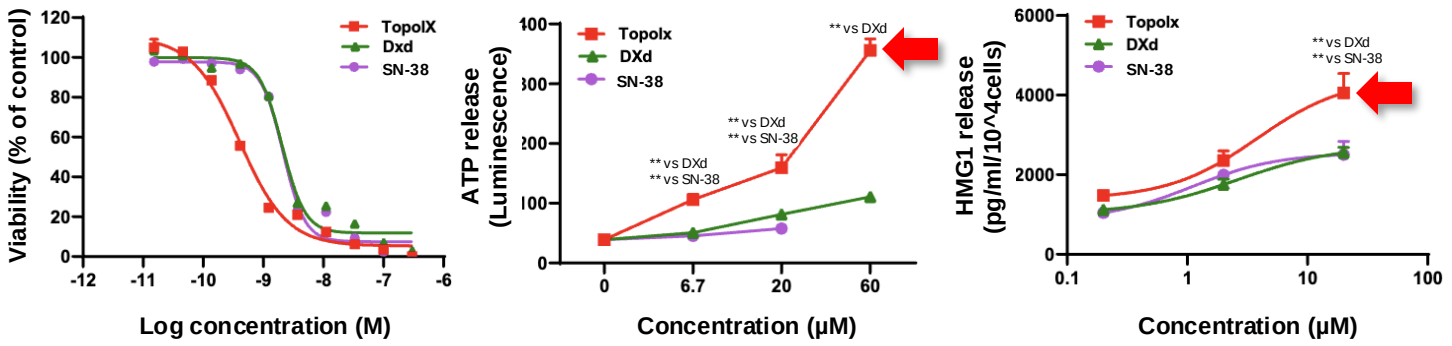
Superior Bystander Activity vs. DS-1062



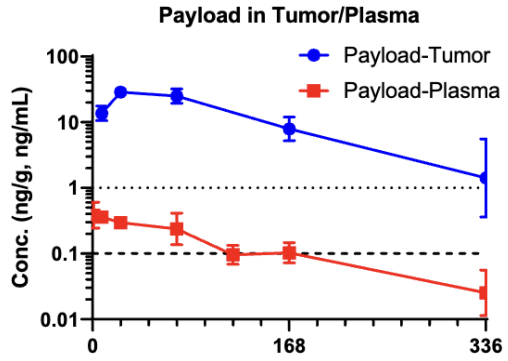
Highly Stable Linker vs. DS-1062



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

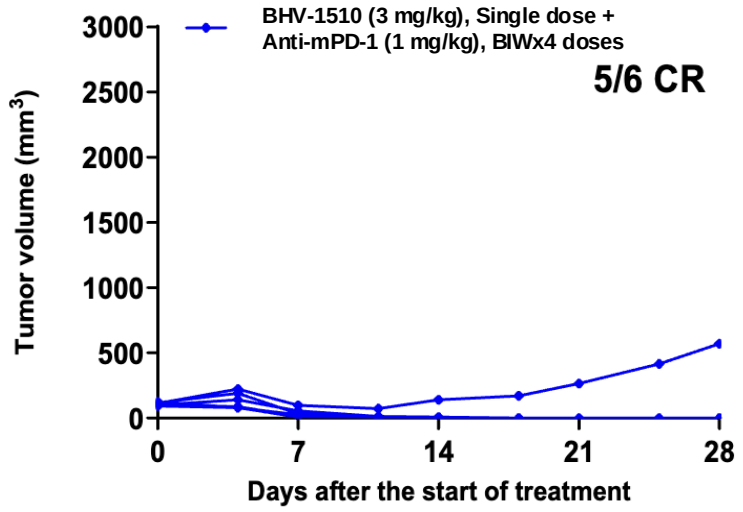


High Payload Delivery to Tumor

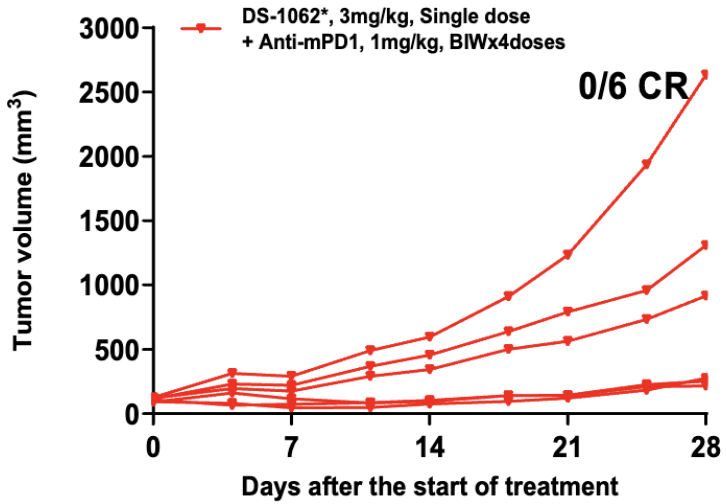


BHV-1510 + Anti-PD-1 Combination Shows Compelling Synergy in Syngeneic Models and Is Superior to DS-1062

BHV-1510 + Anti-PD-1



DS-1062 + Anti-PD-1



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 Trop-2 combinations with safer more efficacious ADC

Phase 1/2 Study in Advanced Epithelial Tumors

Key eligibility

Select advanced refractory epithelial tumors

Tumor tissue available for testing (Trop-2 expression level not required for study entry)

Phase 1: Dose escalation

Phase 1/2: Cohort expansion(s)

Select advanced epithelial tumors

DESIGN	Open label, dose escalation (Ph1) and dose expansion (Ph2)
POPULATION	Advanced epithelial tumors having failed SOC therapy
SAMPLE SIZE	170 patients
