DAYS MATTER™

BHVN
LISTED
NYSE

biohaven®

42nd Annual J.P. Morgan Healthcare Conference

Vlad Coric, M.D.
Chairman and Chief Executive Officer

January 8, 2024

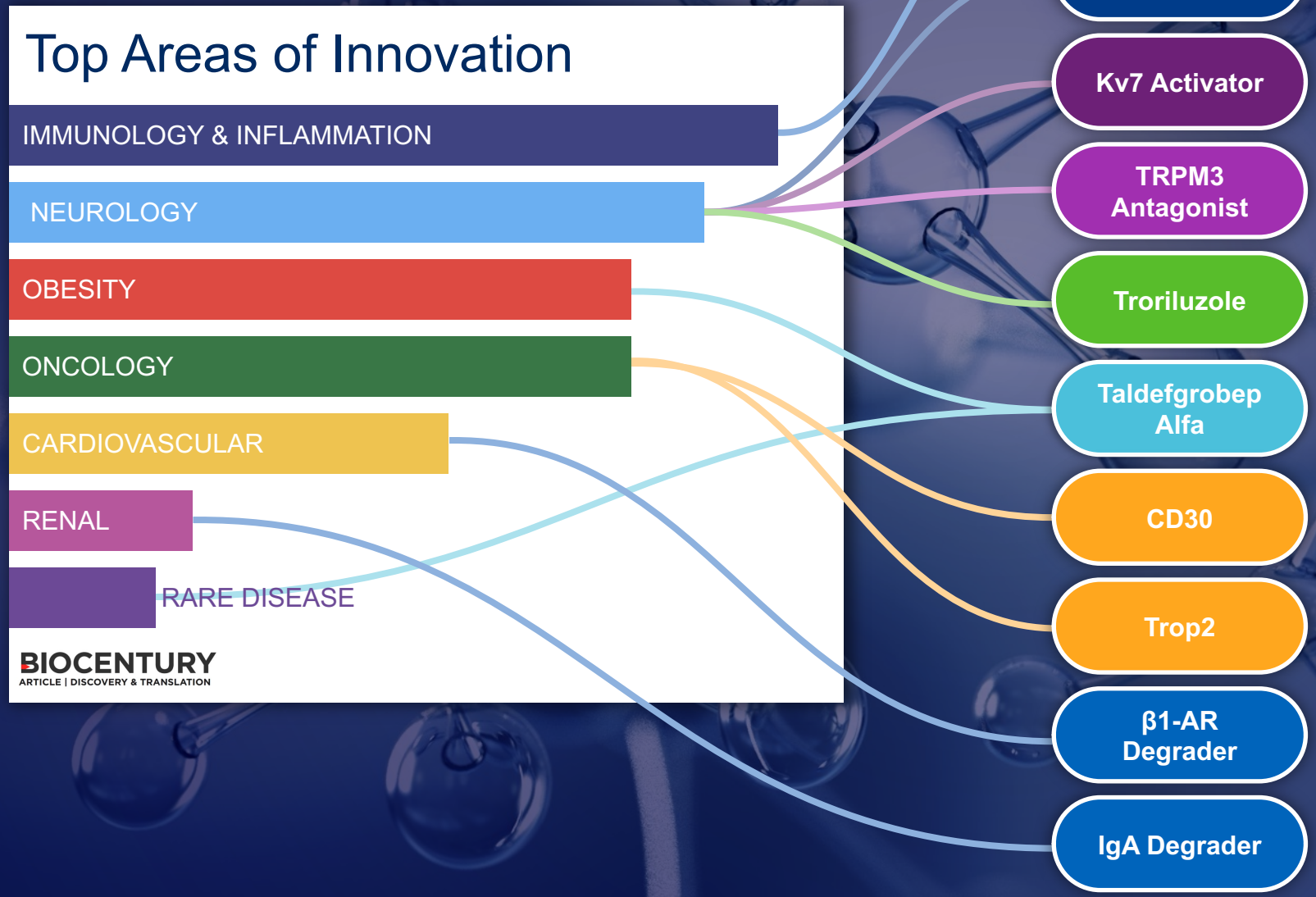
TIA, Living with OCD
AND HELPING RECRUIT IN
BIOHAVEN CLINICAL TRIALS

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, the timing of and the availability of data from those 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. 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 FDA; the timing and outcome of expected regulatory filings; complying with applicable U.S. regulatory requirements; the potential commercialization of Biohaven's product candidates; the potential for Biohaven's product candidates to be first in class and best in class therapies; the anticipated consummation of the Trop2 transaction, 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". The forward-looking statements are made as of the date of this presentation, and Biohaven does not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. 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.

biohaven


GROUNDBREAKING LEGACY OF SUCCESS IN MIGRAINE
Nurtec® ODT
(rimegepant)
Zavzpret™
(zavegepant)
Biohaven has reemerged for countless patients and is growing one of the most innovative portfolios in life sciences.
biohaven®
NEUROSCIENCE | IMMUNOLOGY | ONCOLOGY



IgG Degrader

TYK2/JAK1

Kv7 Activator

TRPM3 Antagonist

Troriluzole

Taldefgrobep Alfa

CD30

Trop2

β1-AR Degrader

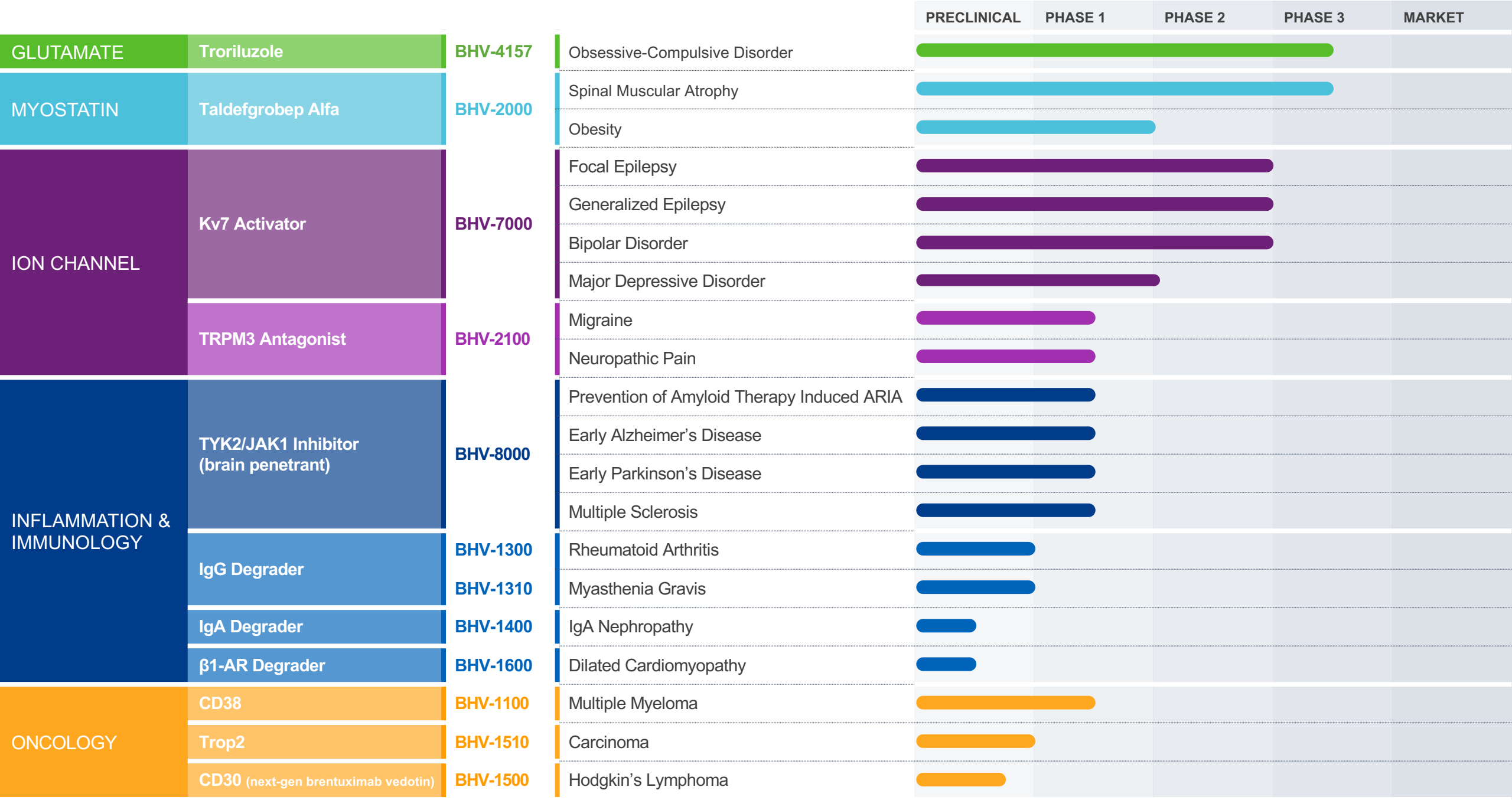
IgA Degrader

BIOHAVEN PORTFOLIO

Positioned for Future Value Creation for Patients and Investors

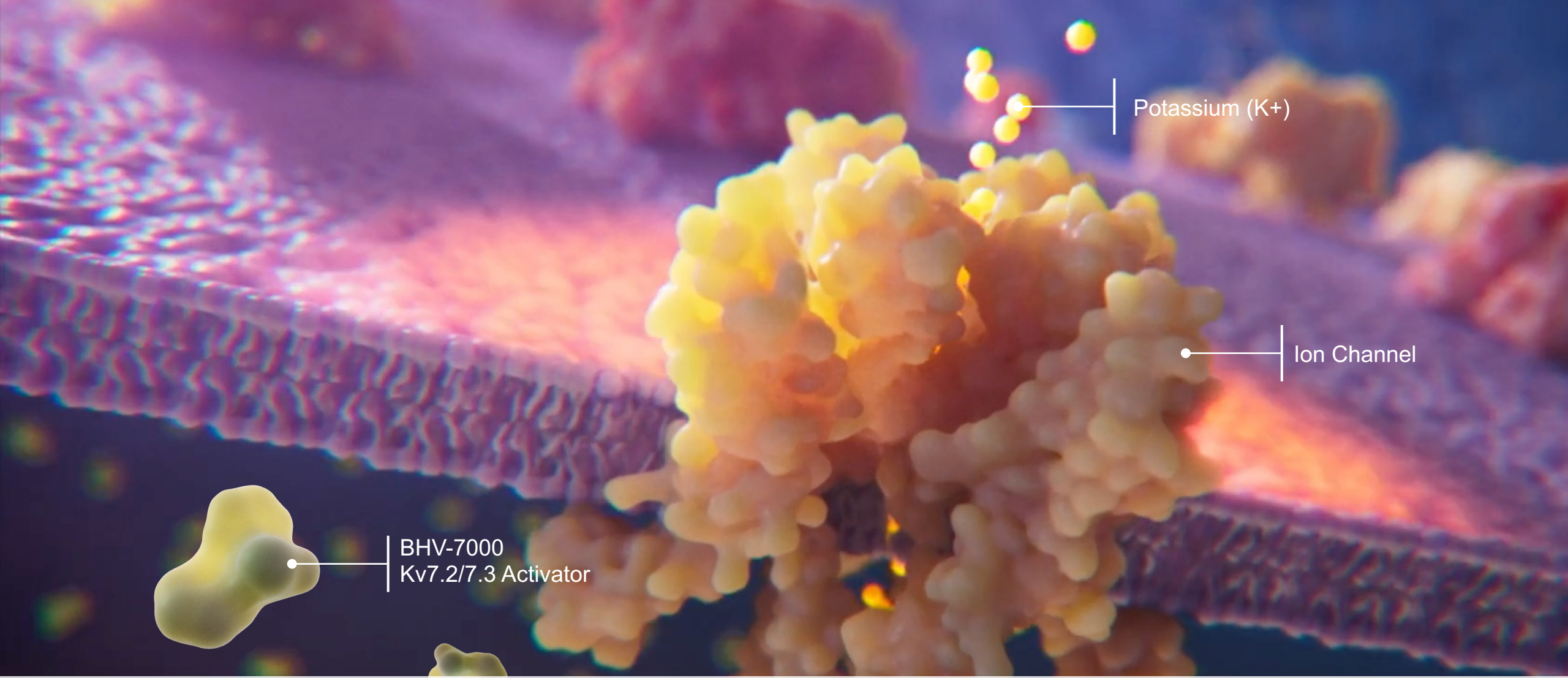
1. Adapted from BioCentury survey: https://www.biocentury.com/article/650883/move-over-oncology-i-i-will-write-the-next-big-stories-in-innovation#

biohaven



ARIA, Amyloid-related imaging abnormalities

biohaven



Ion Channels

biohaven®

BHV-7000
SELECTIVE
Kv7 ACTIVATOR

Kv7 is Breakthrough Target in Neurology and Neuropsychiatry
- Selective Kv7 activation avoids unwanted CNS side effects
- Clinically validated in epilepsy and major depressive disorder

BHV-7000 is Potentially Best-in-class Selective Kv7 Activator with Blockbuster Potential
- Rationally designed to eliminate $GABA_A$ receptor activation
- No dose-limiting CNS side effects in Phase 1 studies
- CNS target engagement confirmed in a dose proportional manner in Phase 1 EEG study

BHV-7000 Has Compelling Preclinical Efficacy Profile
- Highly effective in epilepsy model
- Ketamine-like efficacy in neuropsychiatry model
- Wide therapeutic index to explore full dose range

BREAKING NEWS

Phase 2/3 Epilepsy Update: >110 global clinical sites selected, FPFV 1Q24
Phase 2 MDD and Bipolar Studies expected to initiate FPFV 1Q24

biohaven

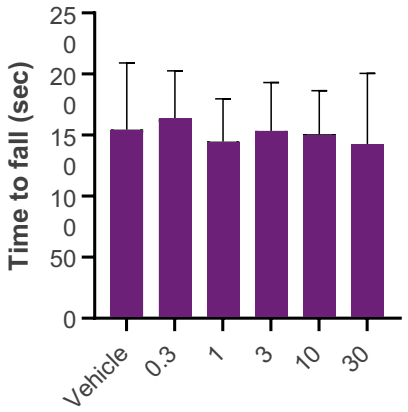
ION CHANNELS

BHV-7000: Epilepsy Update

biohaven®

Dialing Out $GABA_A$ Receptor Activation Now Clinically Proven to Reduce CNS Side Effects

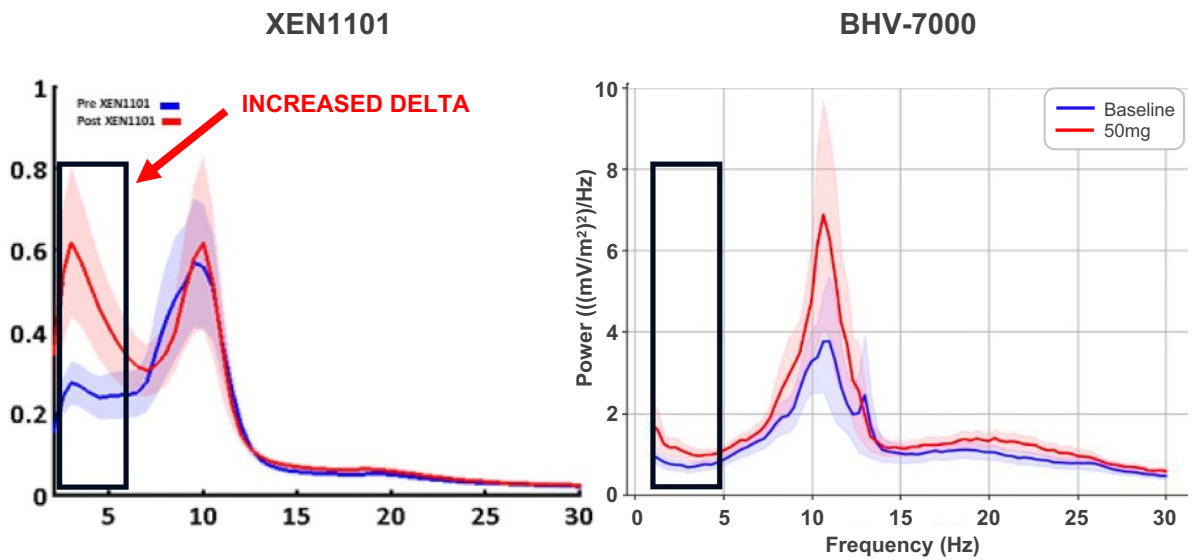
PRECLINICAL
No effects on motor performance on rotarod



PHASE 1
Not associated with CNS AEs typical of other ASMs in healthy volunteers

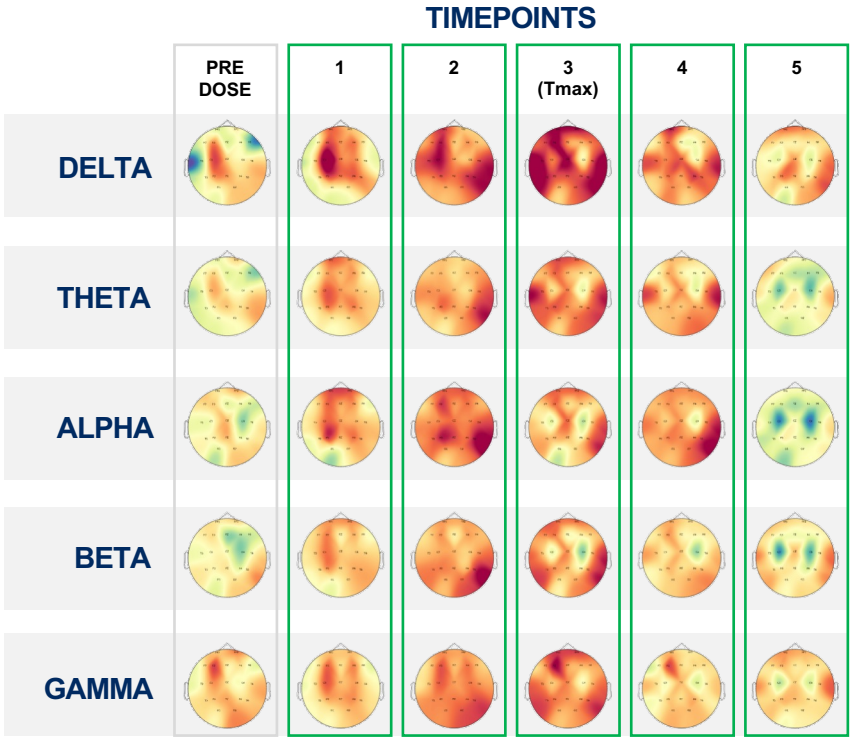
Pooled CNS AEs	BHV-7000 MAD Pooled N=29	XEN1101 MAD Pooled N=18
Somnolence	0%	39%
Headache	21%	39%
Balance disorder/ dizziness	10%	34%
Memory impairment	0%	28%
Sensory disturbance	0%	11%
Speech disorder	0%	33%

EEG
Minimal impact on spectral power in slower frequencies (i.e., delta) consistent with lack of somnolence in Phase 1

