UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 8-K
CURRENT REPORT
Pursuant to Section 13 or 15(d) of
The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 27, 2023

Biohaven Ltd.
(Exact name of registrant as specified in its charter)

British Virgin Islands	**001-41477**	**Not applicable**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

c/o Biohaven Pharmaceuticals, Inc.
215 Church Street
New Haven, Connecticut 06510
(Address of principal executive offices, including zip code)
(203) 404-0410
(Registrant's telephone number, including area code)
Not applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol	Name of each exchange on which registered
Common Shares, no par value	BHVN	New York Stock Exchange

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 7.01 Regulation FD Disclosure

On September 27, 2023, Biohaven Ltd. (the "Company") began utilizing a new corporate presentation (the "Corporate Presentation"). A copy of the Corporate Presentation is attached as Exhibit 99.1 to this Current Report on Form 8-K, which includes pharmacodynamic updates for BHV-1300, the Company's bispecific IgG degrader, showing greater than 90% reductions in IgG after repeat dosing and is incorporated herein by reference.

The information in this Current Report on Form 8-K, including the information set forth in Exhibit 99.1, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Corporate Presentation, dated September 2023
104	The cover page of this Current Report on Form 8-K formatted as Inline XBRL.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 27, 2023

Biohaven Ltd.

By: /s/ Matthew Buten
Matthew Buten
Chief Financial Officer


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Investor Presentation
BHVN
LISTED
NYSE
DAYS MATTER

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 trials for our BHV-2100, troriluzole, BHV-5500, BHV-1100, Taldefgrobep Alfa, BHV-8000, BHV-7000, and BHV-7010 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 ARM™, MATE™, MODE™, TRPM3, UC1MT, TYK2/JAK1, and Kv7. 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 U.S. 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.

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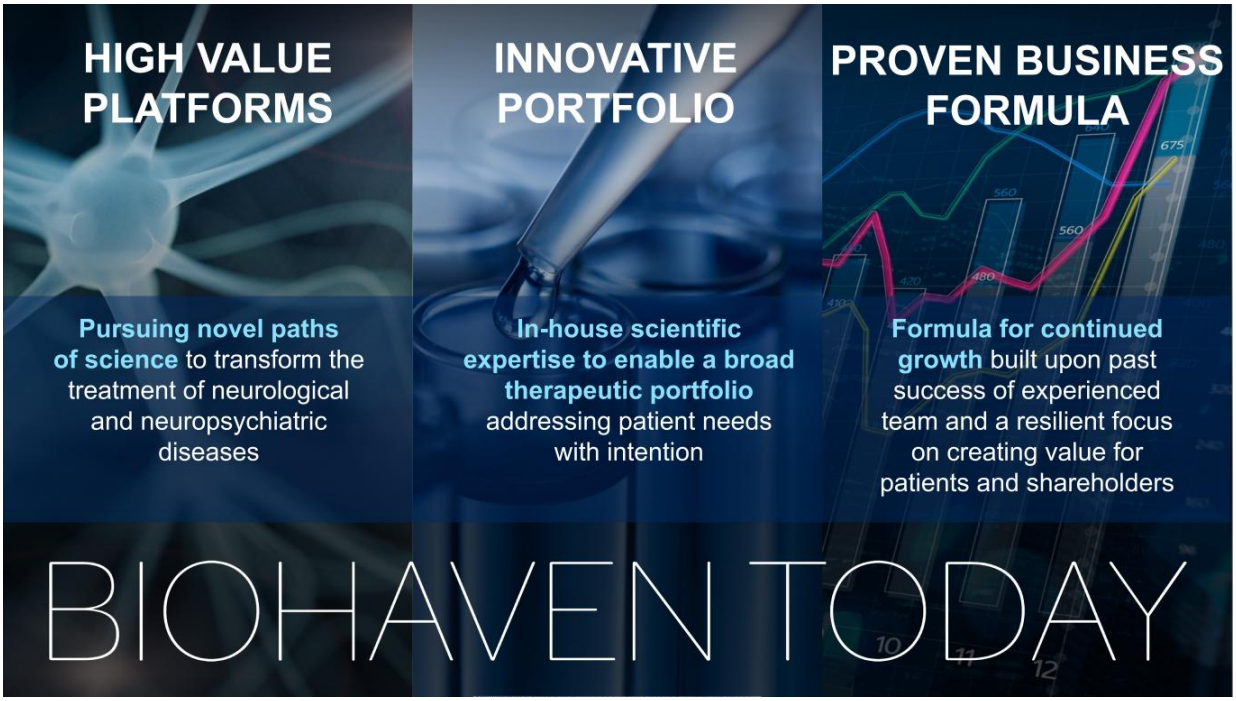
WE SUCCEEDED BY FOLLOWING THE
THE SCIENCE
FOR PATIENTS
#1
MIGRAINE
TREATMENT
IN ITS CLASS
Nurtec® ODT
(rimegepant)
orally disintegrating tablets 75 mg
Pfizer
Pfizer
Acquisition of
CGRP Platform
$13B