TREATMENT	BHV-1510
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.

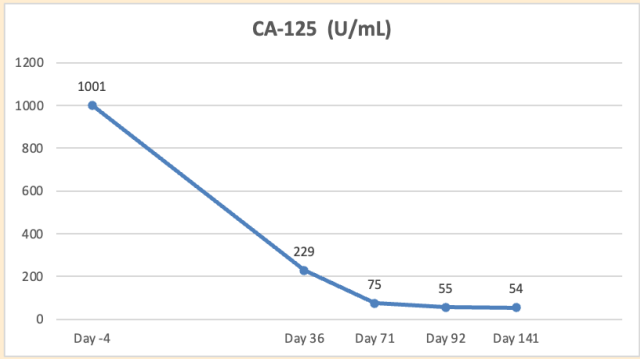
KEY POINTS

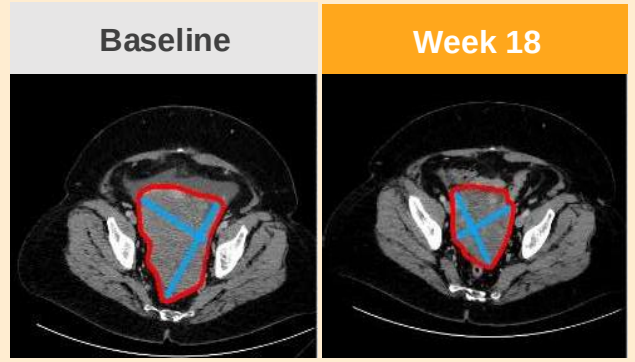
- Phase 1 monotherapy dose escalation initiated
- Combination with PD-1 initiated

BHV-1510 (Trop2 ADC with TopoIx) with Early Clinical Activity in Phase 1

- Clinical activity across doses starting at the lowest dose (2 mg/kg, Q3W)
  - Tumor reduction observed in tumor types including ovarian, SCLC, NSCLC
- Favorable preliminary safety and PK profile
  - No payload-associated ILD, diarrhea, or significant hematological toxicity
  - Main toxicity observed is on-target Trop2 ADC class mucositis; an expected and manageable effect
  - Very low free payload in serum, demonstrates high ADC stability
- Dose escalation (mono and Libtayo® combo) and dose/schedule optimization ongoing

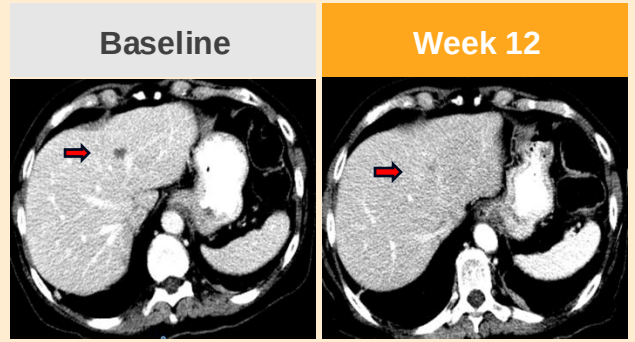
Case 1: 71 y/o, Platinum-resistant ovarian cancer, 2 mg/kg, Q3W
25% tumor reduction at week 18 with dramatic drop in CA-125