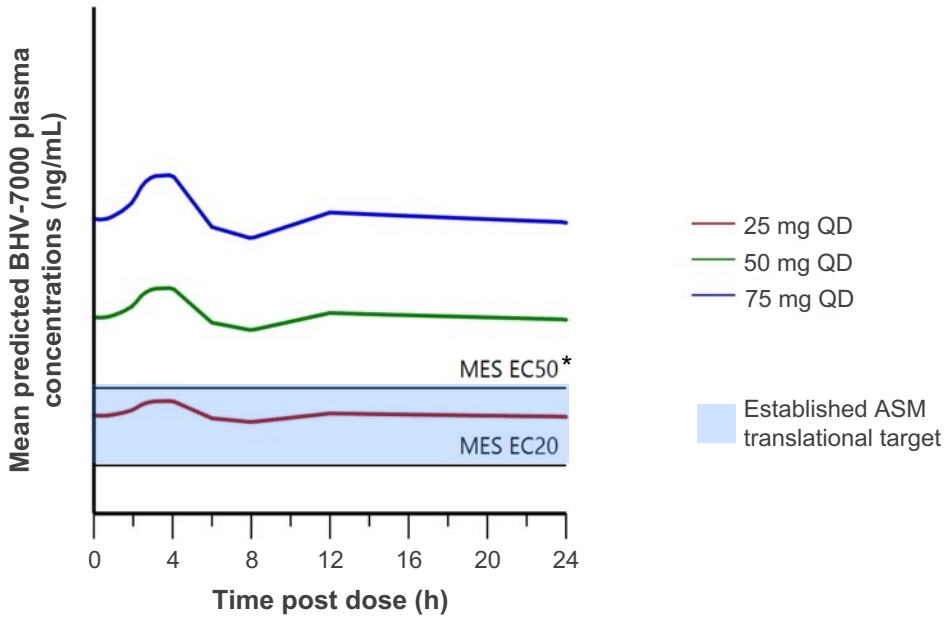


CNS Target Engagement Confirmed at Concentrations Well-Tolerated and Exceeding Predicted Therapeutic Target Levels

Demonstrated CNS target engagement in EEG spectral power across all frequency bands, in a dose proportional manner



Formulated an extended release once-a-day tablet predicted to achieve target concentrations



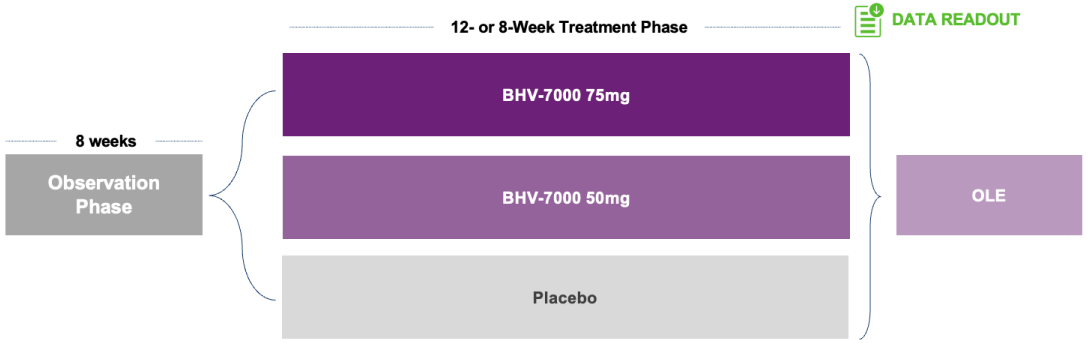
*EC50 based on preclinical maximal electroshock seizure (MES) models

KEY POINT

Dose/time dependent EEG changes confirm target engagement

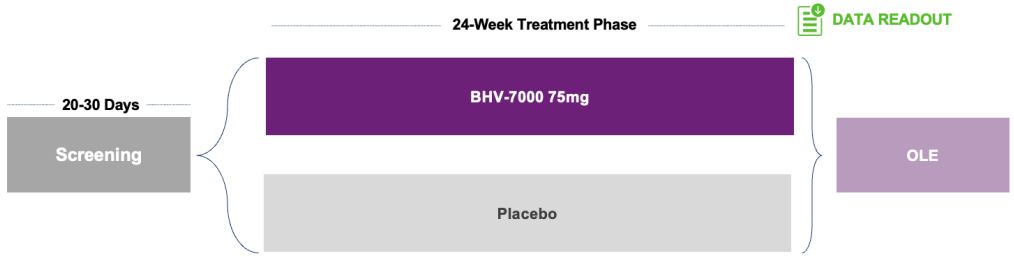
Epilepsy Phase 3 Studies in Focal and Idiopathic Generalized Epilepsy

Focal Design



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Subjects 18–75 years old with intractable focal epilepsy
SAMPLE SIZE	390 subjects (randomized 1:1:1)
TREATMENT	BHV-7000 (75/50 mg) and (50/25 mg) vs. placebo
TREATMENT DURATION	12- or 8-week treatment phase
ENDPOINTS	Change in seizure frequency, 50% seizure reduction, seizure freedom, safety

Generalized Design



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:), study ends with the 127th seizure event
TREATMENT	BHV-7000 75 mg vs. placebo
TREATMENT DURATION	Up to 24-week double-blind phase, subject will transition to open label extension
ENDPOINTS	Time to event (2nd day with generalize tonic-clonic seizure)

KEY POINT

Focal Epilepsy Study — 110 global clinical sites selected, FPFV 1Q24

ION CHANNELS

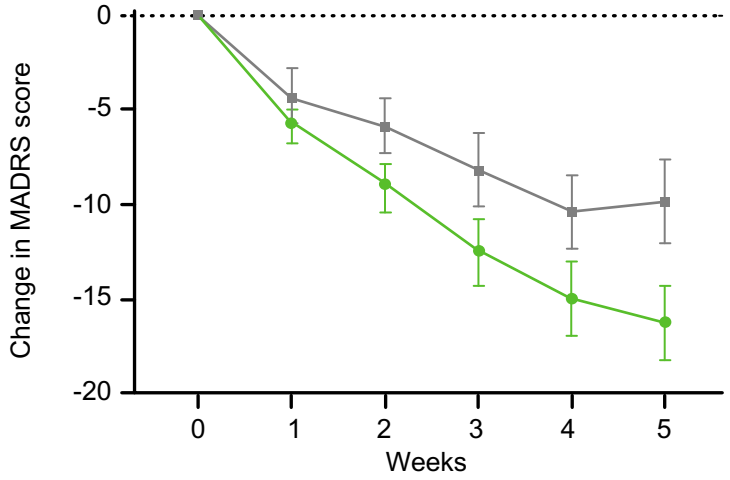
BHV-7000: Neuropsychiatry Updates

biohaven®

Kv7 Activation Validated in the Clinic for Major Depressive Disorder

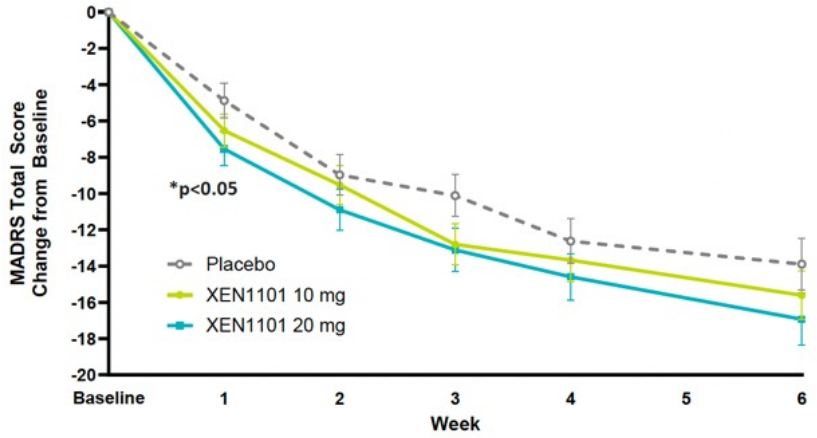
Randomized clinical trials in MDD with two nonselective Kv7 activators have demonstrated potential for rapid onset of clinically meaningful benefit in symptoms of depression and anhedonia

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**

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



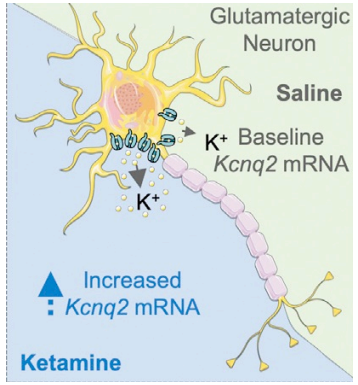
- Benefit on MADRS (p=0.135) vs. placebo in 20 mg group
- Benefit on MADRS at week 1 (p<0.05) vs. placebo in 20 mg group
- **Efficacy not optimized likely due to dose limiting tolerability concerns**

KEY POINT

BHV-7000 has ideal profile for potential in MDD due to low rates of CNS AEs vs. nonselective Kv7 activators

BHV-7000:
Potential for Ketamine and Psilocybin-Like Anti-Depressant Effect

Kv7 (KCNQ2) Mediates Therapeutic Benefits of Ketamine[1]

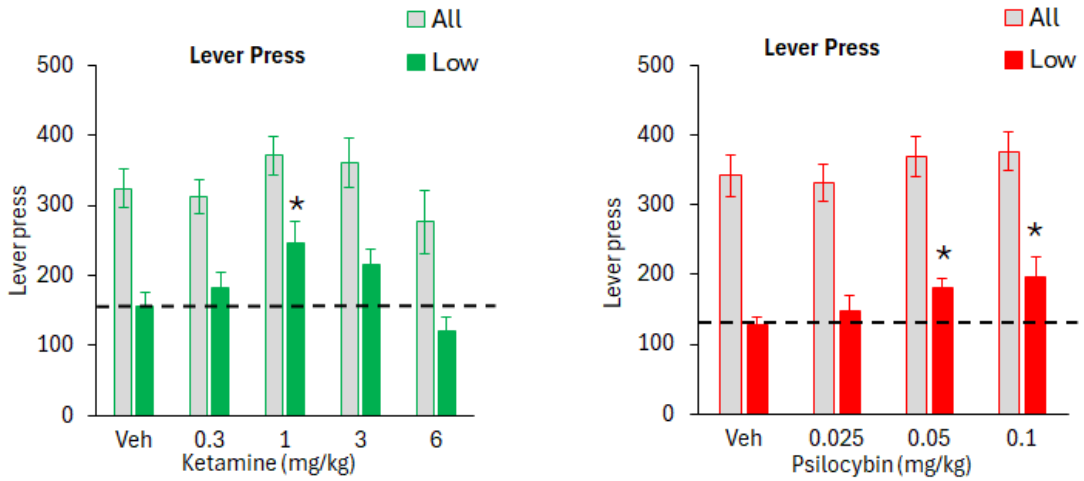


- Chronically stressed mice show downregulation of Kv7 gene expression
- Kv7 mediated ketamine anti-depressant effects abolished when Kv7 is inhibited or Kv7 expression reduced

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

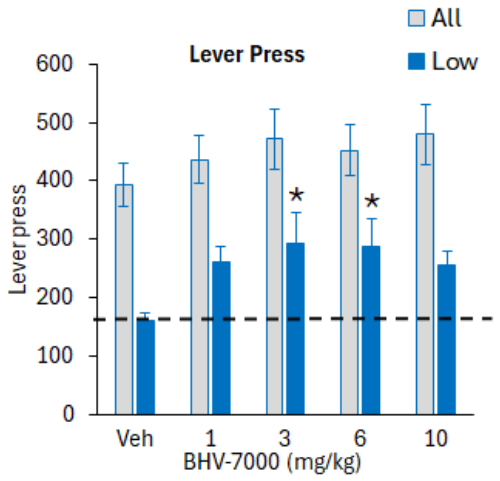
Ketamine, psilocybin, and BHV-7000 all enhance motivation in poor performing rats in operant model

Ketamine and Psilocybin



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

BHV-7000

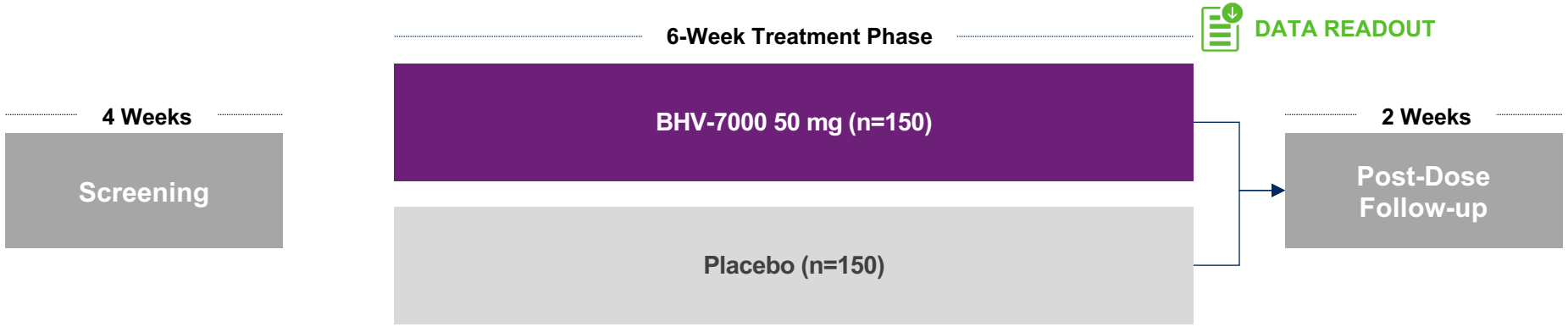


Biohaven data on file.

KEY POINT

BHV-7000 shows similar or greater magnitude of anti-depressant behavioral effects to ketamine and psilocybin

BHV-7000: Phase 2 Study in Major Depressive Disorder



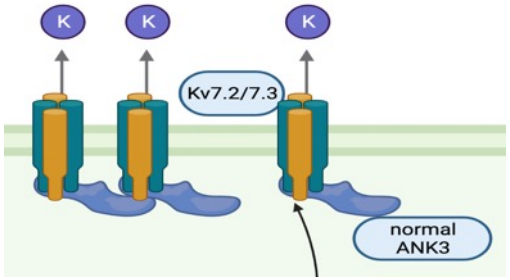
DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Subjects with Major Depressive Disorder (MDD) with at least one prior depressive episode who are currently experiencing a depressive episode with anhedonia (HAM-D ≥ 20, SHAPS ≥ 20)
SAMPLE SIZE	300 subjects (randomized 1:1)
TREATMENT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

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

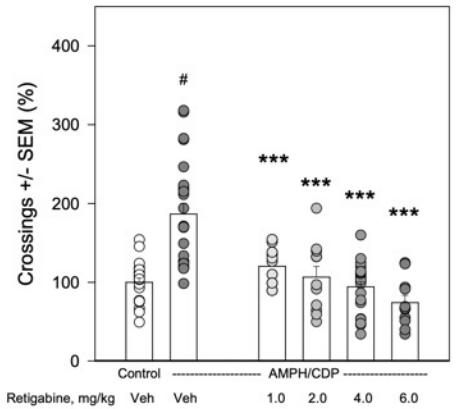
Compelling Evidence for Targeting Kv7 in Bipolar Disorder

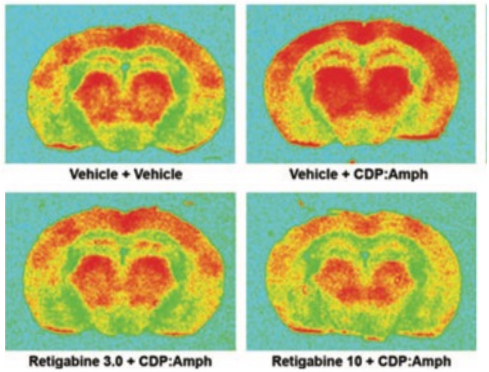
- **HUMAN GENETICS** ANK3 gene link to Kv7 and disease risk[1, 2, 3, 4]
- **MOLECULAR PROFILING OF BIPOLAR DISORDER PATIENT TISSUES** demonstrating epigenetic, transcriptomic and proteomic Kv7 deregulation
- **PRECLINICAL MODELS** Kv7 activation corrects disease-related phenotypes and behaviors
- **ANTISEIZURE MEDICINES ARE CORNERSTONE BIPOLAR TREATMENTS**

Human Genetics Links Kv7 to Risk of Bipolar Disorder



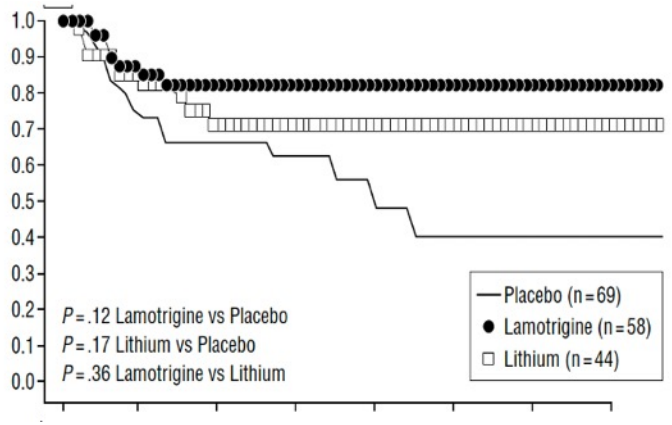
Kv7 Activation With Ezogabine Normalizes Hyperactive Locomotion and Brain Hypermetabolism in Mania Model





Feng et al., 2019.

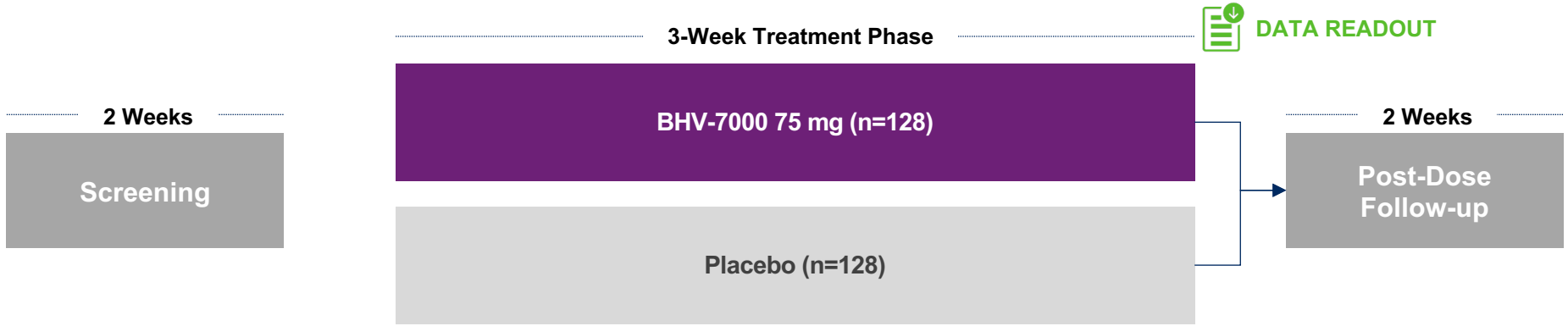
ASMs Such as Lamotrigine Are Cornerstone Bipolar Treatments



Bowden et al. 2003;60:392-400

1. Pan et al. Journal of Neuroscience, 2006. 2. Ferreira et al. Nat. Genet. 40, 1056–1058. 3. Psychiatric GWAS Consortium Bipolar Disorder Working Group. (2011). 4. Judy et al. Front Genet (2013).