HIGH VALUE PLATFORMS
Pursuing novel paths of science to transform the treatment of neurological and neuropsychiatric diseases
INNOVATIVE PORTFOLIO
In-house scientific expertise to enable a broad therapeutic portfolio addressing patient needs with intention
PROVEN BUSINESS FORMULA
Formula for continued growth built upon past success of experienced team and a resilient focus on creating value for patients and shareholders
BIOHAVEN TODAY


PRECLINICAL
PHASE 1
PHASE 2
PHASE 3
FILED
ION CHANNEL: Kv7 ACTIVATOR
Kv7
BHV-7000 | Epilepsy, Bipolar Disorder
BHV-7010 | Epilepsy, Mood Disorders
ION CHANNEL: TRPM3 INHIBITOR
TRPM3
BHV-2100 | Chronic Pain Disorders
INFLAMMATORY: TYK2/JAK1 INHIBITOR
TYK2/JAK1
BHV-8000 | Neuroinflammatory Disorders
GLUTAMATE PLATFORM
Troriluzole
BHV-4157 | Obsessive-Compulsive Disorder
MYOSTATIN PLATFORM
Taldefgrobep Alfa
BHV-2000 | Spinal Muscular Atrophy
BHV-2000 | Metabolic Disorders
BISPECIFIC TARGETED CELL THERAPY
CD-38
BHV-1100 | Multiple Myeloma
DISCOVERY RESEARCH
IgG Degrader
BHV-1300 | Immune-Mediated Diseases
IgA Degrader
IgA Nephropathy
Next-Gen ADC Platform
Oncology

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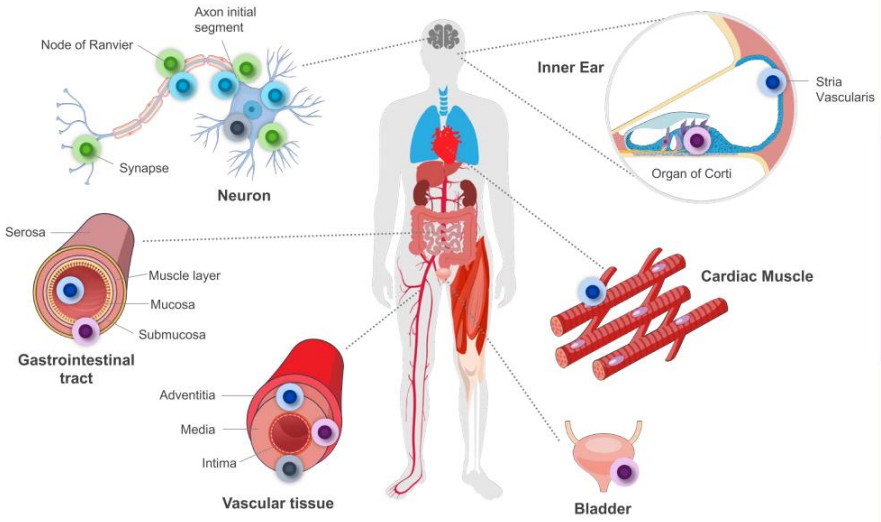
Kv7 Platform Is Broadly Applicable to Hyperexcitability Disorders Beyond Epilepsy



Source: Adapted from Soldovieri et al. *Physiology.* 2011;26(5):365-376.