Case 2: 70 y/o, SCLC post carboplatin+durvalumab and lurbinectedin, 4 mg/kg Q3W

PR (~60% reduction) at week 12



KEY POINT

Observed clinical activity and safety supports broad investigation of ADCs incorporating novel TopoIx payload and highly stable linker

Advancing TopoIx Payload in Next-Gen ADC to Target Urothelial Cancer and Other Solid Tumors

- Novel and proprietary FGFR3 mAb
- Enzymatic, site-specific conjugation
- Favorable nonclinical tox profile

Validated target with limited competition

- No ADCs approved or in advanced development
- Core opportunity in FGFR3-altered metastatic urothelial cancer (mUC) – only 1 Tyrosine Kinase Inhibitor approved
- Potential extension into other FGFR3-driven solid tumors
- ~$400M to > ~$1B peak US gross sales potential

Synergistic Efficacy With Checkpoint Inhibitors *In Vivo*

- BHV-1530/anti-PDL1 combination showed synergy similar to BHV-1510
- PD1 synergy with PADCEV® (Nectin-4 ADC with MMAE payload) showed dramatically improved survival in mUC

Milestones Achieved

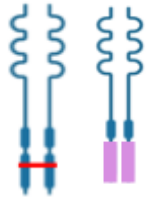
- US FDA IND May Proceed Letter granted

BREAKING NEWS

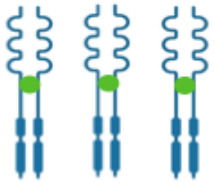
First-in-Human study planned to initiate in 1H 2025

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

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



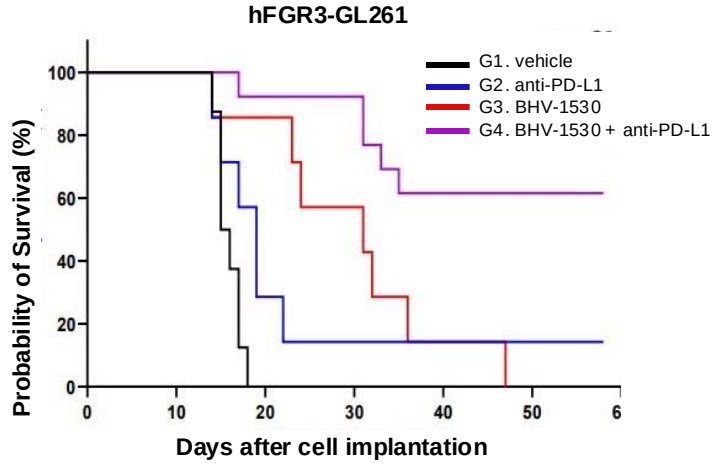
FGFR3 mutation/fusion in ~20% mUC



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



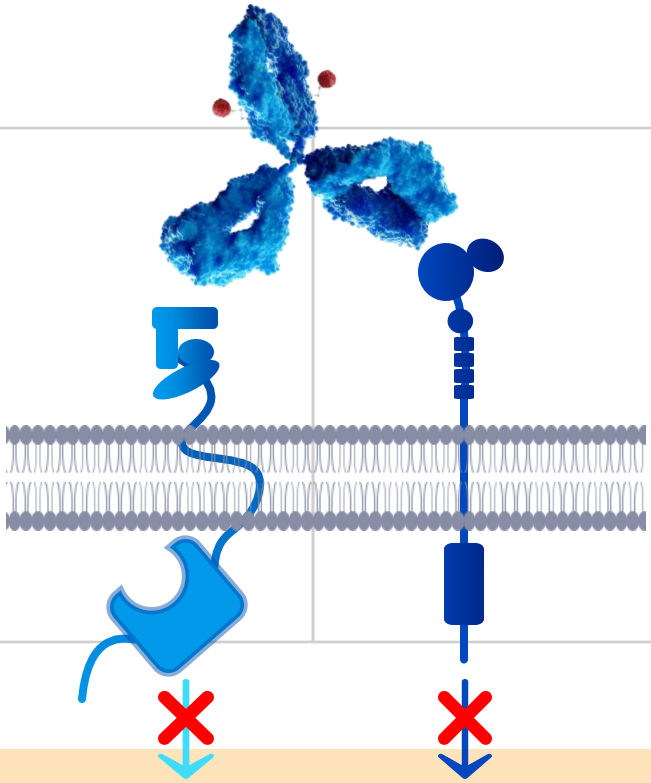
Group	% Increased Life Span (ILS)	Median Survival (days)
G1	-	15
G2	27%	19
G3	107%	31
G4	>300%	>63