BHV-7000: Phase 2/3 Study to Evaluate Safety and Efficacy for the Acute Treatment of Mania in Bipolar Disorder I



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, safety and tolerability

YMRS: Young Mania Rating Scale; **CGI-S**: Clinical Global Impression, Severity

biohaven

BHV-2100
TRPM3 ANTAGONIST

BREAKING NEWS

- **Biohaven is back in migraine with novel agent, BHV-2100**
- **Phase 1 SAD study ongoing**
- **Phase 2 in migraine and neuropathic pain planned 2H 2024**

Despite the CGRP Revolution, Significant Unmet Need Remains for 40M Migraine Sufferers in the US and 1B Worldwide

- 30–40% of patients do not respond to treatments that block CGRP or its receptor
- Migraine is 2nd leading cause of disability worldwide and 1st among young women[1]

First-in-Class TRPM3 Antagonist — Novel Mechanism for the Treatment of Migraine and Pain

- BHV-2100 is the only TRPM3 antagonist in clinical development
- 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 Preliminary Data Supports Evaluation in Acute Migraine

- SAD study: 2 cohorts completed dosing (25 and 75 mg)
- MAD study: initiating
- Rapidly absorbed (Tmax 1–2 hours)
- Projected therapeutic concentrations achieved (IC90 exceeded within 1 hour)
- Well tolerated with only mild adverse events (flatulence, constipation, upper respiratory tract infection, dysesthesia) and no evidence of temperature dysregulation to date

1. Steiner. J Headache Pain 2020

biohaven

Myostatin

biohaven®

TALDEFGROBEP ALFA (Anti-myostatin)

Differentiated Profile Balancing Both Efficacy and Safety

- Taldefgrobep alfa inactivates free myostatin (GDF-8), an inhibitor of muscle growth
- Pharmacology uniquely sustained by taldefgrobep alfa/myostatin complex
- Taldefgrobep alfa/myostatin complex inhibits skeletal muscle ActRIIB receptor signaling, and thus, enhances muscle mass

Potential Paradigm Shift in the Treatment of Obesity

- Taldefgrobep alfa treatment of >350 subjects with favorable safety and tolerability observed in children, adolescents, and adults
- Reductions in fat mass while increasing lean mass in healthy adults
- Maintains muscle gains after cessation of administration
- Weekly SC administration with the potential for extended dosing intervals

Phase 3 in SMA

- Global Phase 3 study in broad-population of SMA patients now fully enrolled
- Weekly SC taldefgrobep alfa on top of stand of care continues to be well tolerated
- Orphan designation granted in the US and EU, along with Fast Track designation by FDA

BREAKING NEWS

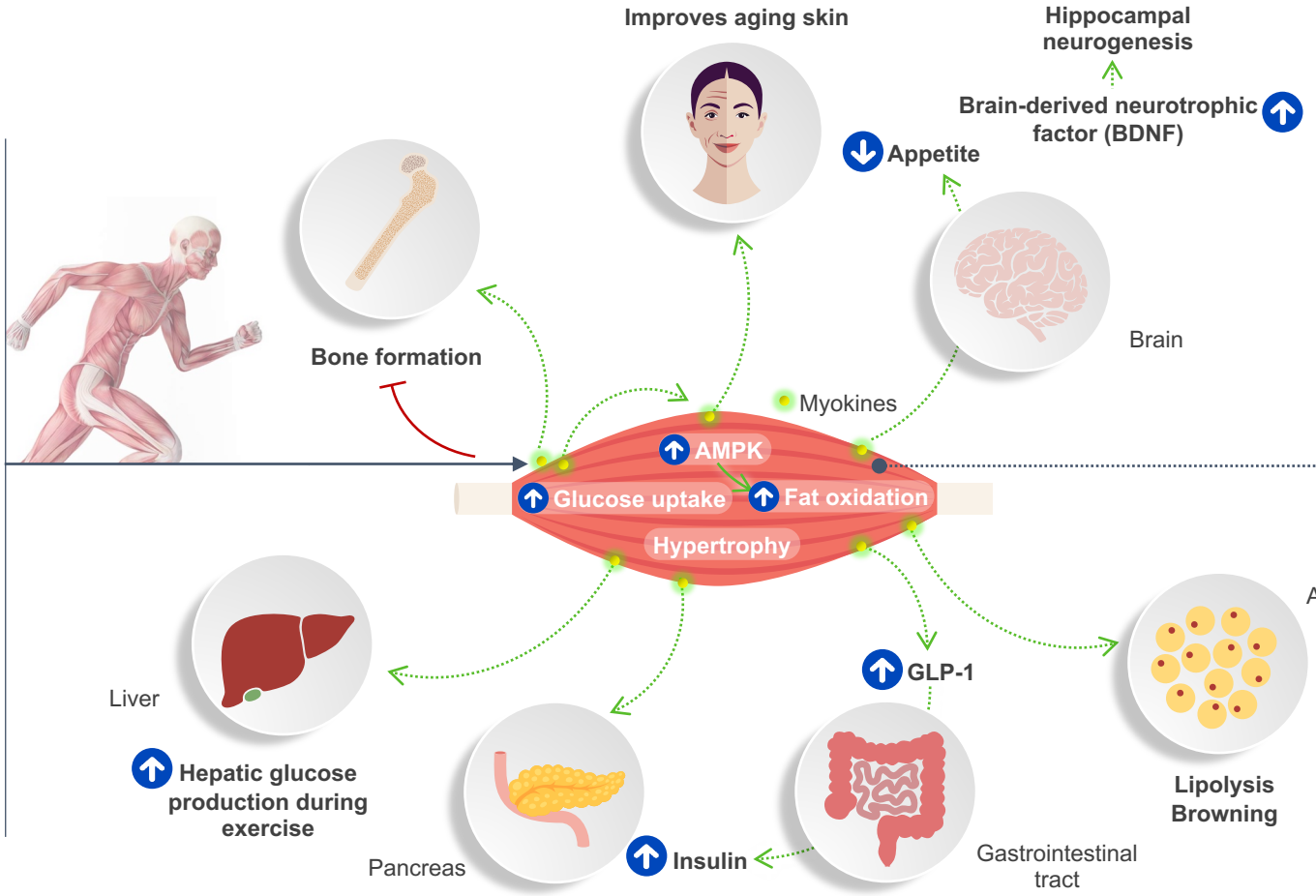
- **Obesity Phase 2 to initiate in 2Q 2024**
- **Topline Phase 3 Results in SMA in 2H 2024**

biohaven

Muscle Is an Important Endocrine Organ in Metabolic Activity

MYOKINES
play an important role in regulating fat metabolism, inflammation, appetite, glucose control, bone density, and basal metabolic rate

LEAN MUSCLE MASS -DERIVED MYOKINES
signal to numerous organ systems impacting overall health and wellness, beyond physical performance[1]



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

KEY POINT

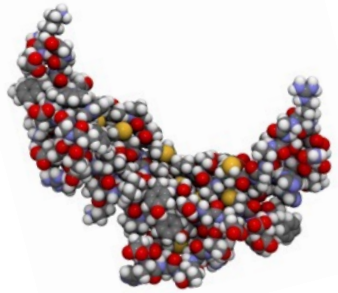
Taldefgrobep alfa increases lean muscle mass leading to improvements in metabolism and weight management

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.

Inhibiting Myostatin Increases Muscle Mass and Metabolic Health

- Increased lean mass
- Improved insulin sensitivity
- Increased basal metabolic rate
- Improved bone mineral density

Myostatin as a Pharmacologic Target



- Reduction in total body fat mass
- Reduction in visceral fat
- Reduction in intramuscular fat
- Reduction in intrahepatic fat

biohaven

Taldefgrobep Alfa:
A Differentiated Therapeutic Approach Balances Efficacy and Safety

Apitegromab
Scholar Rock

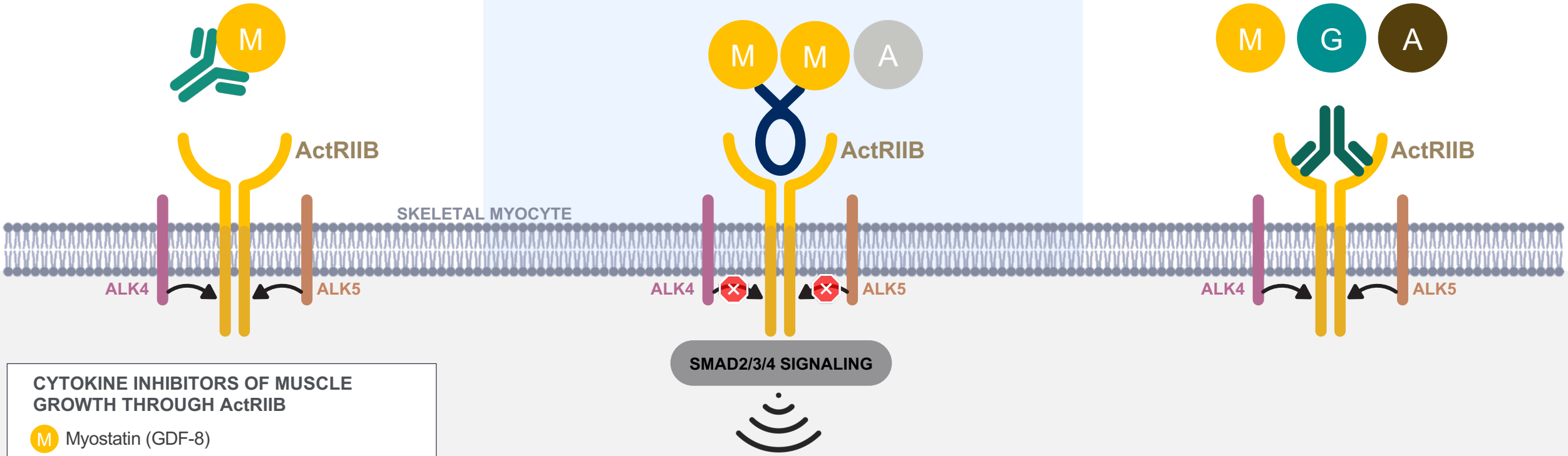
TARGETS pro- and latent myostatin

Taldefgrobep alfa
Biohaven

BLOCKS active myostatin and
INHIBITS ActRIIB signaling

Bimagrumab
Versanis-Lilly

BLOCKS ActRIIB signaling
with very high affinity



CYTOKINE INHIBITORS OF MUSCLE GROWTH THROUGH ActRIIB

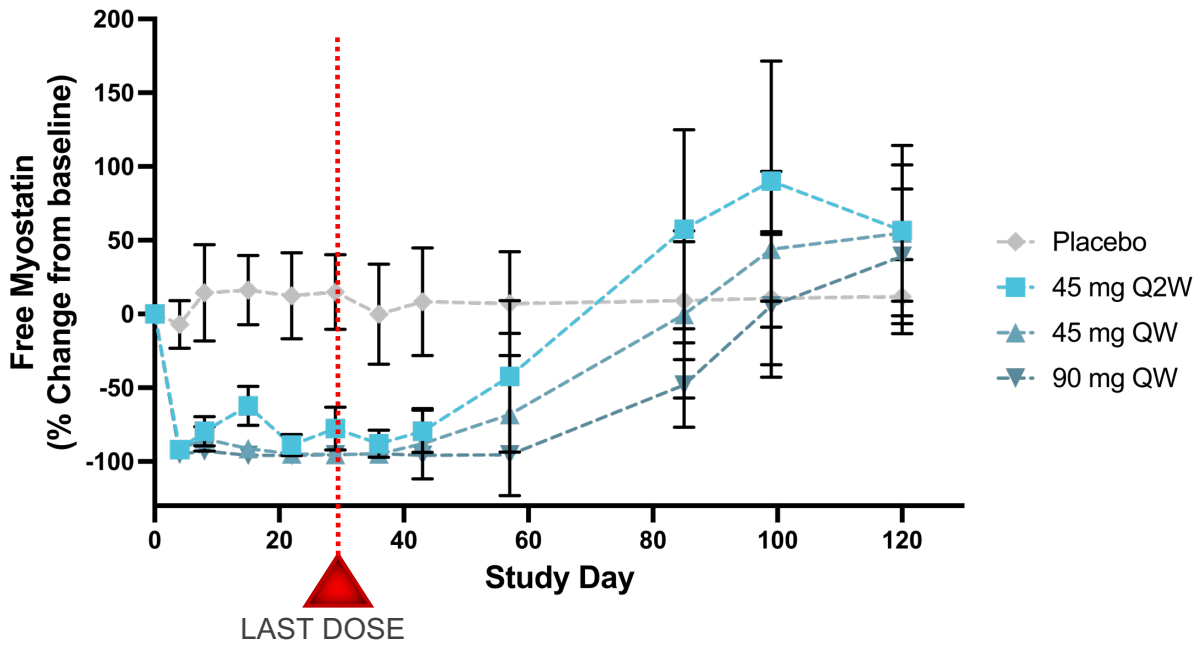
- M Myostatin (GDF-8)
- G Growth Differentiation Factor 11 (GDF-11)
- A Activin

Signal transduction of muscle growth inhibition through ALK4/5 and ActRIIB

SC Taldefgrobep Effectively Suppresses Free Myostatin in Healthy Adults

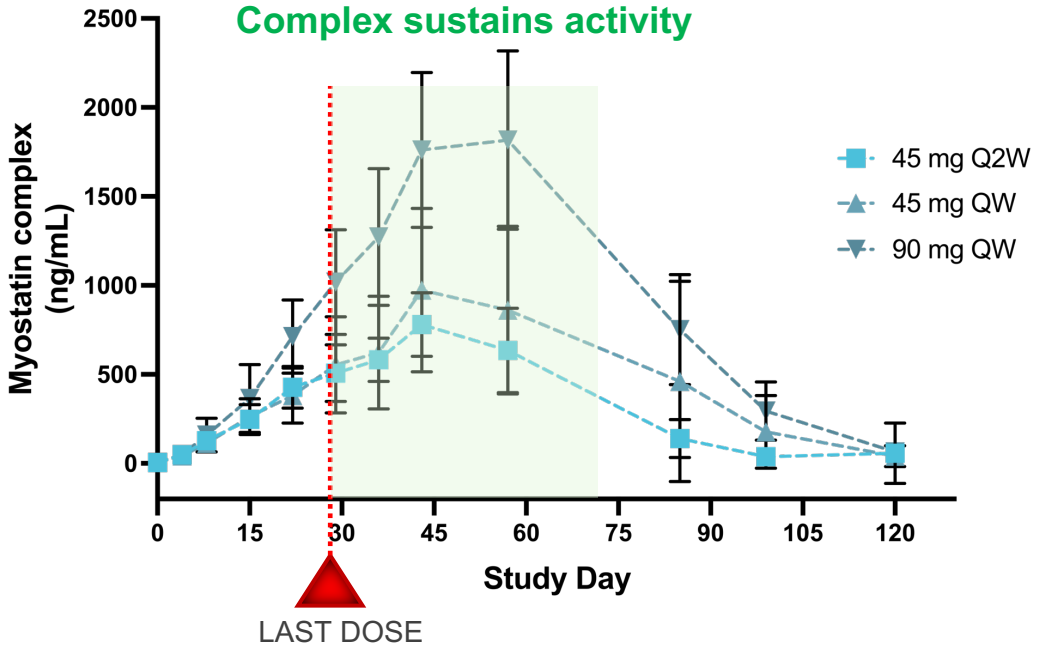
Taldefgrobep alfa activity sustained by circulating taldefgrobep-myostatin complex

Free Myostatin Levels



Biohaven Phase 1 data on file

Myostatin Complex Levels



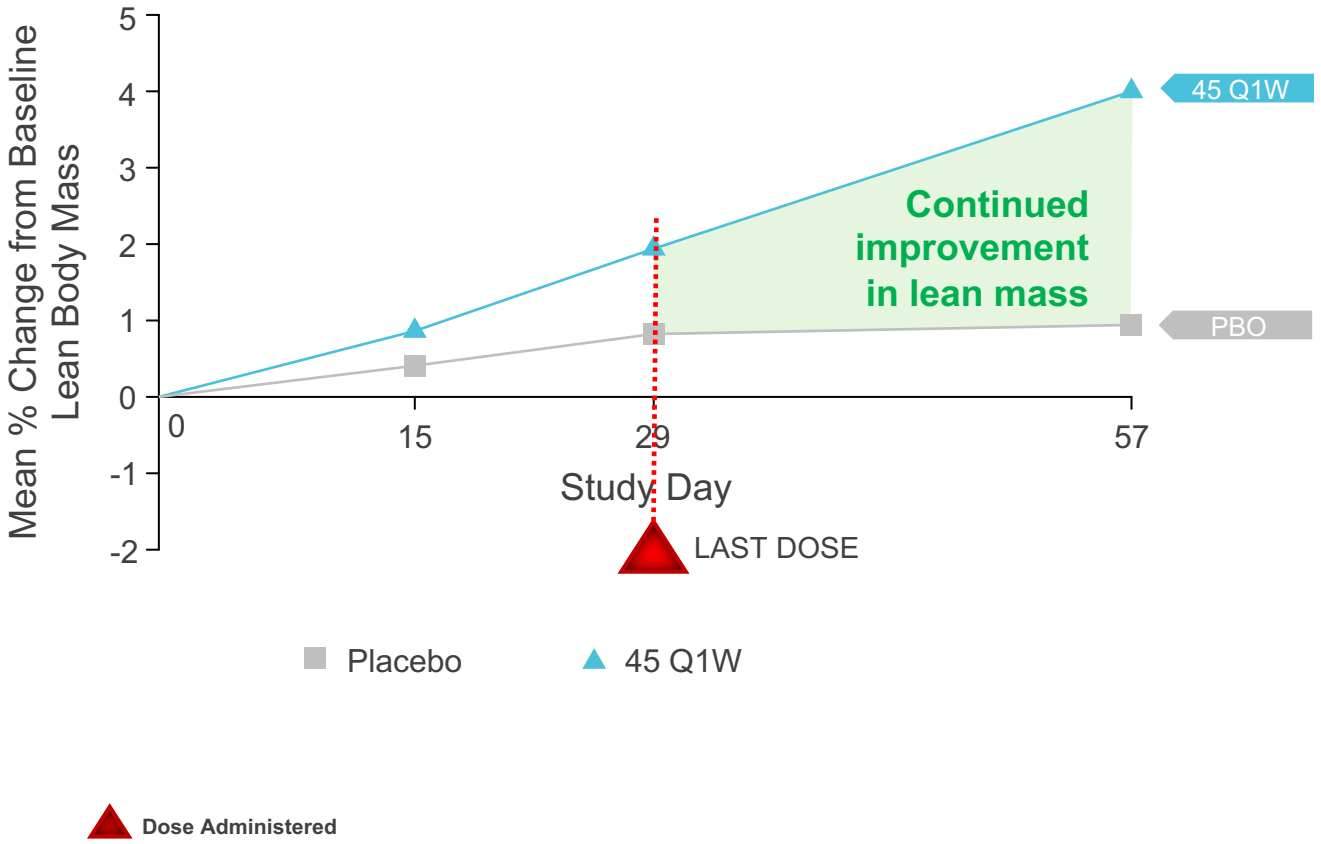
Biohaven Phase 1 data on file

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**
- **Continued improvement in muscle mass after cessation of dosing**