5 FAMILY SUBTYPES
Primary localizations:

- Kv7.1: cardiac
- Kv7.2: CNS **BHV-7000 activator**
- Kv7.3: CNS **BHV-7000 activator**
- Kv7.4: smooth muscle and inner ear
- Kv7.5: vascular tissue, neurons, skeletal muscle

Significant Unmet Needs Remain for the 3.5 Million Patients Living with Epilepsy in the US

1/3 people are treatment refractory despite availability of anti-seizure medications (ASMs), surgery, and diet modifications

After starting an ASM, **80% of patients experience burdensome adverse events**, which can include:

- Somnolence
- Dizziness
- Cognitive dysfunction
- Mood disturbances

Devinsky et al. *Nat Rev Dis Primers*. 2018;4:18024; Kanner, Bicchi. *JAMA*. 2022;327(13):1269-1281.

1st and 2nd Gen Kv7 Activators Show Clinical Anti-seizure POC, But Off-target Activities, Opportunity for 3rd Gen Kv7 Differentiation

EZOGABINE

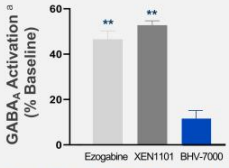
- **Unstable** when exposed to light
- **Label warnings** for skin discoloration
- **Black box warning** for retinal abnormalities/vision loss

FDA Drug Safety Communication: Potiga (ezogabine) [04-26-2013]

BHV-7000 is chemically stable to photo-oxidation

XEN1101

- **XEN1101** and ezogabine **significantly greater** $GABA_A$ receptor allosteric activators than BHV-7000 in vitro[a]
- $GABA_A$ receptor activation: somnolence, dizziness, fatigue, diplopia

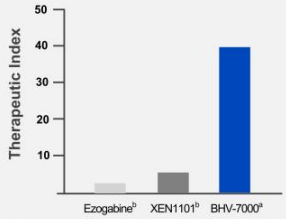


** significantly different from BHV-7000, all tested at 10 µM

BHV-7000 is selective for Kv7 over $GABA_A$ receptors [a]

BHV-7000

- **Potent activator** of Kv7 channels
- **Effective and well-tolerated** in preclinical seizure assays



BHV-7000 has a wide therapeutic index preclinically [a]

a. Biohaven data on file (2022). **b.** Calculated as ratio of TD_{50} (rotarod) to ED_{50} (MES seizure assay) data presented by Xenon at Epilepsy Foundation Pipeline Conference, San Francisco (Feb 2018).
Preclinical results are consolidated from separate reports and graphed together.
Data presented is not the result of any head-to-head clinical trials and does not mean or suggest that BHV-7000 is clinically more safe and effective.

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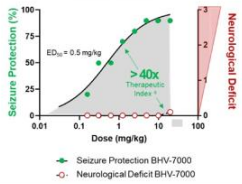
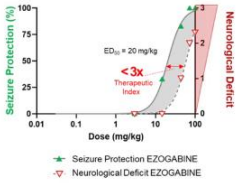
BHV-7000: First Kv7.2/7.3 Activator in Clinical Development Designed Specifically to Exclude $GABA_A$ Receptor Activation

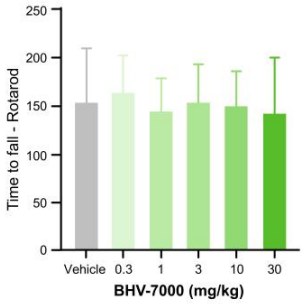
BHV-7000



Ezogabine

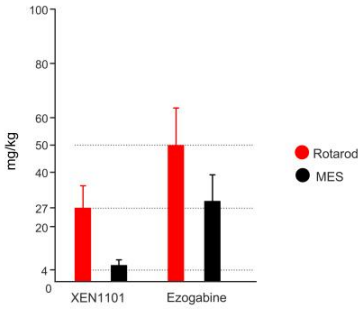


Rat Rotarod



No impact on motor function observed with BHV-7000 across effective dose range

*Mouse ED_{50} or TD_{50} (Mean 95% CI)