Biohaven-Merus Collaboration Represents a Leading-Edge Approach to Developing Highly Optimized Bispecific ADCs

Merus

A leader in developing differentiated bispecific mAbs for oncology

- Clinically validated platform
- Lead program (Zenocutuzumab) granted US FDA accelerated approval in December 2024



biohaven

Next-generation ADC conjugation and payload platform technologies

- Potential for superior specificity and benefit/risk profile vs. single target ADCs
- Co-development maximizes expertise and efficiencies

Potential advantages of dual-target bispecific ADCs

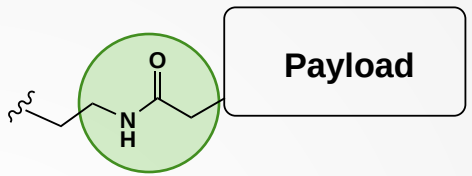
- Preferential binding
- Improved internalization
- Optimal tumor penetration
- Multiple MOA of tumor cell killing

BREAKING NEWS

Multi-target collaboration, leveraging each company's innovative tech for ADC co-development

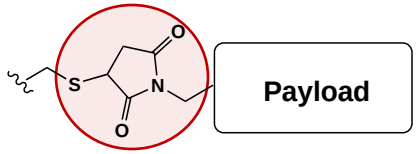
Multimodal Antibody Therapy Enhancers (MATE™): Biohaven's Next-Generation Site-Specific ADC Technology

Biohaven chemistry



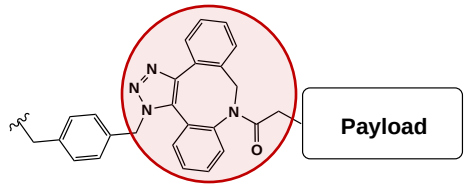
Stable, physicochemically benign amide linkage

Industry standard maleimide



Poorly stable linkage

Click chemistry to engineered antibody



Undesirably large, lipophilic linkage

IMPROVED CONJUGATION TECHNOLOGY

Efficient conjugation of single heavy chain lysine provides stable and precise DAR

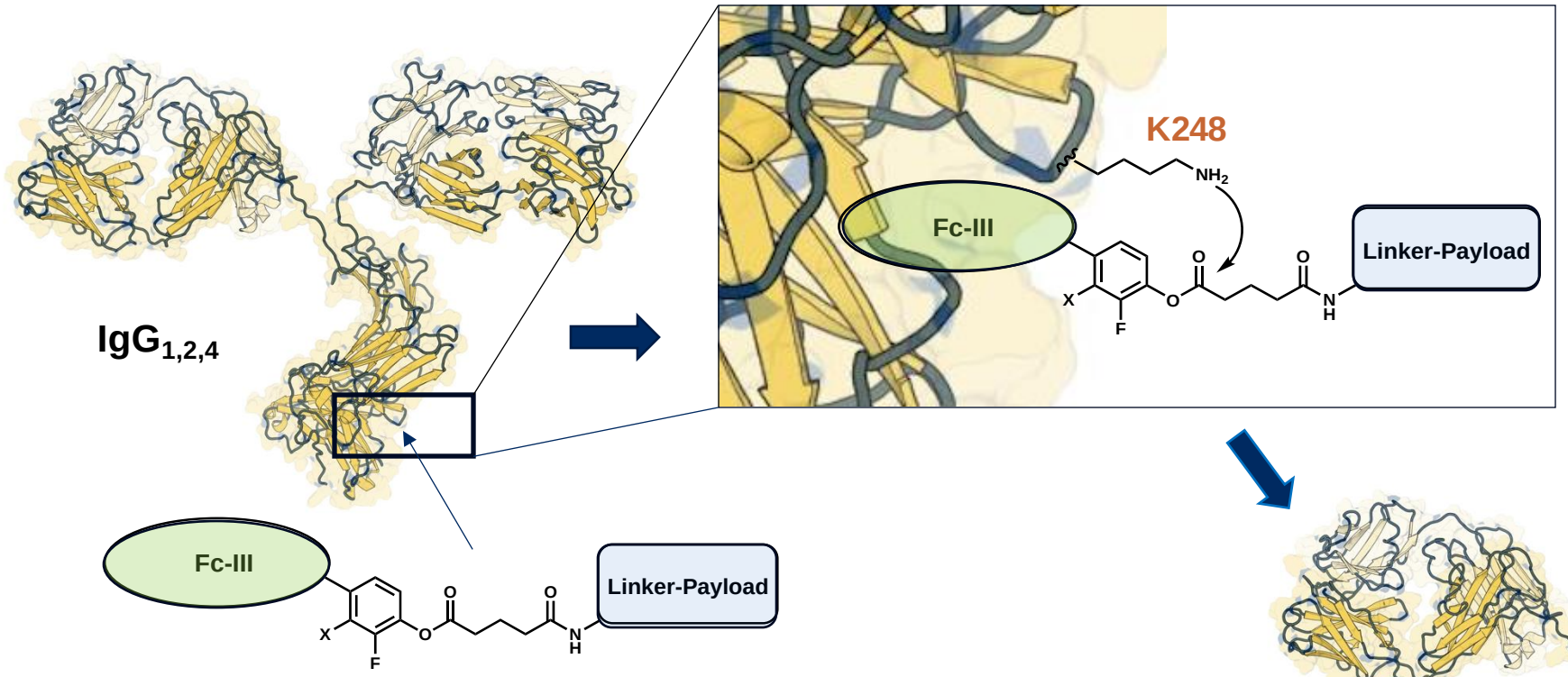
- ✓ **Improved safety:** Reduced untargeted payload in systemic circulation driving toxicity
- ✓ **Improved efficacy:** Increased targeted payload reaches tumor, higher doses possible
- ✓ **IP filed globally for conjugation technology footprint compositions** — applies to many antibodies / NMEs: 2042 patent expiration