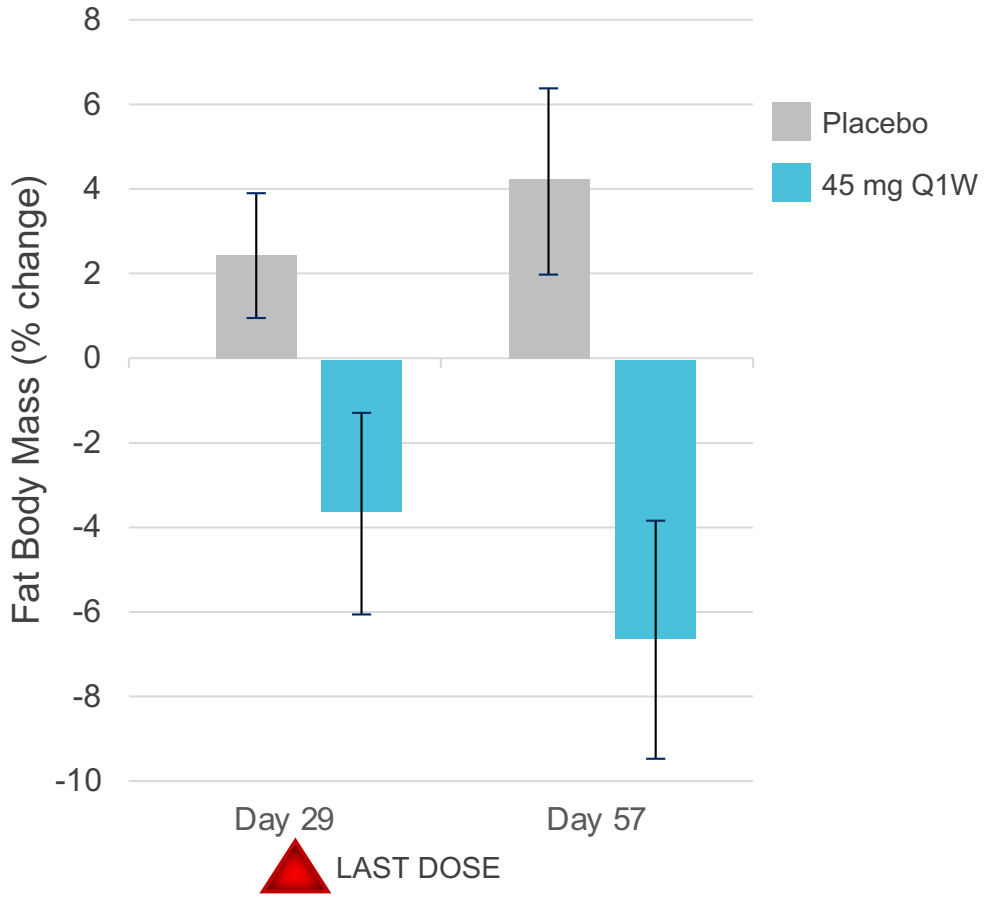
Taldefgrobep Alfa: Demonstrates Fat Reduction While Improving Lean Mass in Healthy Adults

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



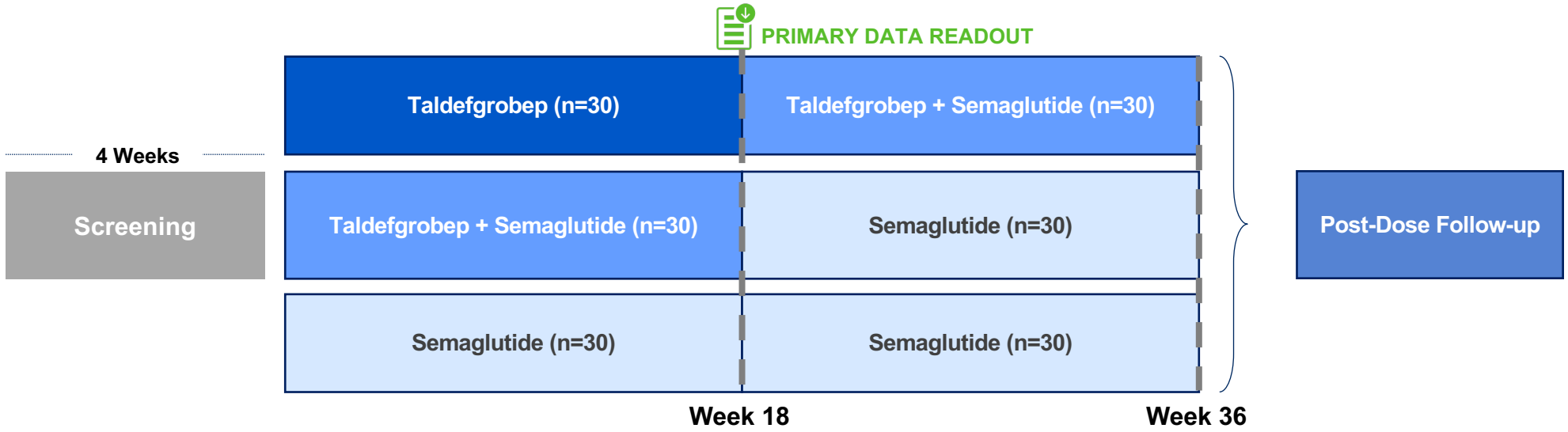
Biohaven Phase 1 data on file

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



Biohaven Phase 1 data on file

Taldefgrobep Alfa: Phase 2 Study to Evaluate Taldefgrobep +/- Semaglutide in the Treatment of Overweight and Obesity



Innovative study design allows for early insight into a number of key clinical questions

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

KEY UPDATE

Phase 2 Proof of Concept Study Initiation in 1H24

TRORILUZOLE
OCD

BREAKING NEWS

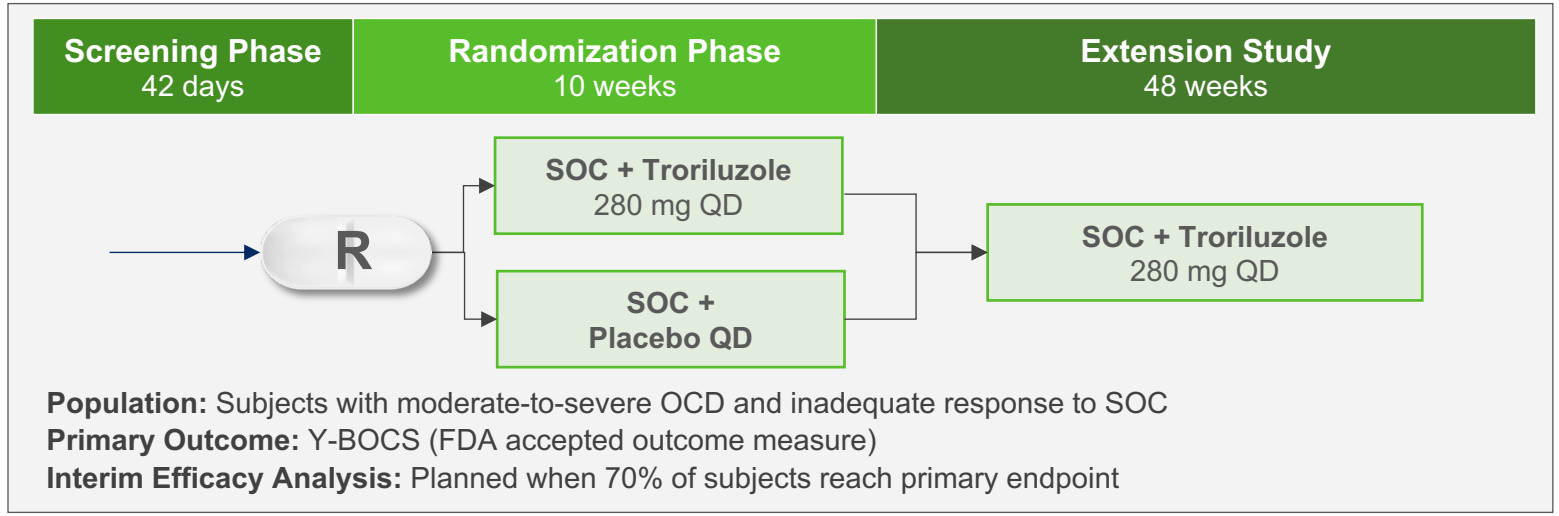
3M+ OCD Patients in US With High Unmet Medical Need

- 40–60% do not respond to first line treatment
- 10–40% are treatment refractory potentially requiring ablative neurosurgery or deep brain stimulation

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

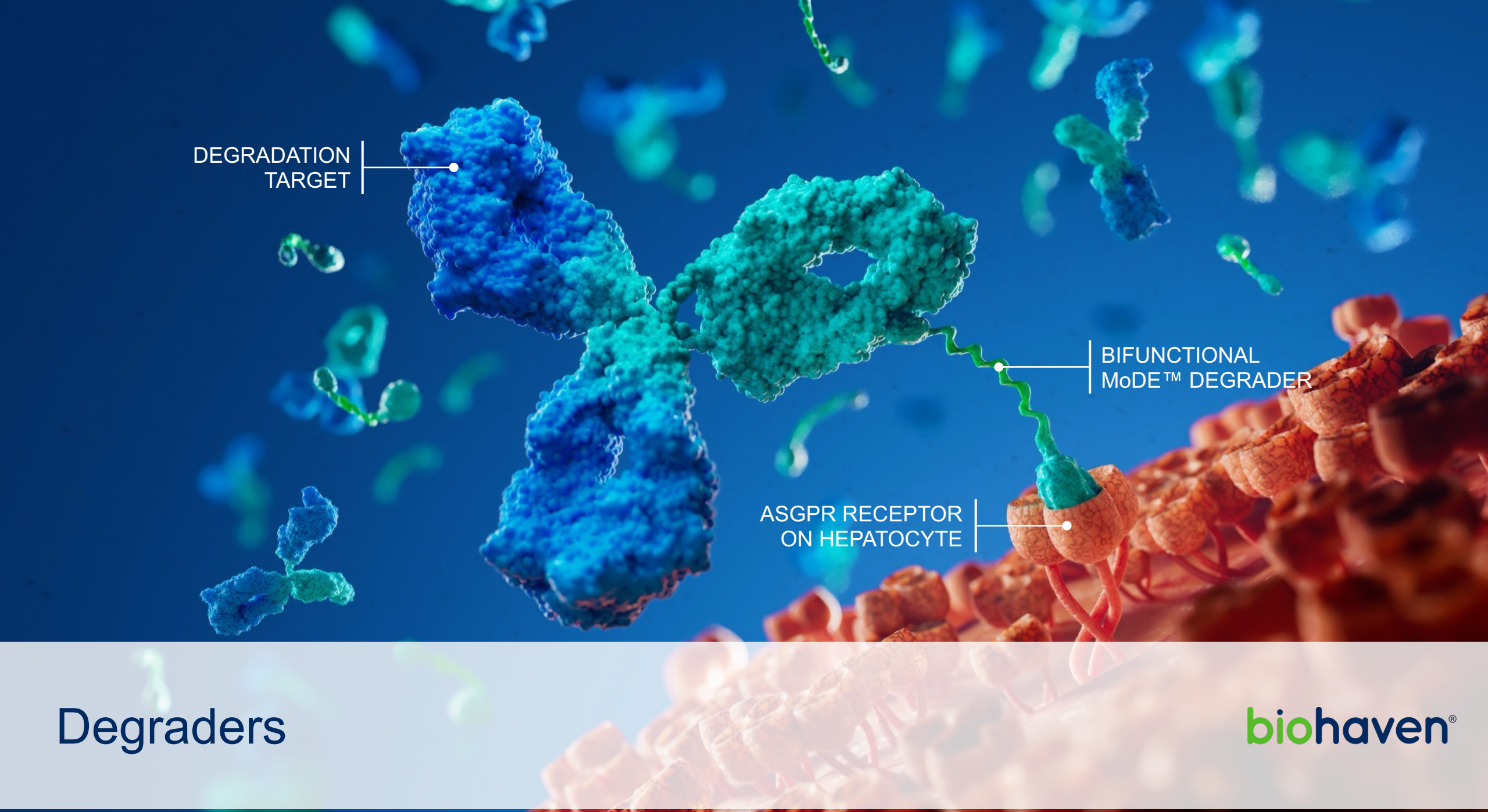


Population: Subjects with moderate-to-severe OCD and inadequate response to SOC
Primary Outcome: Y-BOCS (FDA accepted outcome measure)
Interim Efficacy Analysis: Planned when 70% of subjects reach primary endpoint

Database Lock for Interim Efficacy Analysis in 1Q 2024

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

biohaven



Degraders

biohaven®

PAN IgG DEGRADERS

Potent Extracellular Pan-IgG Lowering Agents

- Degrading and depleting pathogenic IgG presents multiple disease opportunities
- BHV-1310 has further optimized properties over first-generation BHV-1300

Innovative Mechanism of Action

- Protein degradation rather than inhibition
- Low projected human dose range
- Small molecule allows for small-volume subcutaneous dosing
- Next-gen technology allows for selective targeting of a variety of proteins

Faster and Deeper Depletion

- NHP studies showed 80% IgG depletion with a single dose of BHV-1300; increasing to ~90% after multiple doses
- Safe in doses up to 500 mg/kg
- More rapid IgG reduction vs. competitors
- Allows for co-administration with biologics

Potential in Multiple Diseases

- Common diseases — RA, lupus erythematosus, lupus nephritis
- Rare diseases — Generalized myasthenia gravis, transplant, oncology, etc.

BREAKING NEWS

- **BHV-1300: First-in-human Phase 1 start and data expected 1Q 2024**
- **BHV-1310: ~90% IgG depletion with a single dose**
- **New NHP data showing that Biohaven's IgG Degrader technology allows for co-administration with biologics (Humira® — PK unaltered)**

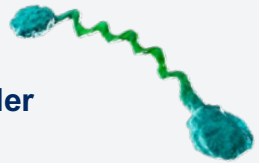
biohaven

A First-in-Class Mechanism: Hepatic ASGPR Receptor Harnessed for Efficient and Safe Removal of Circulating Pathogenic Targets

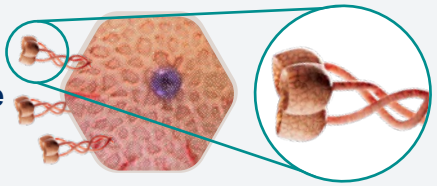
Legend

Degradation Target

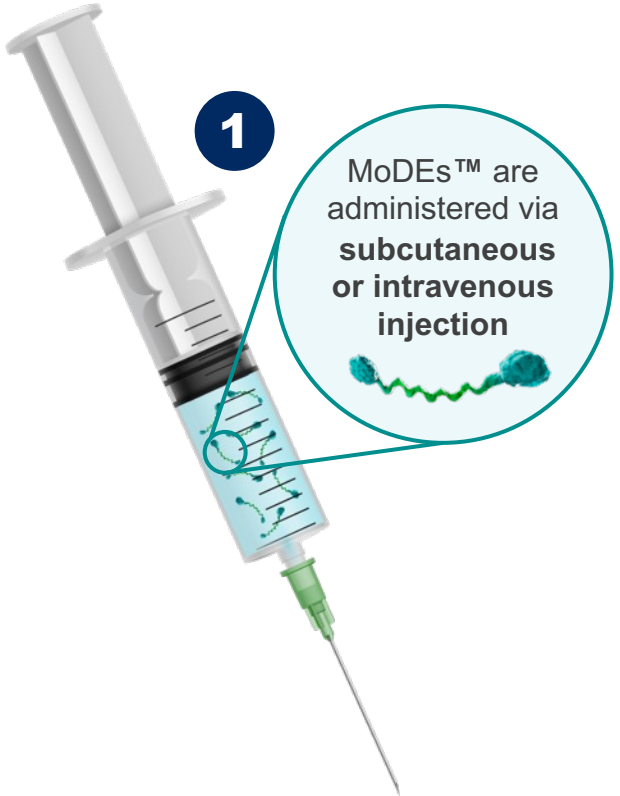
Bifunctional MoDE™ Degrader



Hepatocyte



Asialoglycoprotein Receptor (ASGPR)*

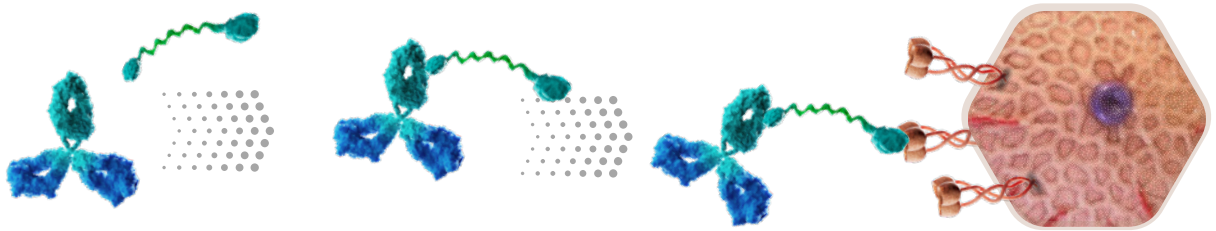


1

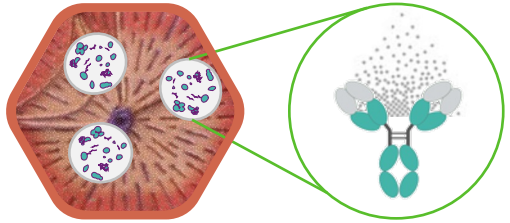
MoDEs™ are administered via **subcutaneous or intravenous injection**

2

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

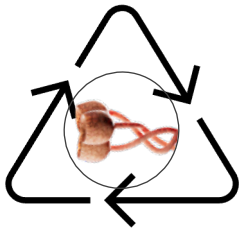


3



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

4



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

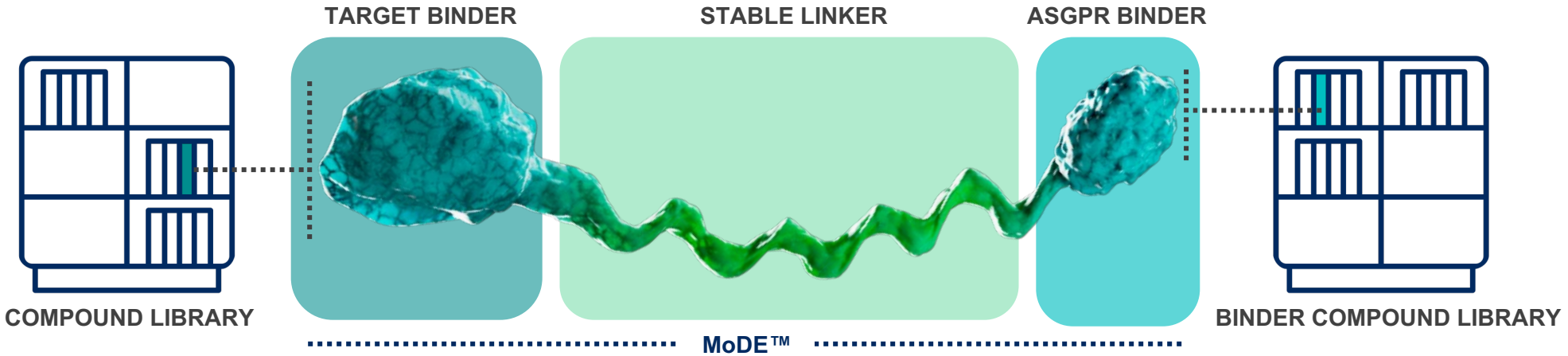
*Stylistic representation

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

biohaven

A Transformational 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
- Allows for selective targeting of proteins to avoid broad immunosuppression
- Ability to adjunctively dose Fc biologics
- Accelerated new drug candidate timelines (12–18 months)

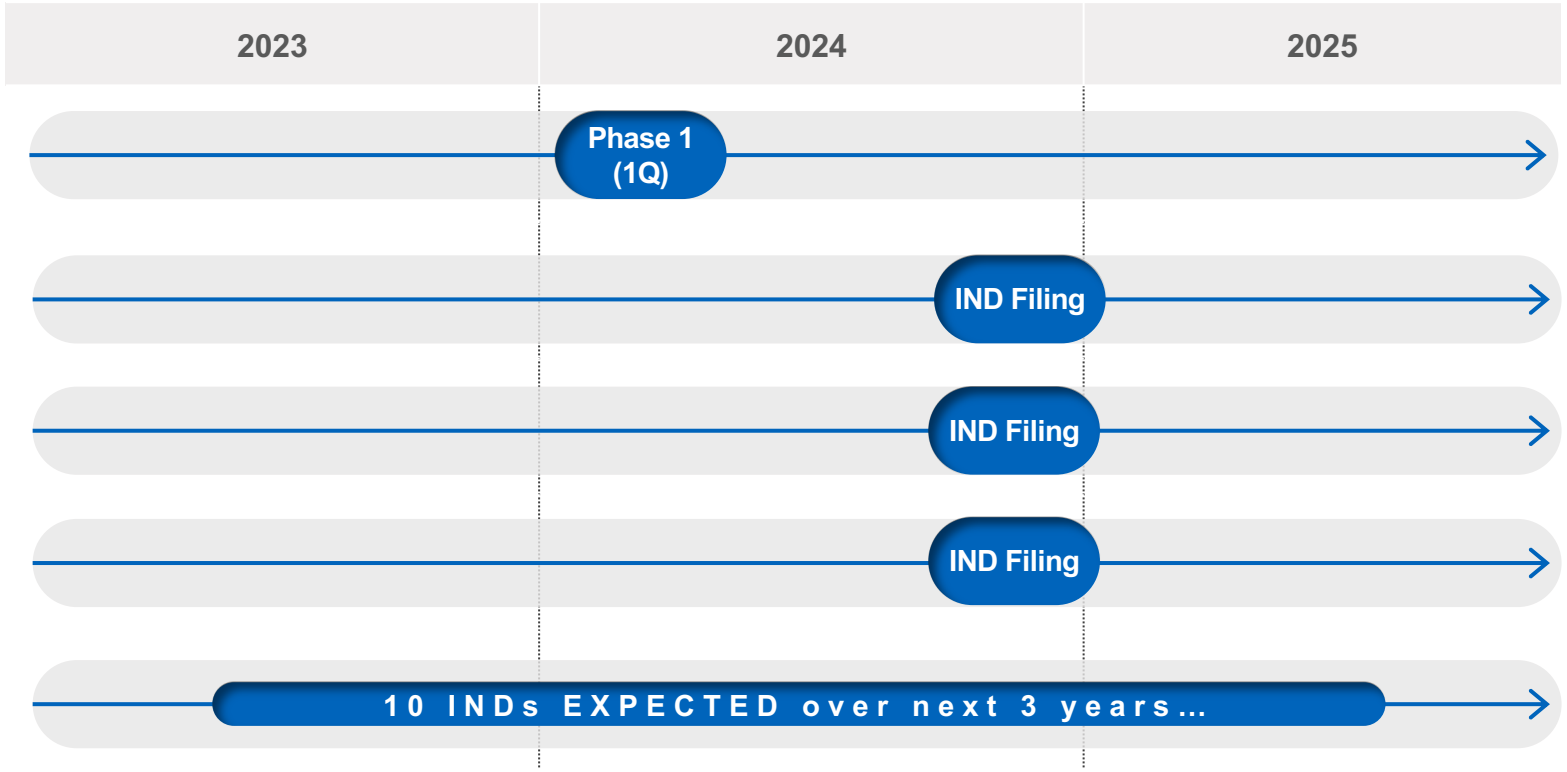
KEY POINT

Platform allows for new compound generation in only 12–18 months!

MoDE™ Degraders: Multiple Asset Opportunities and Potential Timelines

IgG, IgA and β1-AR antibodies are the first targets for Biohaven's powerful degradation platform

KEY INFLECTION POINTS



Realization of value inflection points will be project specific and aligned with cohesive portfolio strategy, Late timelines are considered approximate
AutoAb, autoantibody; **Ig**, immunoglobulin; **IND**, Investigational New Drug; **MoDE™**, molecular degrader of extracellular proteins; **RA**, rheumatoid arthritis

biohaven

DEGRADERS

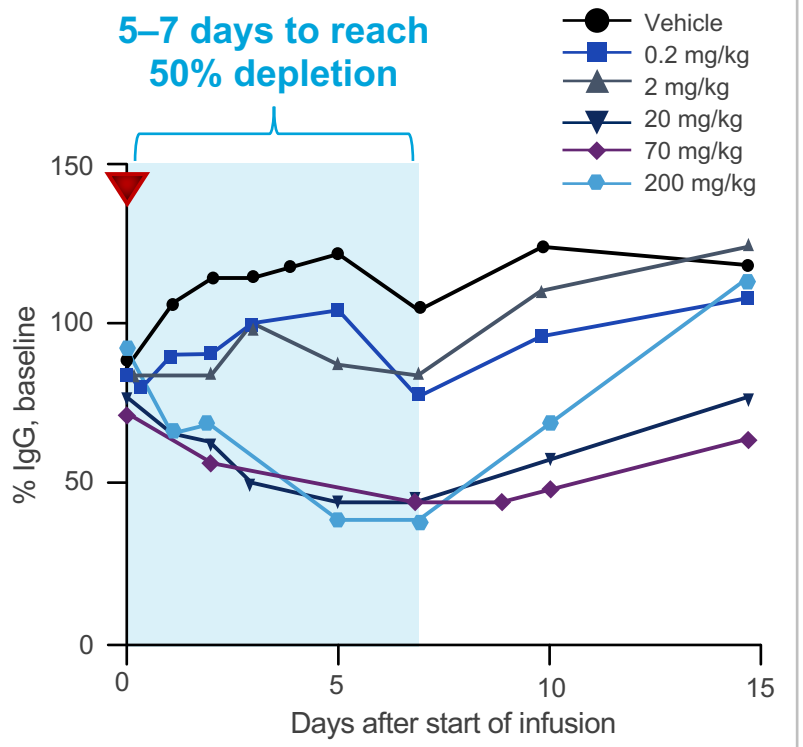
BHV-1300

biohaven®

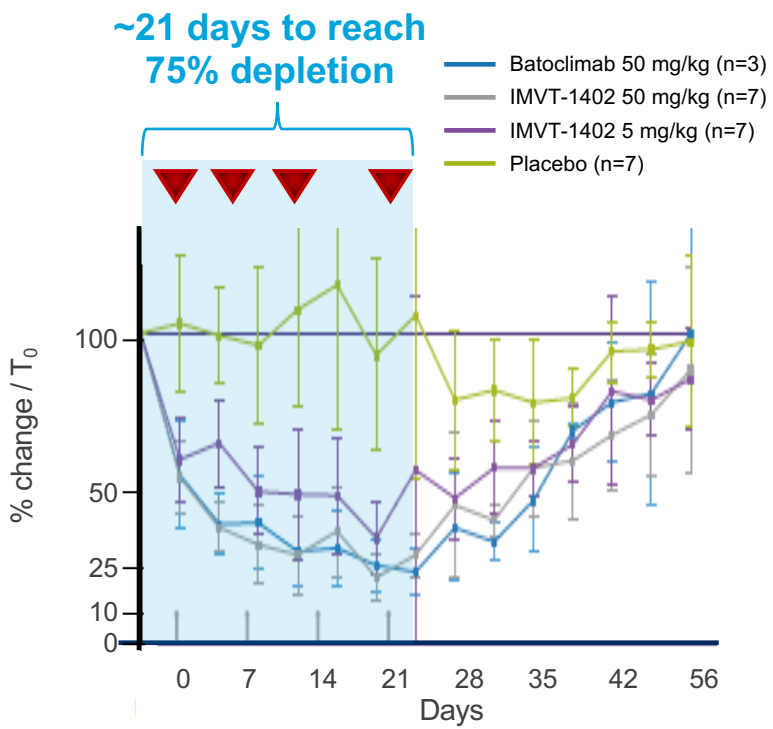
BHV-1300: Shows Potential for Superiority Over Competition

BHV-1300 demonstrated faster depletion of IgG in non-human primates

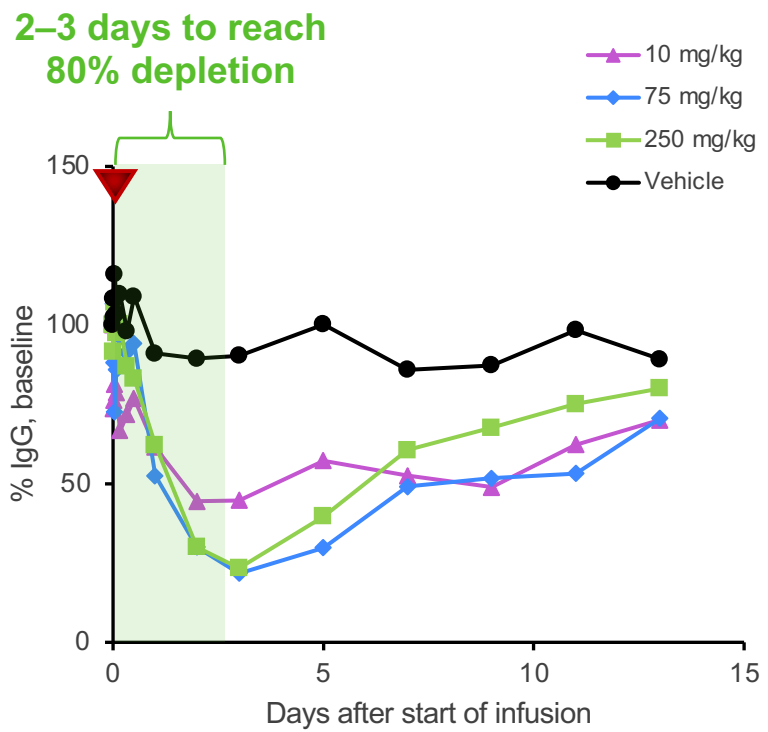
Efgartigimod NHP Pharmacodynamics



Immunovant NHP Pharmacodynamics



BHV-1300 NHP Pharmacodynamics



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

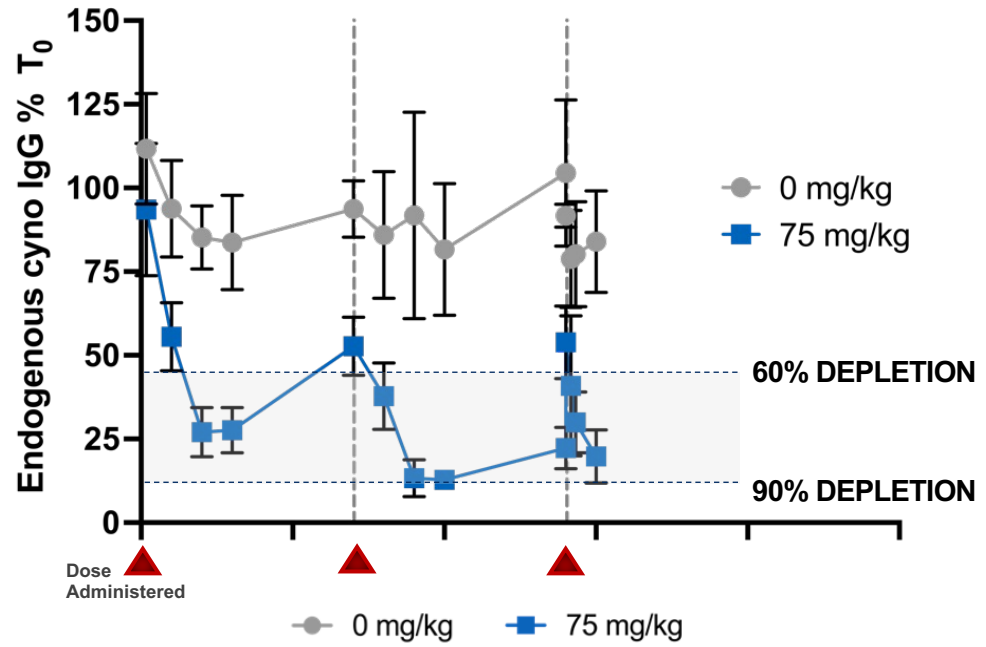
Excerpted from Immunovant Corporate Presentation, August 2023.

▼ Dose Administered

biohaven

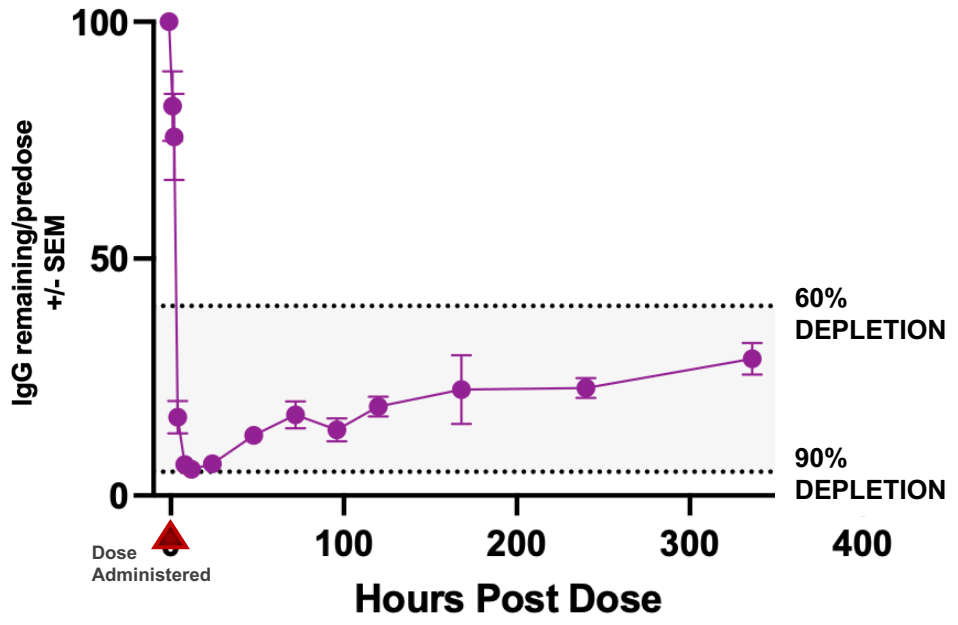
Unique Properties of BHV-1300 and BHV-1310 Matched to Indications

BHV-1300 Preclinical Pharmacodynamics (multiple dose)



CHRONIC indications — e.g., rheumatoid arthritis

BHV-1310 Preclinical Pharmacodynamics (single dose)



ACUTE indications — e.g., myasthenia gravis

KEY POINT

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

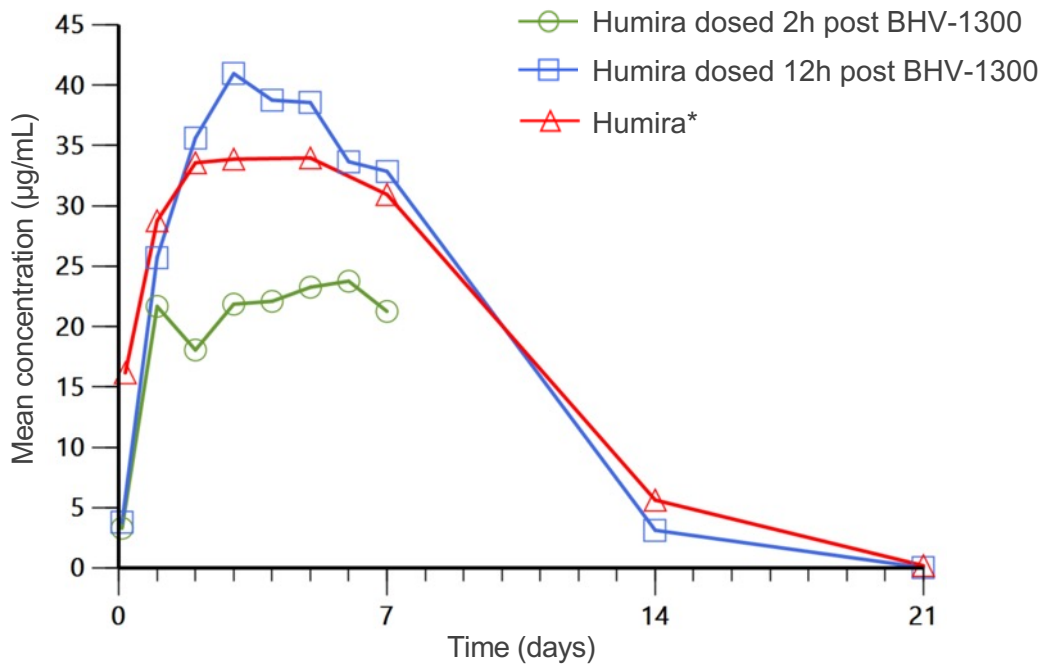
BHV-1300 pharmacodynamics in NHP and BHV-1310 pharmacodynamics in rabbit

Biohaven Pan-IgG Degraders Allow for Co-Administration with mAbs

Frequently Administered Fc-Containing Biologics

Humira®
Enbrel®
Remicade®
Cosentyx®
Rituxan®
Actemra®
Tremfya®
Repatha®
Prolia®

Humira 3 mg/kg SC, After a 30 mg/kg SC Dose of BHV-1300 to NHP



KEY POINTS

- **First NHP data to show that BHV-1300 does not alter PK of Humira® when dosed 12 hours earlier**
- **Allows for same-day dosing with biologics**
- **FcRns reduce effectiveness of Fc-containing biologics and should not be used chronically together**