USES NATIVE ANTIBODY

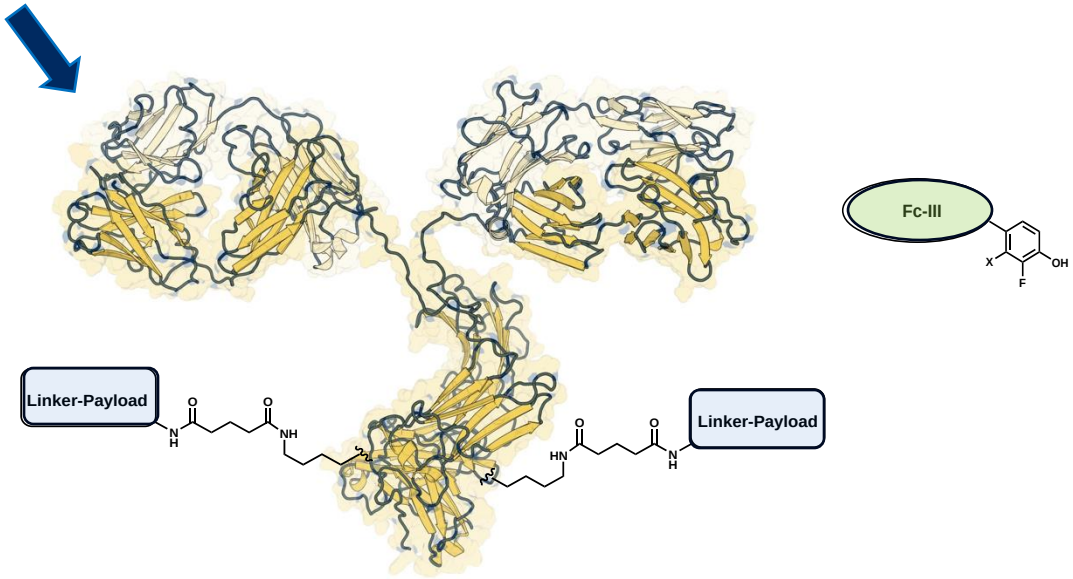
Improved CMC vs. current site-specific technologies

NME, new molecular entity.