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

DEGRADERS

BHV-1600, Next-Generation Selective Degrader Targeting β1-AR Autoantibodies

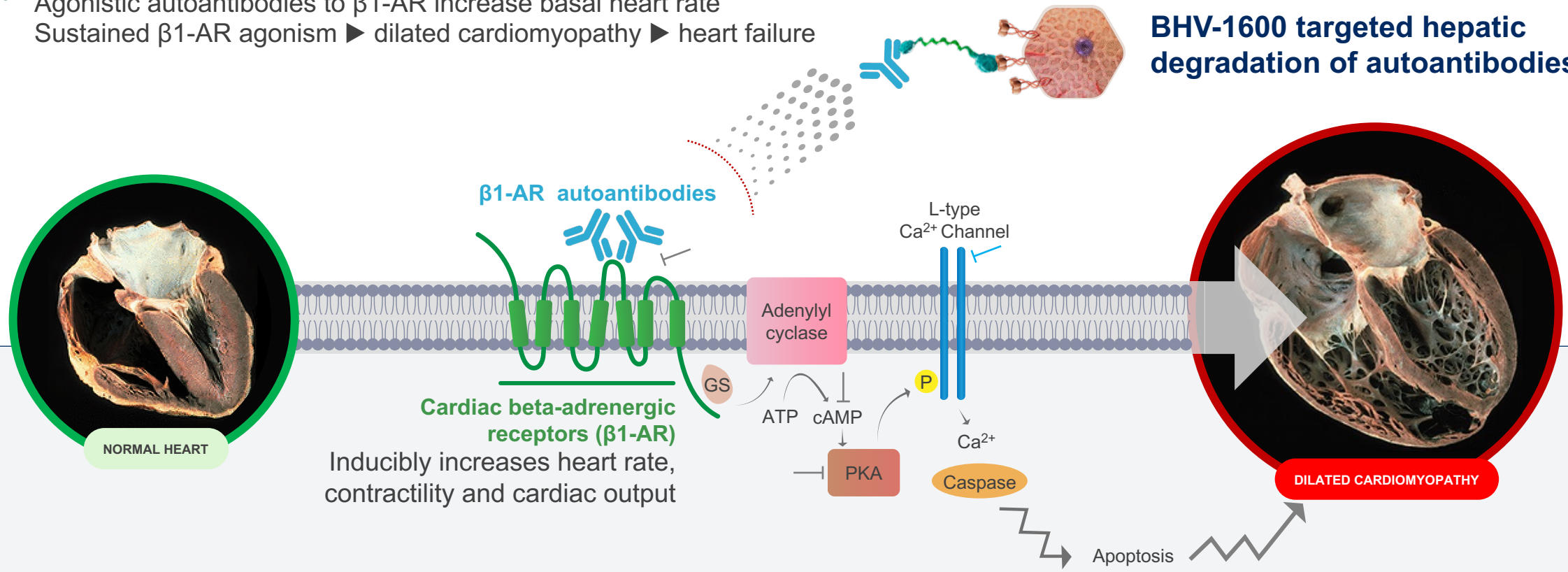
biohaven®

Selective Targeting of β1-AR Autoantibodies for Dilated Cardiomyopathy

β1-AR autoantibodies

Agonistic autoantibodies to β1-AR increase basal heart rate
Sustained β1-AR agonism ▶ dilated cardiomyopathy ▶ heart failure

BHV-1600 targeted hepatic degradation of autoantibodies



Cardiac beta-adrenergic receptors (β1-AR)
Inducibly increases heart rate, contractility and cardiac output

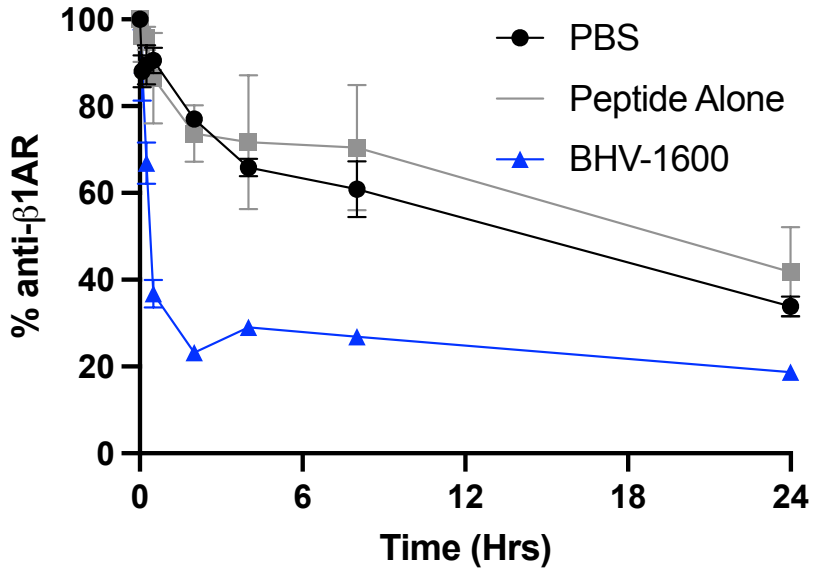
CURRENT TREATMENT FOR β1-AR AUTOANTIBODY-DRIVEN CARDIAC DISEASE:

- **BETA BLOCKERS:** Ineffective treatment limited to supportive treatment, diuresis, etc.
- **REMOVAL OF ANTIBODIES:** Plasmapheresis[1,2] demonstrates POC but requires hospitalization

1. *Eur J Heart Fail.* **2013**; 15(7): 724–729. 2. *Nat. Rev. Nephrol.* **2014**; **10**(3): 125-125. Illustration adapted from European Journal of Heart Failure (2013) 15, 724–729. Heart image adapted from https://thoracickey.com/clinical-presentation-and-therapy-of-cardiomyopathies/

BHV-1600: *In Vitro* and *In Vivo* Properties Ideal for Degrading β-1AR Abs

Marked Degradation of Anti-β-1AR Antibody in Mice

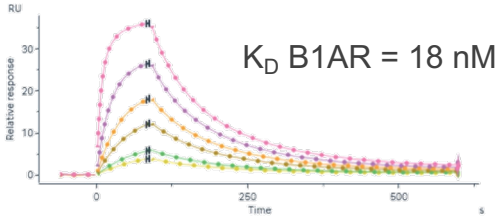


- Rapid ASGPR-mediated hepatic clearance in mouse and rat
- Stoichiometric degradation of exogenously administered anti-β-1AR Ab in mice compared to controls

KEY UPDATE **IND Filing and FIH Phase 1 Study 2H 2024**

High Affinity to the Target

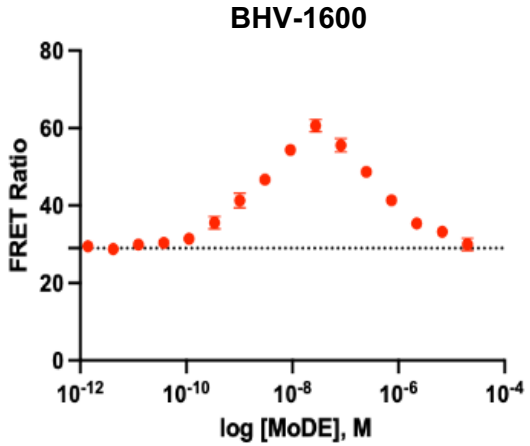
High affinity for monoclonal mouse anti-β1-AR antibody and ASGPR protein construct by SPR



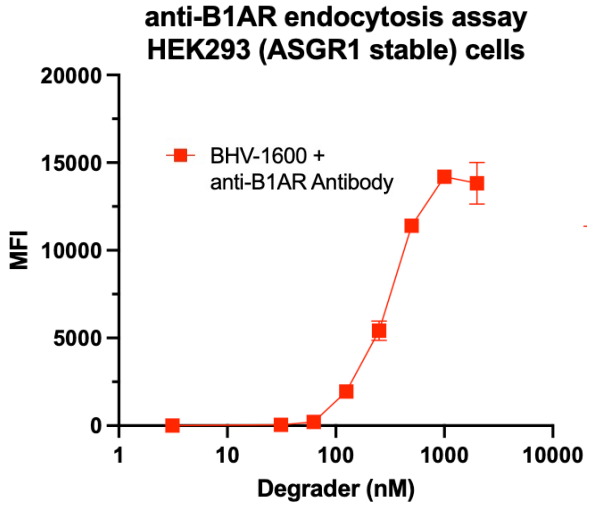
K_D B1AR = 18 nM

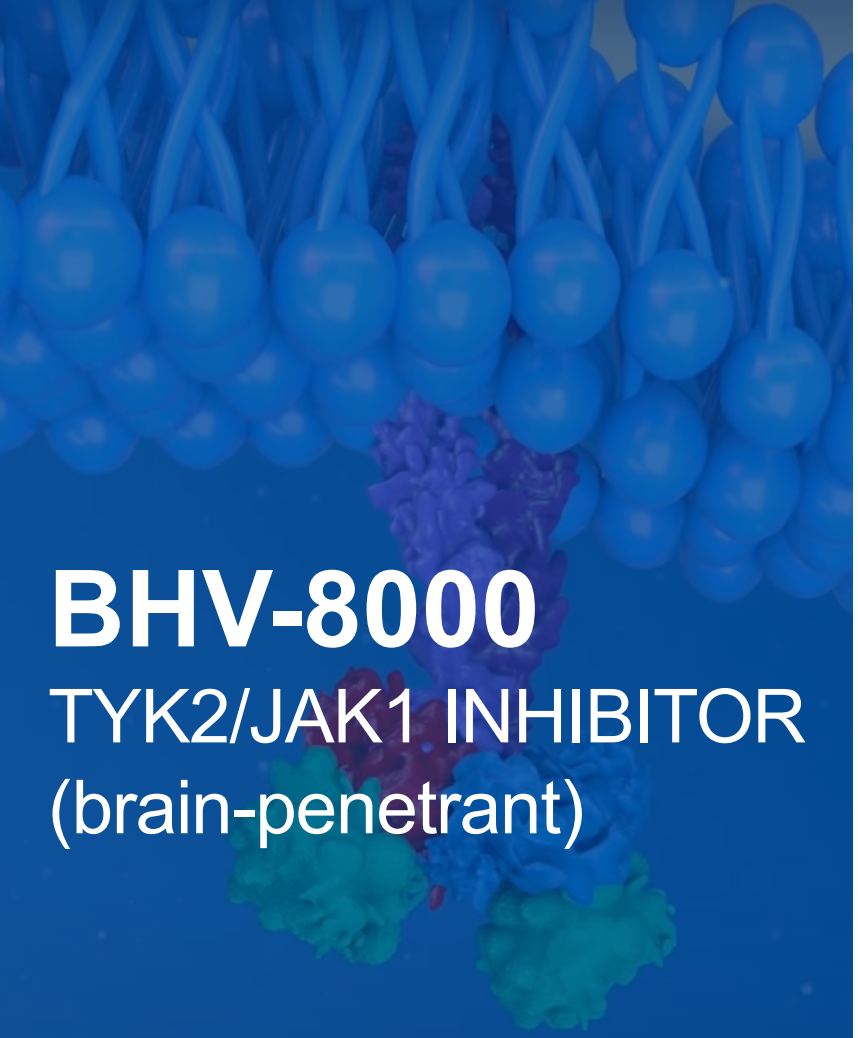
Ternary Complex and Endocytosis

Formation of ternary complex confirmed in TR-FRET assay



Cellular internalization of anti-β-1AR Ab demonstrated in HEK293 (hASGPR) cells





BHV-8000

TYK2/JAK1 INHIBITOR (brain-penetrant)

PROGRAM UPDATE

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

- Uniquely potent, TYK2/JAK1 selective, brain-penetrant inhibitor
- Selectivity profile should avoid 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

Evidence supports efficacy in prevention of amyloid therapy induced ARIA, Alzheimer's disease, Parkinson's disease, Multiple Sclerosis and other disorders

Encouraging Preliminary Results from Ongoing Phase 1 Trial

- Projected therapeutic concentrations achieved
- Well tolerated with only mild adverse events to date (loose bowel movements, headache, and constipation)

Upcoming Milestones

Anticipate initiating multiple clinical trials in 2024

- **SAD study: SAD cohorts completed dosing (10, 20 and 30 mg)**
- **MAD study: Completed 10 mg dose cohort and began 20 mg dose**

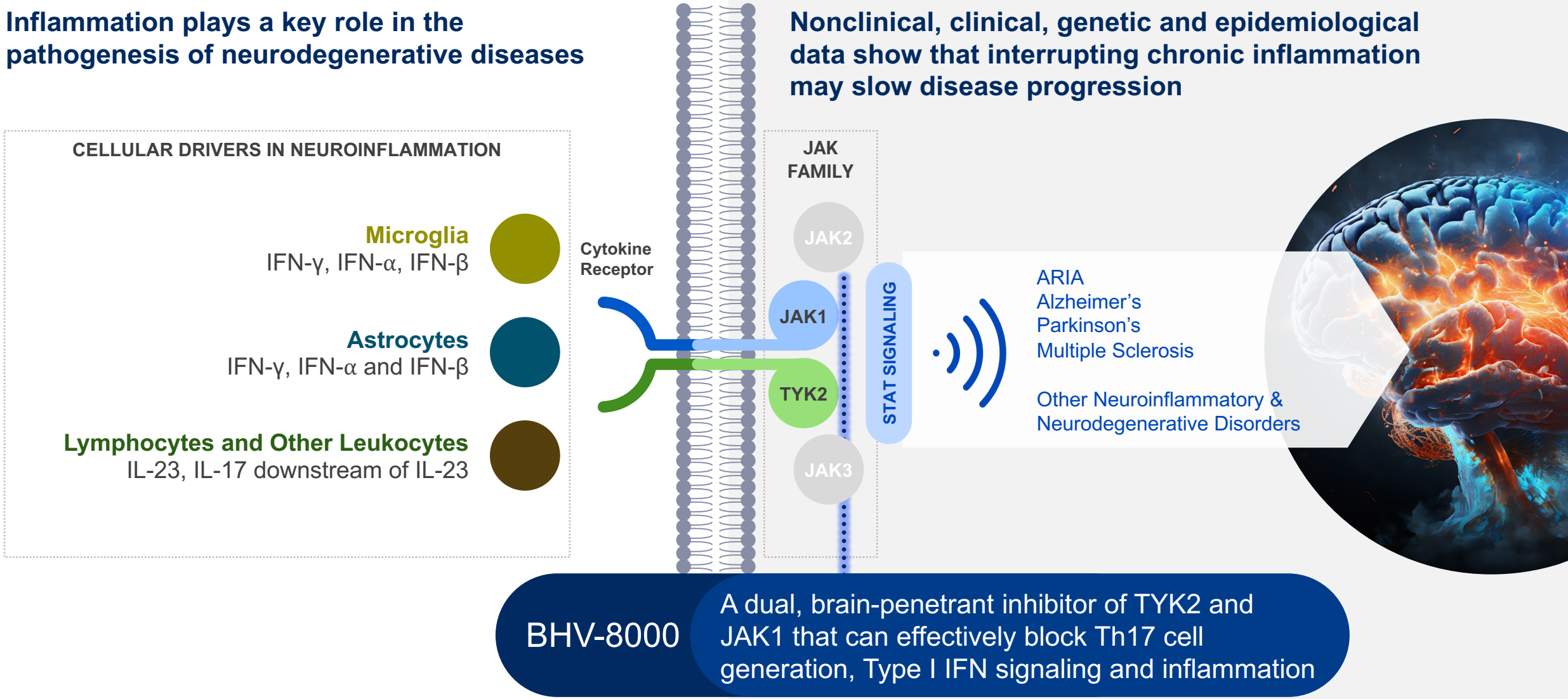
ARIA, Amyloid-related imaging abnormalities

biohaven

BHV-8000: TYK2/JAK1 in Neuroinflammatory 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 A dual, brain-penetrant inhibitor of TYK2 and JAK1 that can effectively block Th17 cell generation, Type I IFN signaling and inflammation

Biohaven's Real-World Analytics of Large Healthcare Database: Parkinson's Disease Risk Reduction with IL-17/TNF 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
- Result provides MOA rationale for the effectiveness of a TYK/JAK inhibitor in 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		

BHV-8000: Unique Clinical Trial Approach in 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)

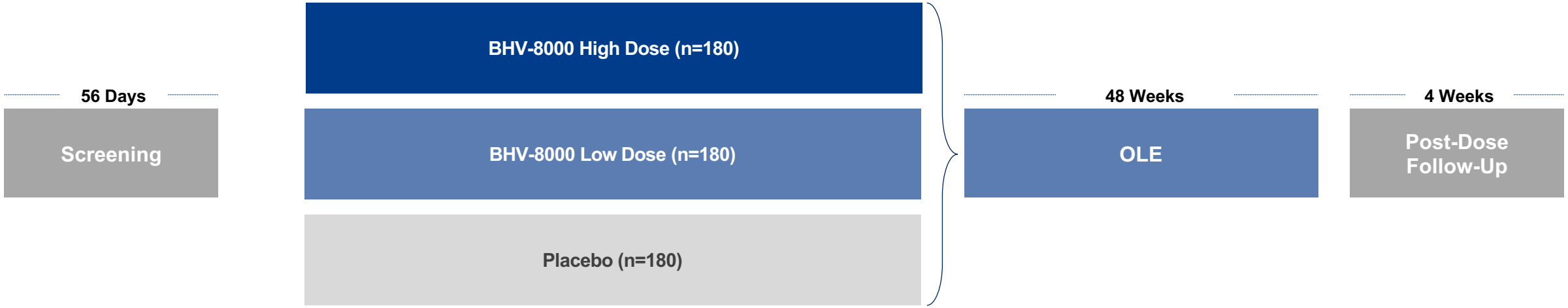
Provides a meaningful efficacy endpoint with a smaller sample size

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

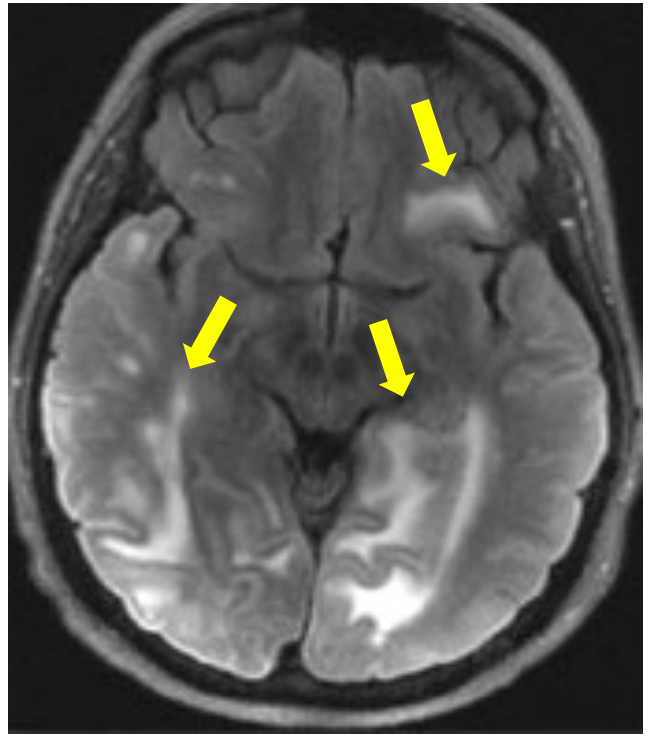


ARIA: A Potential Therapeutic Target for TYK2/JAK1 Inhibition

ARIA events typically occur early (8–12 weeks) after initiation of anti-amyloid mAb therapy[1] and can complicate the benefit-risk assessment in certain patient groups

ARIA-E EVENTS WITH ANTI-AMYLOID THERAPY				
	Overall	APOE4 carriers (het)	APOE4 carriers (homo)	Non-carriers APOE4
EMERGE & ENGAGE TRIALS				
Aducanumab[2]	35.2%		43.0%	20.3%
Placebo	2.7%			
TRAILBLAZER-ALZ2				
Donenamab[3]	24.0%	22.8%	40.6%	15.7%
Placebo	1.9%	1.9%	3.4%	0.8%
CLARITY-AD				
Lecanemab[4]	12.6%	14%	39%	11.9%
Placebo	1.7%	8.6%	21%	4.2%

Severe ARIA-E (Edema) in a Patient Receiving Anti-Amyloid Therapy for AD



Axial MR images of the brain show multifocal subcortical edema (arrows) with FLAIR hyperintensity

Agarwal A. Published Online: August 31, 2023. https://doi.org/10.1148/rg.230009

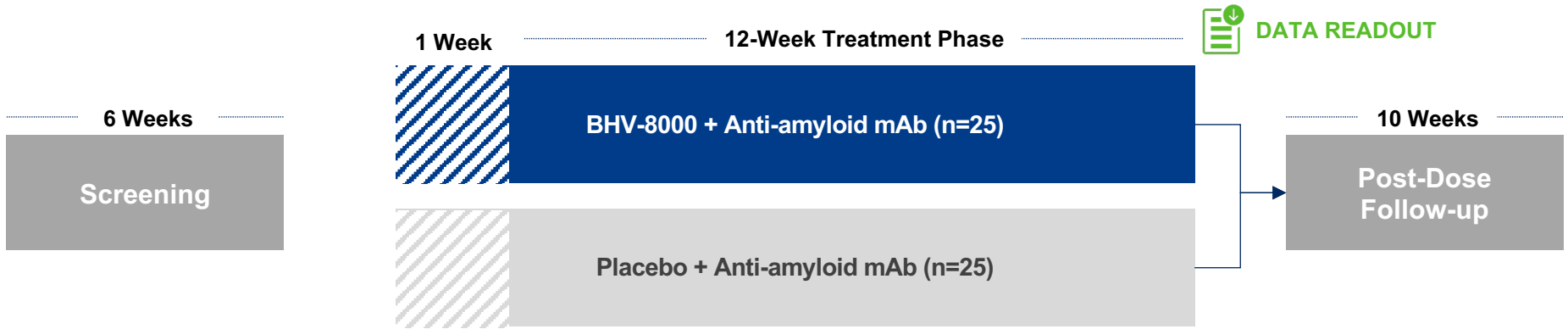
1. Cummings et al, *J Prev Alz Dis.* 2023;3(10):362-77. 2. Aducanumab Budd Haeberlein S, et al J Prev Alzheimers Dis. 2022;9(2):197-210. 3. Donenamab Sims JR, et al JAMA. 2023 Aug 8;330(6):512-527. 4. Cummings J, et al J Prev Alzheimers Dis. 2023;10(3):362-377.

BHV-8000: A Potential Therapy for the Prevention of ARIA

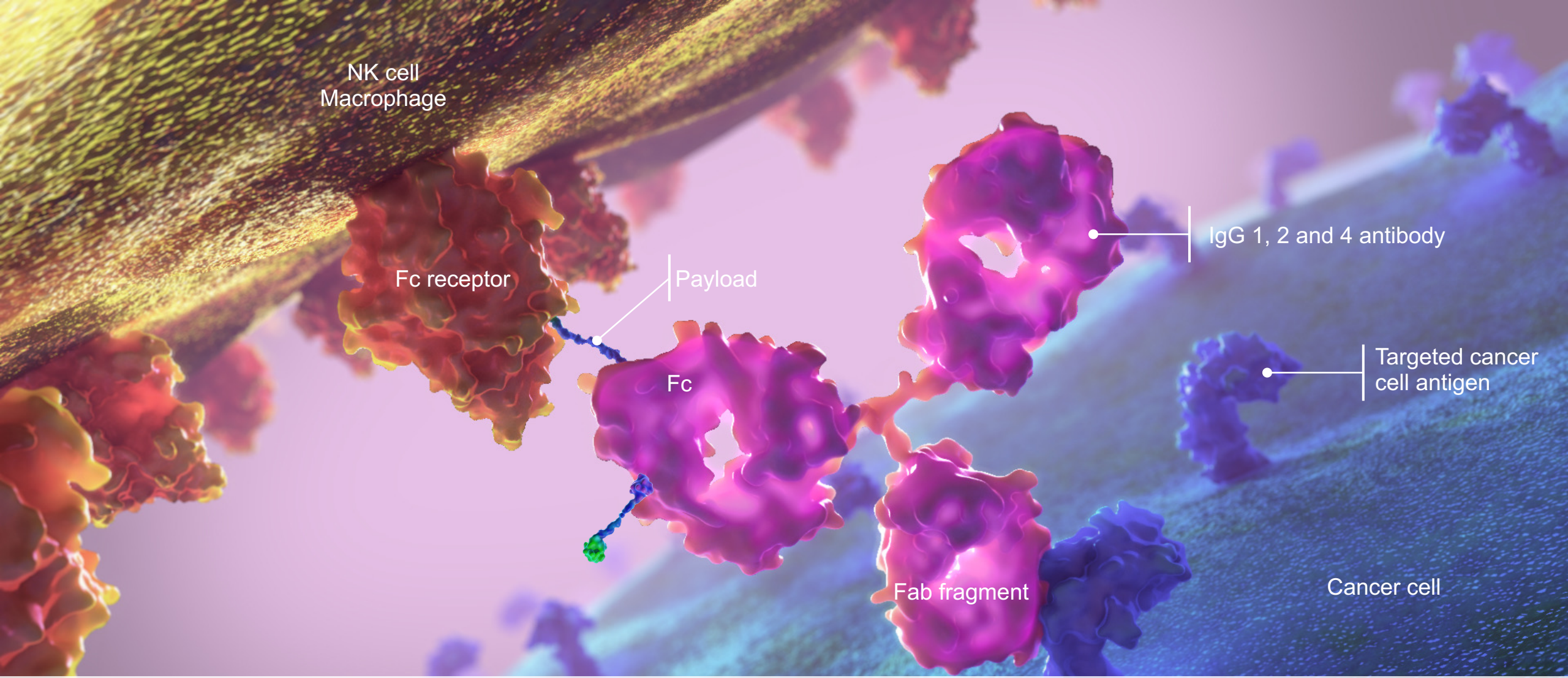
Therapeutic hypothesis:

- TYK2/JAK1 inhibition reverses activated glial- and T-cell mediated pathology and general inflammation
- Corticosteroids and other immunosuppressive drugs show benefit in treating and reducing the risk of ARIA[1,2,3]
- TYK2/JAK1 inhibition has a favorable benefit-risk profile over corticosteroids and other immunosuppressive drugs
- BHV-8000 has the potential to reduce incidence of ARIA associated with anti-amyloid therapies

Biohaven plans to conduct a Phase 2 study to assess events of ARIA in Alzheimer's disease in APOE4 homozygous adults living with early Alzheimer's disease who are initiating anti-amyloid therapy



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.



Oncology

biohaven®

ADC PLATFORM

Conjugation Chemistry Superior to Industry Standard

Maleimide and lipophilic click chemistry

Attached to Two Specific Lysines

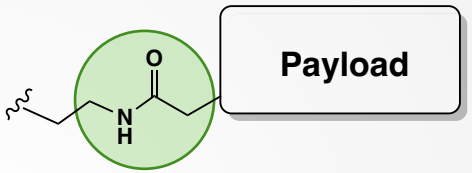
Provides stable and consistent drug antibody ratio (DAR)

- ✓ **ADAPTABLE** Complements and improves multiple existing ADC payload-linker technologies
- ✓ **STABLE** Improved ADC plasma stability with controlled DAR potentially improves therapeutic index
- ✓ **EFFECTIVE** Improved efficacy in mouse tumor model also suggests potential for increased therapeutic index
- ✓ **MULTIPURPOSE** Conjugates IgG1, 2 and 4; Single step conjugation with predictable favorable yields, low aggregation
- ✓ **NOVEL** IP filed globally in key markets

Current Status

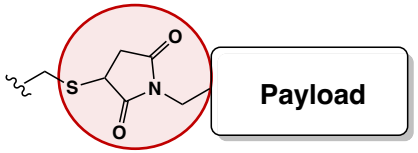
- Two INDs planned for 2024

Biohaven chemistry



Stable, physicochemically benign amide linkage

Industry standard maleimide



Poorly stable linkage

BREAKING NEWS

- **Two INDs planned for 2024**
- **TROP2 Phase 1 2Q 2024**
- **5–7 new ADCs in next two years**

biohaven

BHV-1510 is a Potential Best-in-Class TROP2 ADC

TROP2 IS A HIGHLY VALIDATED TARGET WITH LARGE MARKET OPPORTUNITY

- Trodelvy® only drug approved with 2022 actual sales of $680M (+65%y/y)
- Significant opportunities for indications beyond current approvals and in anti-PD1 combination

BHV-1510 HAS POTENTIAL BEST-IN-CLASS PROFILE COMPARED TO OTHER TROP2 ADCS

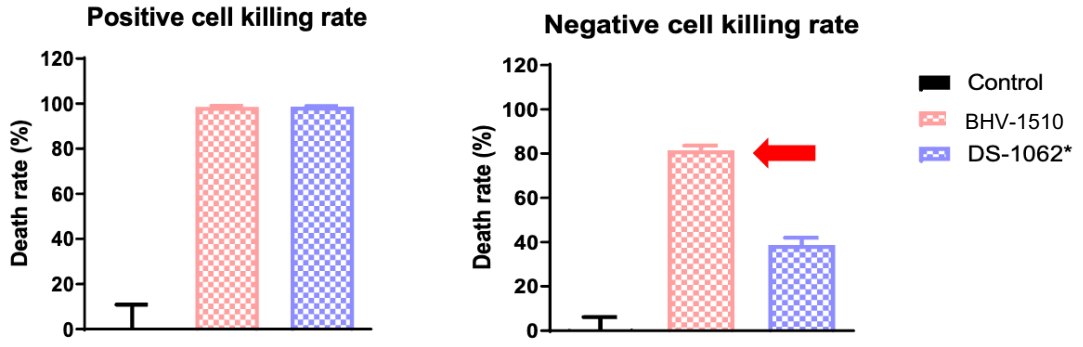
- Fully optimized next-generation ADC with potential best-in-class payload and enhanced stability
- Synergistic and superior efficacy with anti-PD1
- Highly differentiated efficacy and safety profile provide an opportunity to broaden therapeutic margin, increase time on treatment and improve efficacy

	Trodelvy®	DS-1062	SKB264 / MK-2870	BHV-1510	Point of Differentiation
Antibody	Sacituzumab	Datopotamab	Sacituzumab	**Sacituzumab**	**Higher TROP2 binding affinity vs DS-1062**
Linker	Hydrolyzable CL2A (pH-dependent)	Hydrolyzable, protease cleavable	Similar to Trodelvy (pH-dependent)	**Proprietary highly stable (irreversible) and protease cleavable linker**	**Increased plasma stability to reduce off-target toxicity**
Payload	SN-38 (govitecan)	Dxd (deruxtecan)	Topolx, similar to SN-38	**Proprietary potential best-in-class Topolx**	**Improved *in vitro* cytotoxicity, bystander effect and immunogenic cell death vs Dxd and SN-38**
Conjugation	Chemical, non-specific	Cysteine, non-specific	Cysteine, non-specific	**Enzymatic (non-cysteine), site-specific**	**Increased homogeneity**
DAR	7–8	4	7–8	**4**	

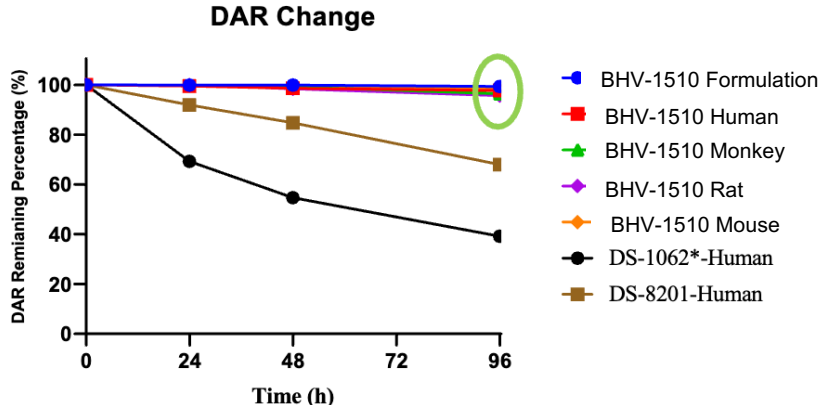
biohaven

BHV-1510: Improved Efficacy, Cell Killing and Linker Stability

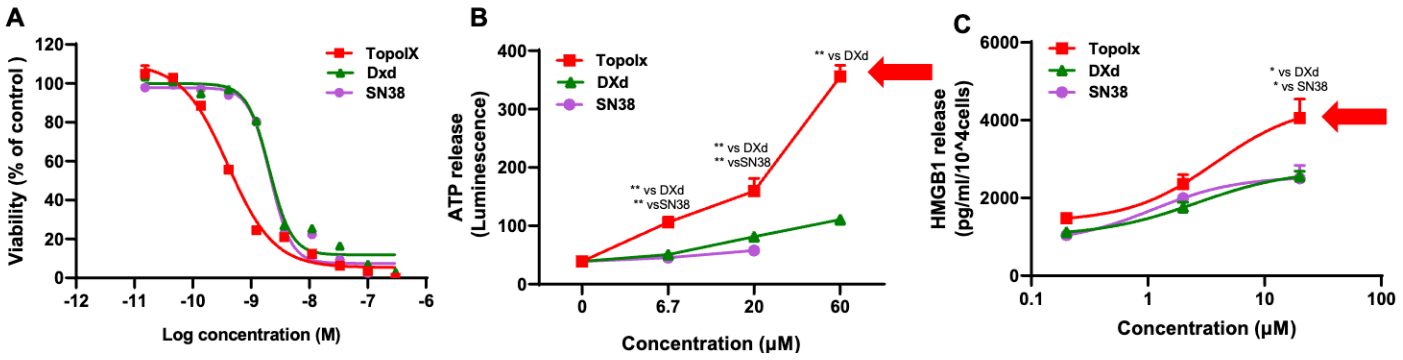
Superior Bystander Activity vs. DS-1062



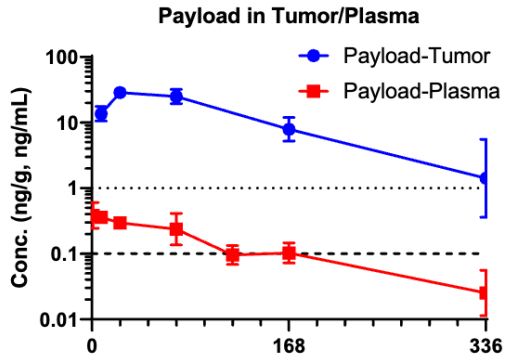
Highly Stable Linker vs. DS-1062



Superior Immunogenic Cell Death with Topolx Compared to Other Payloads (DxD and SN38)

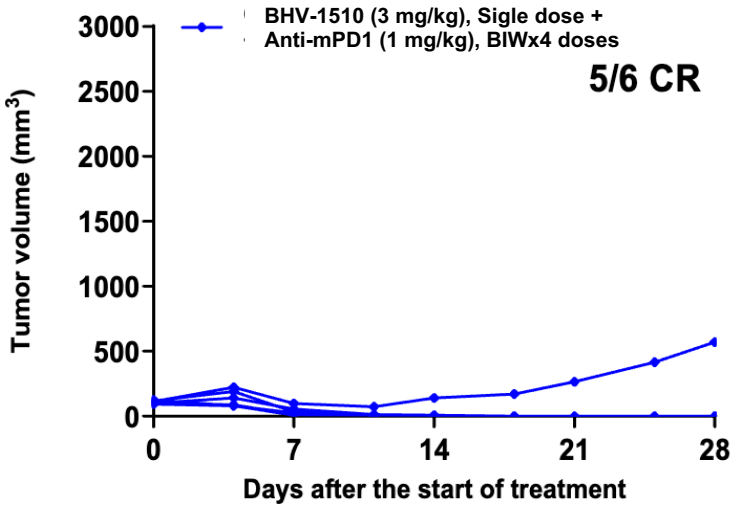


High Payload Delivery to Tumor

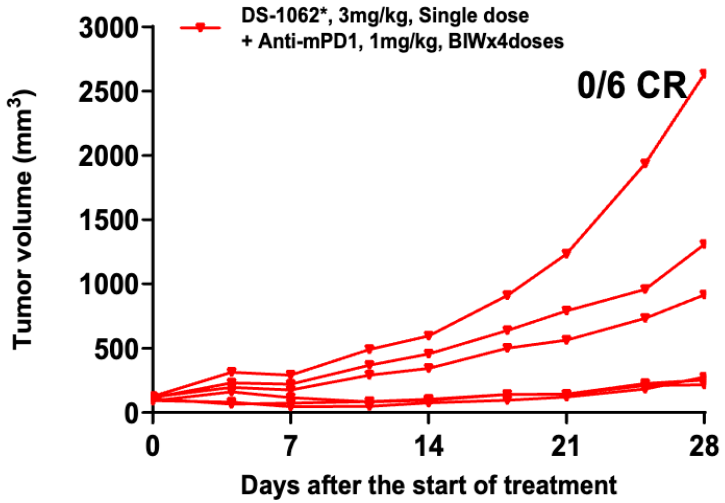


BHV-1510 + Anti-PD1 Combination Shows Compelling Synergy in Syngeneic Models and is Superior to DS-1062

BHV-1510 + Anti-PD1



DS-1062 + Anti-PD1



- Preclinical profile of BHV-1510 positions it for superiority in ADC therapy with anti-PD1
- Landscape open for TROP2 combinations with safer more efficacious ADCa

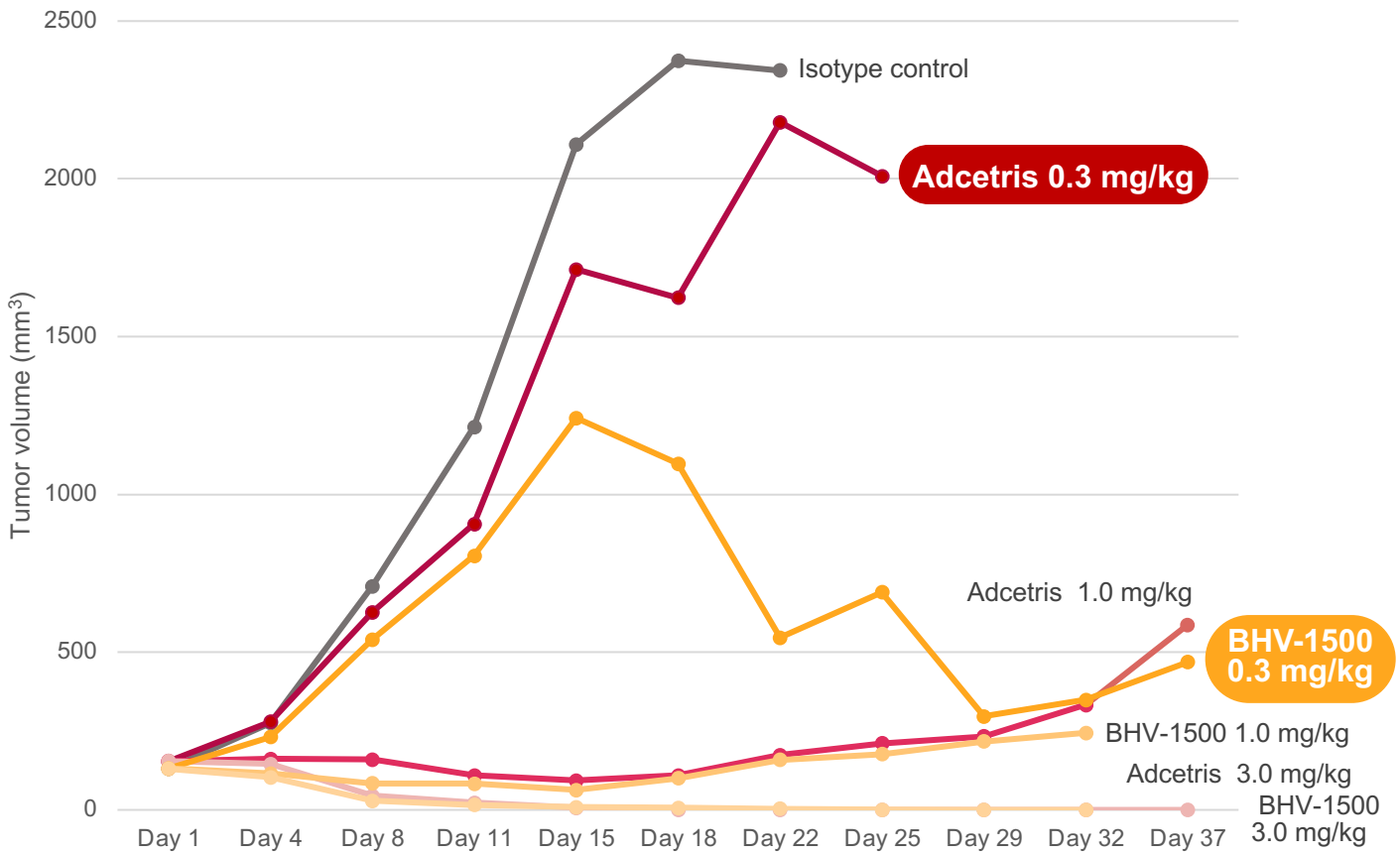
KEY POINT

BHV-1510 with potential best-in-class TopoIx payload shows superior bystander killing and immunogenic cell death to Dxd or SN-38 payloads