One-Step Preparation: Site-Specific ADCs Using Native IgGs



Chemically modified Fc-III cyclic peptide binds site-specifically, allowing lysine (K248) to form stable amide bond with payload-linker



Chemistry has been scaled to prepare 1.1 kg of GLP conjugate (> 90% yield) and a diverse set of 12 ADCs

(Global IP filings on "fingerprint" of conjugation technology and individual composition of matter IP for specific ADC molecules)

Validation of Biohaven's ADC MATE™ Technology

- 11 unique oncology targets selected from marketed compounds/lead Phase 3s for industry leading ADCs, demonstrating platform capabilities across a diverse range of payloads, targets, and tolerability
- Biohaven's ADC technology applied to each of these 11 and evaluated for key attributes translatable to improvements in clinical efficacy and safety

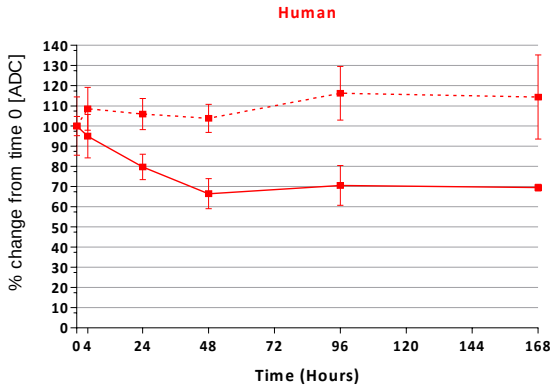
Attribute	Outcome
5 different payloads* in 11 ADCs	**Successful conjugation of each payload**
Cross-species plasma stability assessment	**Substantial stability improvements in 7/7 evaluated**
Cell target cytotoxicity	**Comparable in 7/8 evaluable culture systems**

*MMAE, Eribulin, DM1, DXd, PBD dimer.

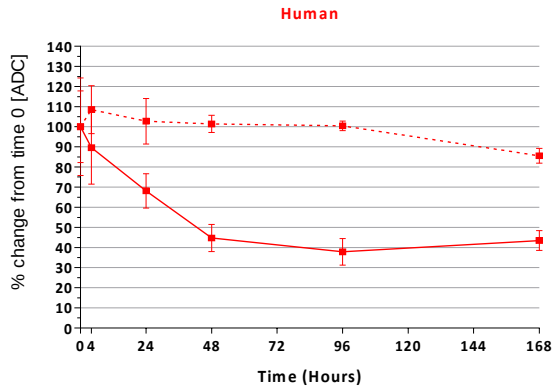
MATE™ Conjugation Platform Consistently Improved Plasma Stability

Biohaven ADC — Clinical Comparator

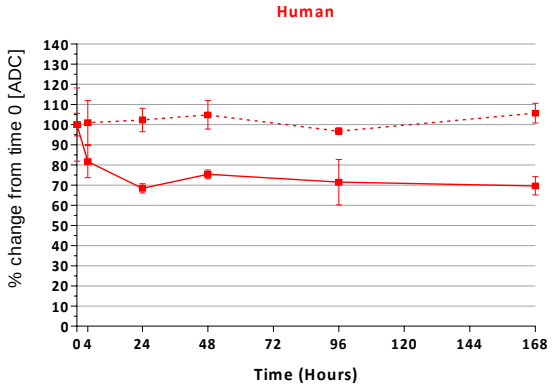
Total ADC @ 37˚
Target A vs. BH-3974



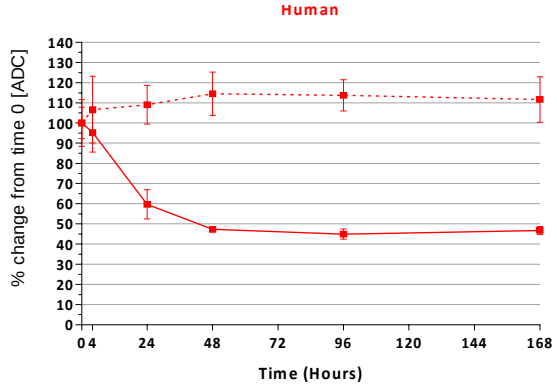
Total ADC @ 37˚
Target B vs. BH-3946016



Total ADC @ 37˚
Target C vs. BH-6015



Total ADC @ 37˚
Target D vs. BH-6028

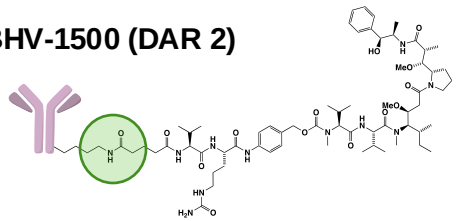


- Highly stable conjugation observed in vitro across multiple ADCs
- Able to generate a wide portfolio of stable constructs using native mAbs
- Potential to broaden therapeutic margin, increase time on treatment and improve efficacy