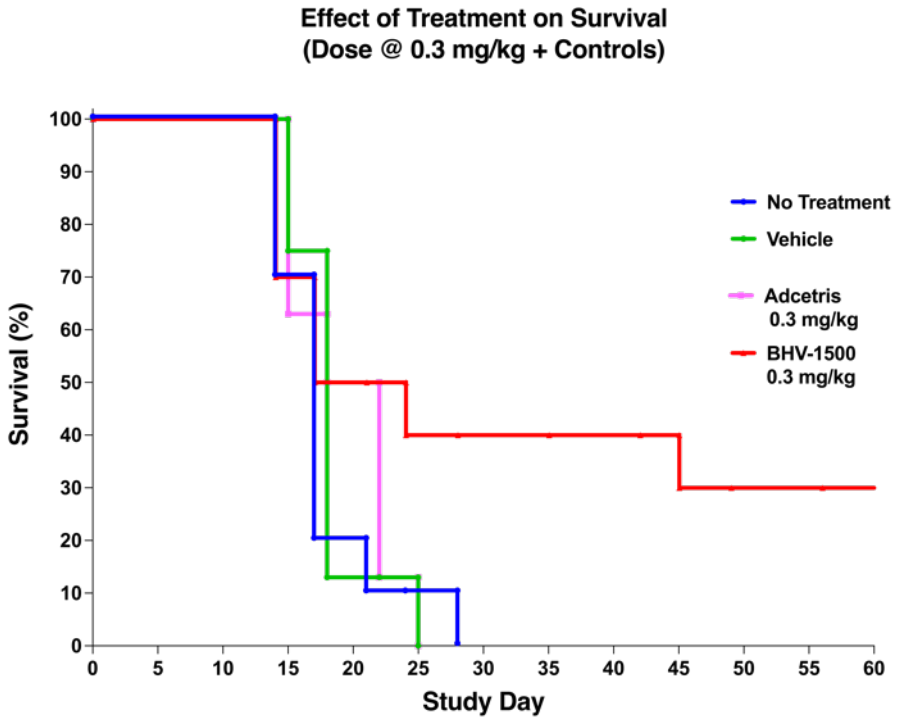
AACR 2023 annual meeting, abstract #1549

BHV-1500: Compares Favorably to Adcetris and Potential Best-In-Class Profile

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



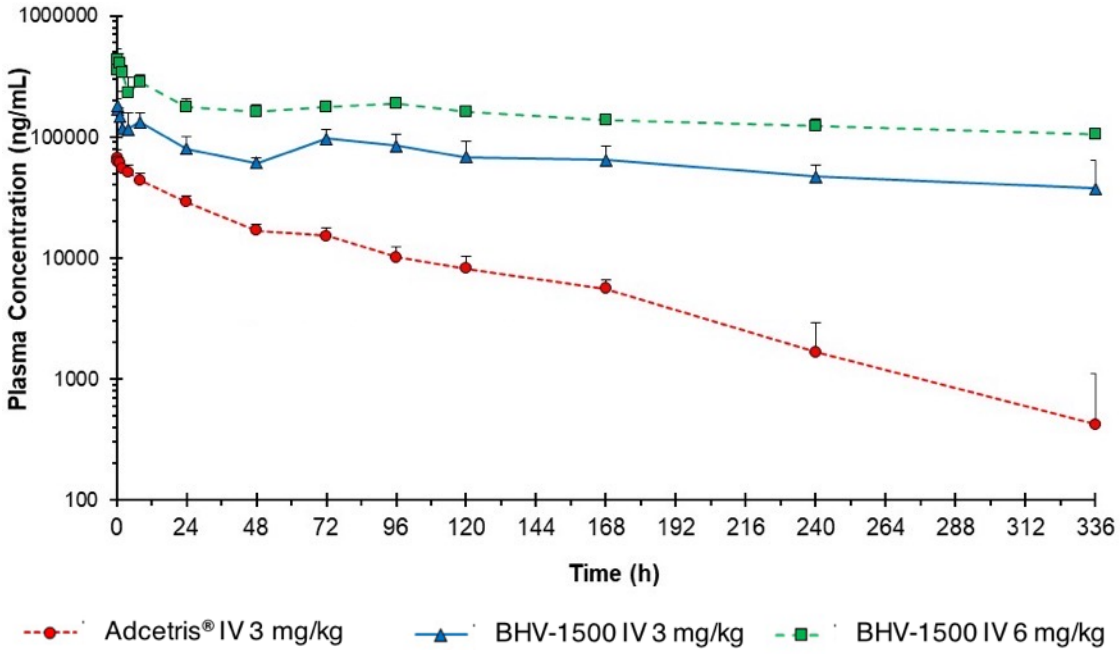
BHV-1500 Improved Survival in Mouse Compared to Adcetris®



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

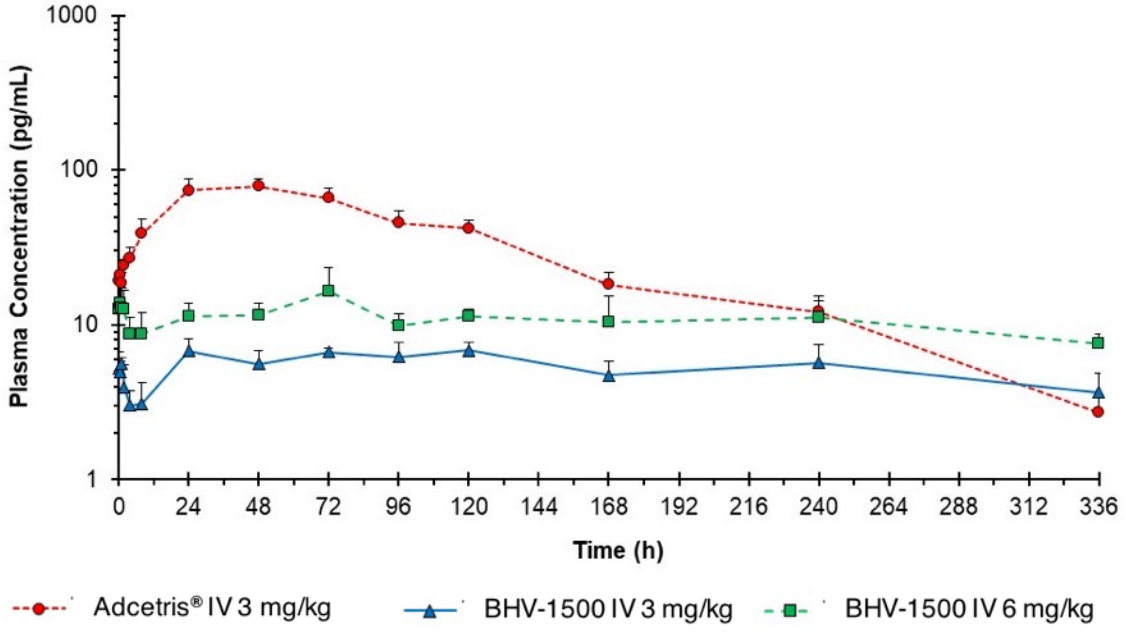
BHV-1500: Improved PK and Decreased Payload Release Compared to Adcetris®

ADC



- Markedly improved PK
- Increased exposure does not increase risk

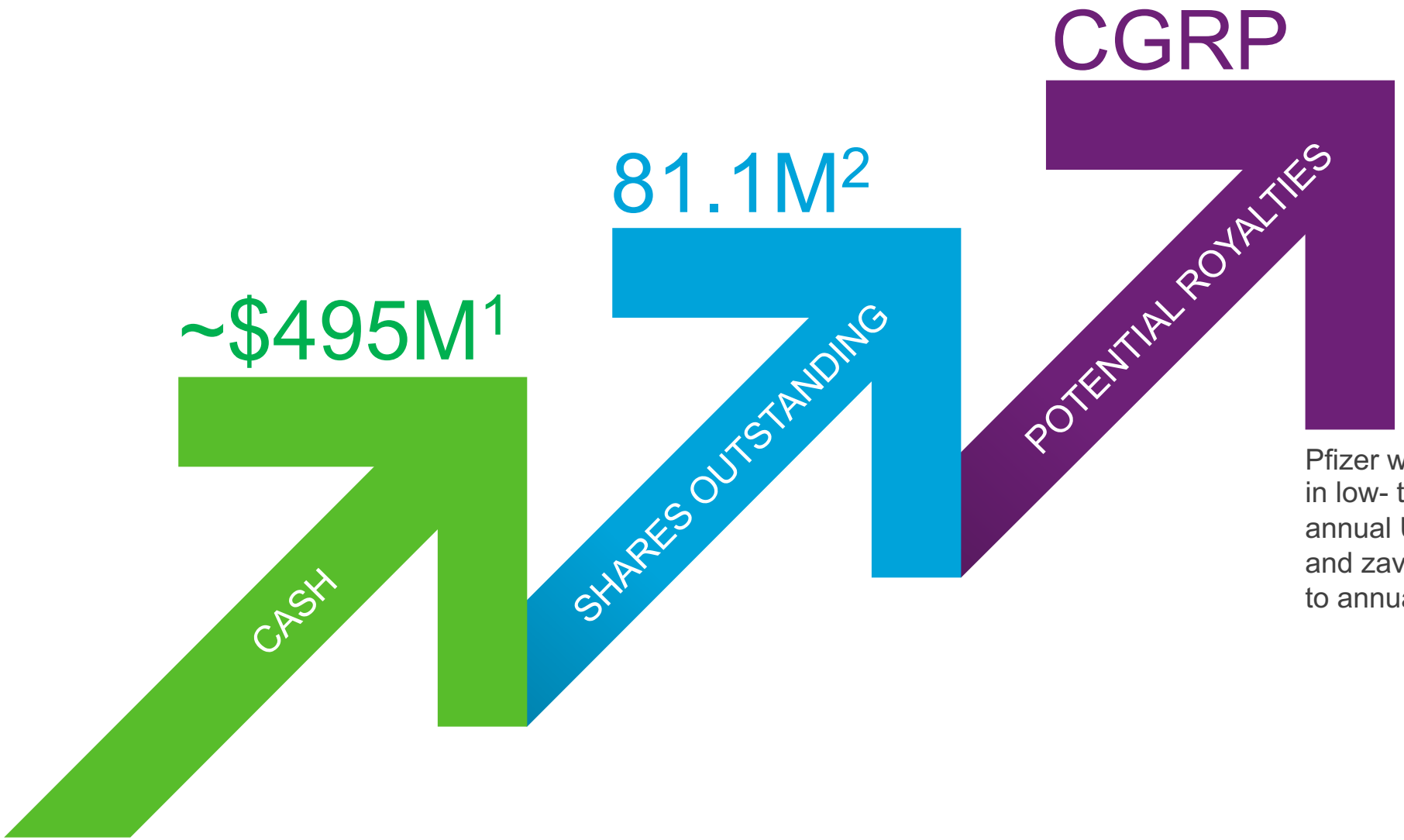
Free MMAE



- Marked reduction in release of free payload
- Free payload drives toxicity

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

Capitalization Updates



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)[3]

1. As of October 5, 2023, including cash from the completed Oct 2023 common offering, marketable securities, and investments. 2. Excludes outstanding options. 3. Cap reach 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.

Top Areas of Innovation

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

BIOCENTURY SURVEY[1]

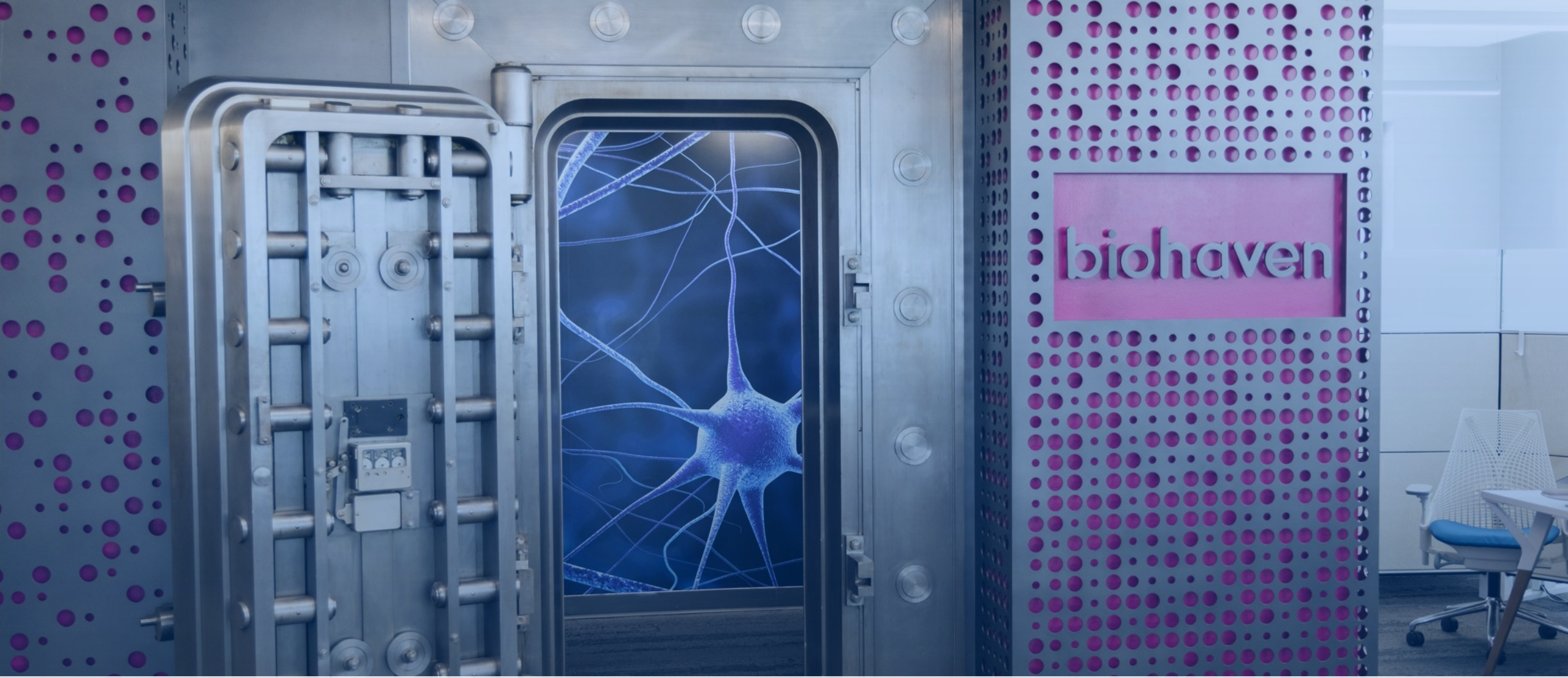
	PATIENTS[2] INDICATION	
IgG Degrader	**80–130K** RHEUMATOID ARTHRITIS	**100K** MYASTHENIA GRAVIS
TYK2/JAK1	**3.5M** ARIA PREVENTION[2]	**0.5M** EARLY PARKINSON'S DISEASE
	3.5M EARLY ALZHEIMER'S DISEASE[3]	**950K** MULTIPLE SCLEROSIS
Kv7 Activator	**2M** FOCAL EPILEPSY	**7M** BIPOLAR DISORDER
	1.2M GENERALIZED EPILEPSY	**21M** MAJOR DEPRESSIVE DISORDER
TRPM3 Antagonist	**40M** MIGRAINE	**36M** PAIN
Troriluzole	**2.6M** OBSESSIVE-COMPULSIVE DISORDER	
Taldefgrobep Alfa	**10K** SPINAL MUSCULAR ATROPHY	**10M** OBESITY
CD30	**173K** HODGKIN'S LYMPHOMA	
Trop2	**660K** EPITHELIAL TUMORS	
β1AR Degrader	**388K** DILATED CARDIOMYOPATHY	
IgA Degrader	**3.5M** IgA NEPHROPATHY	

Biohaven's pipeline working to help millions of patients

1. Adapted from BioCentury survey: https://www.biocentury.com/article/650883/move-over-oncology-i-i-will-write-the-next-big-stories-in-innovation#.
2. Patient numbers are US prevalence from Biohaven market research;
3. With amyloid therapy; 4. Disease modifying

2024 Milestones: Potential for Multiple Value Inflection Points

		1Q 2024	2Q 2024	2H 2024
Troriluzole | BHV-4157	Obsessive-Compulsive Disorder	Database Lock	Phase 3 IA Topline	
Taldefgrobep Alfa | BHV-2000	Spinal Muscular Atrophy			Phase 3 Topline
	Obesity		Initiate Phase 2	
Kv7 Activator | BHV-7000	Focal Epilepsy	Initiate Phase 2/3		
	Generalized Epilepsy		Initiate Phase 2/3	
	Bipolar Disorder	Initiate Phase 2/3		
	Major Depressive Disorder	Initiate Phase 2		
TRPM3 Antagonist | BHV-2100	Migraine			Initiate Phase 2
	Neuropathic Pain			Initiate POC
TYK2/JAK1 | BHV-8000 (brain-penetrant)	Prevention of Amyloid Therapy Induced ARIA			Initiate Phase 2a
	Early Alzheimer's Disease			Initiate Phase 2/3
	Early Parkinson's Disease			Initiate Phase 2/3
	Multiple Sclerosis		Initiate Phase 2	
IgG Degrader | BHV-1300	Rheumatoid Arthritis	Phase 1 IgG Lowering Data		
IgG Degrader | BHV-1310	Myasthenia Gravis			Initiate Phase 1
IgA Degrader | BHV-1400	IgA Nephropathy			Initiate Phase 1
β1-AR Degrader | BHV-1600	Dilated Cardiomyopathy			Initiate Phase 1
CD30 | BHV-1500	Hodgkin's Lymphoma			File IND
Trop2 | BHV-1510	Carcinoma		Initiate Phase 1	



Our Commitment:
Building Value for Patients and Shareholders

biohaven®