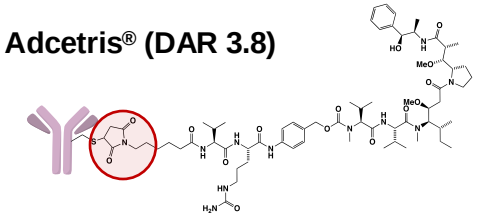
BHV-1500 Is a Differentiated CD30 ADC

- Validated target
- Superior *in vivo* efficacy head-to-head vs. Adcetris® at ***50% lower*** DAR
- Highly stable and site-specific conjugation

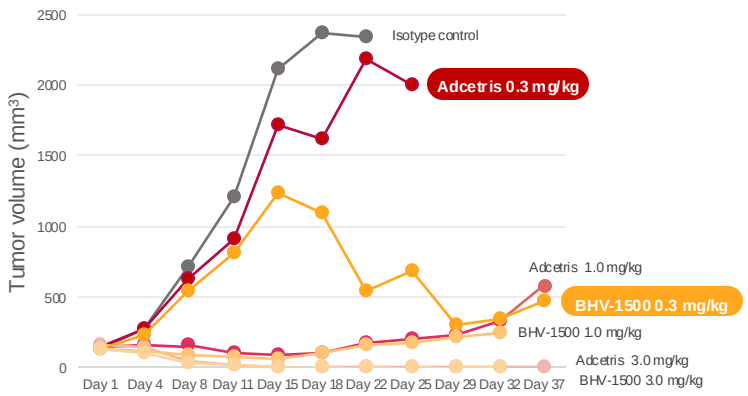
BHV-1500 (DAR 2)



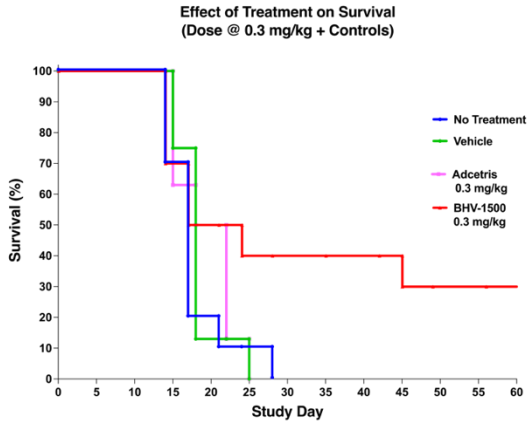
Adcetris® (DAR 3.8)



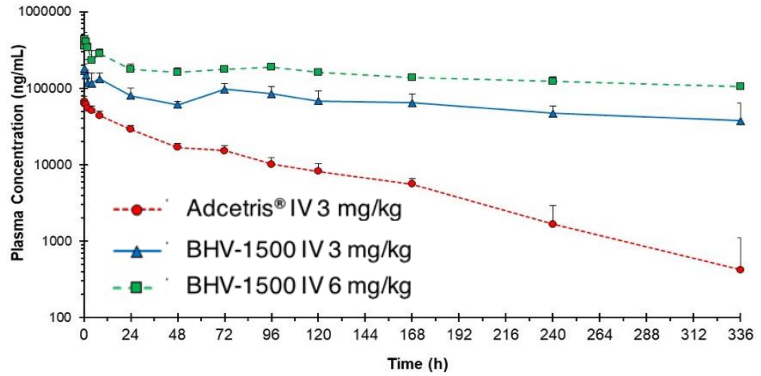
BHV-1500 Demonstrates Superior Efficacy to Adcetris® in a Mouse Xenograft Model



BHV-1500 Improved Survival in Mouse Compared to Adcetris®



Total ADC Stability *in vivo* in Cynomolgous Monkey



BHV-1500 is a CD30 (next-gen brentuximab vedotin) ADC.

KEY POINT

IND anticipated in 1H 2025

Company Capitalization Updates

POTENTIAL ROYALTIES

Pfizer will make royalty payments in low- to mid-teens% in respect of annual US net sales of rimegepant and zavegepant >$5.25B, subject to annual cap ($400M/year)[1]

CGRP

SHARES OUTSTANDING

101.1M[2]

DAYS MATTER™

CASH

~$642M[3]

1. Cap reached if aggregate annual U.S. net sales of rimegepant and zavegepant amount to $8.15B. Royalty payments would be in respect of years ended on or before 12/31/40. 2. As of November 8, 2024; excludes outstanding options. 3. As of October 2, 2024; includes proceeds raised from underwritten public offering

Top Areas of Innovation

- IMMUNOLOGY & INFLAMMATION
- NEUROLOGY
- OBESITY
- ONCOLOGY
- CARDIOVASCULAR
- RENAL
- RARE DISEASE

biohaven®

	PATIENTS[1] INDICATION	
IgG Degraders	**130K** mAB PARTIAL RESPONDER RA[2]	**100K** MYASTHENIA GRAVIS
	350K ATD REFRACTORY GRAVES' DISEASE[2]	
TYK2/JAK1	**3.5M** ARIA PREVENTION[3]	**0.5M** EARLY PARKINSON'S DISEASE
	3.5M EARLY ALZHEIMER'S DISEASE[4]	**950K** MULTIPLE SCLEROSIS
Kv7 Activator	**2.4M** FOCAL EPILEPSY	**7M** BIPOLAR DISORDER
	1.1M GENERALIZED EPILEPSY	**21M** MAJOR DEPRESSIVE DISORDER
TRPM3 Antagonist	**40M** MIGRAINE	**10M** PAIN
Troriluzole	**15K** SPINOCEREBELLAR ATAXIA	**3.2M** OBSESSIVE-COMPULSIVE DISORDER
Taldefgrobep Alfa	**10K** SPINAL MUSCULAR ATROPHY	**10M** OBESITY
CD30	**95K** HODGKIN LYMPHOMA	
Trop2	**316K** EPITHELIAL TUMORS	
FGFR3	**118K** mUC and SOLID TUMORS	
β1AR Degrader	**200K DCM /** PERIPARTUM CARDIOMYOPATHY	
Gd-IgA1 Degrader	**140K** IgA NEPHROPATHY	

Biohaven's pipeline working to help millions of patients

1. Patient numbers are US from Biohaven market research; 2. represents ~12% and ~11% of Graves and RA populations respectively; 3. With amyloid therapy; 4. Disease modifying.

			1H 2025	2H 2025
GLUTAMATE	**Troriluzole | BHV 4157**	Spinocerebellar Ataxia	NDA Submission Filing Decision	
		Obsessive-Compulsive Disorder	Phase 3 Study #1 Topline	Phase 3 Study #2 Topline
MYOSTATIN	**Taldefgrobep Alfa | BHV-2000**	Spinal Muscular Atrophy	FDA Meeting	
		Obesity	Initiate Phase 2	
ION CHANNEL	**Kv7 Activator | BHV-7000**	Focal Epilepsy	Continue Phase 3 Enrollment	
		Generalized Epilepsy	Continue Phase 3 Enrollment	
		Bipolar Disorder	Pivotal Study Topline	
		Major Depressive Disorder		Pivotal Study Topline
	TRPM3 Antagonist | BHV-2100	Migraine & Pain Disorders	POC Topline Data	
INFLAMMATION & IMMUNOLOGY	**TYK2/JAK1 Inhibitor | BHV-8000 (brain-penetrant)**	Prevention of Amyloid Therapy Induced ARIA		
		Parkinson's Disease (PD)	Initiate Phase 2/3	
		Alzheimer's Disease (AD)		
		Multiple Sclerosis		
	IgG Degrader | BHV-1300 | BHV-1310	Common Disease (Graves, RA)	Complete Phase 1	Initiate Phase 2 Graves' Disease
		Rare Disease (Myasthenia Gravis)	Initiate Phase 1	
	Gd-IgA1 Degrader | BHV-1400	IgA Nephropathy	Complete Phase 1	
	β1AR AAb Degrader | BHV-1600	Peripartum Cardiomyopathy	Complete Phase 1	
ONCOLOGY	**Trop2 ADC +/- PD1 | BHV-1510**	Advanced or Metastatic Epithelial Tumors		Phase 1 Interim Data
	FGFR3 ADC | BHV-1530	Urothelial Cancer & Other Tumors	Initiate Phase 1	
	CD30 ADC | BHV-1500	Hodgkin Lymphoma	Regulatory Interaction	
	Undisclosed Targets	*Merus and GeneQuantum Collaborations*		Advance New ADCs

DAYS MATTER™

biohaven®