* Adapted from https://www.xenon-pharma.com/wp-content/uploads/2018/05/XEN1101_EILAT_15May2018_FINAL_YPG_web.pdf

Presented at 2023 American Society for Experimental Neurotherapeutics (ASENT) Annual Meeting March 13-15, 2023.
EC_{50}, half maximal effective concentration; **EZO**, ezogabine

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BHV-7000 Exhibits Highly Differentiated Preclinical Profile

	Ezogabine	XEN1101	BHV-7000
Kv7.2/7.3 Activator	✓ Activator, clinical and preclinical anti-seizure activity	✓ Activator, clinical and preclinical anti-seizure activity	✓ **Activator, clinical and preclinical anti-seizure activity**
$GABA_A$ Activity "dialed-out"	✗ $GABA_A$ activity present	✗ $GABA_A$ activity present	✓ **Negligible $GABA_A$ activity**
Wide Therapeutic Index	✗ <3x reported[a,b]	✗ <5x reported[a]	✓ **>40x[b]**

a. Calculated as ratio of TD_{50} (rotarod) to ED_{50} (MES seizure assay) data presented by Xenon at Epilepsy Foundation Pipeline Conference, San Francisco (Feb 2018). **b.** Biohaven data on file (2022).
Preclinical results are consolidated from separate reports and not a result from head-to-head comparisons Data presented is not the result of any head-to-head clinical trials and does not mean or suggest that BHV-7000 is clinically more safe and effective.

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BHV-7000: Well-Tolerated Across Phase 1 SAD/MAD Cohorts

SAFETY AND TOLERABILITY

No SAEs

No severe TEAEs, 1 moderate TEAE, remaining TEAEs mild by severity

DOSING

SAD: single doses up to 100 mg

MAD: multiple doses up to 40 mg daily x15 days

Exposures exceeded EC_{50} in MES preclinical seizure model

MedDRA System Organ Class	Placebo (N=15) n (%)	BHV-7000 (N=46) n (%)
Nervous system disorders	1 (6.7)	7 (15.2)
Gastrointestinal disorders	1 (6.7)	6 (13.0)
Musculoskeletal disorders	0	5 (10.9)
Infections	0	2 (4.3)
Investigations	1 (6.7)	2 (4.3)
Respiratory disorders	0	2 (4.3)
Skin disorders	0	2 (4.3)
Eye disorders	0	1 (2.2)
General disorders	0	1 (2.2)
Procedural complications	1 (6.7)	1 (2.2)
Psychiatric disorders	0	1 (2.2)
Renal disorders	1 (6.7)	1 (2.2)

BHV-7000: Phase 1 SAD/MAD CNS TEAEs by Dose and Cohort

Single Ascending Dose

CNS AEs[a]	Placebo N=10	4 mg N=6	10 mg N=6	25 mg (Fasted) N=6	25 mg (Fed) N=6	50 mg N=6	100 mg N=5	BHV-7000 Overall N=29
Headache	0	0	1 (16.7)	1 (16.7)	0	1 (16.7)	0	3 (10.3)
Dizziness	0	0	1 (16.7)	0	0	0	0	1 (3.4)
Myoclonus	0	0	0	1 (16.7)	0	0	0	1 (3.4)

[a]MedDRA® Preferred Term within the System Organ Class of "Nervous System Disorders"

Multiple Ascending Dose

CNS AEs[a]	Placebo N=5	10 mg N=5	25 mg N=6	40 mg N=6	BHV-7000 Overall N=17
Headache	1 (20.0)	0	0	3 (50.0)[1]	3 (17.6)

[a]MedDRA® Preferred Term within the System Organ Class of "Nervous System Disorders"

1. Incidents of headache were classified as mild

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BHV-7000: Not Associated with CNS AEs Typical of Other ASMs

Challenges with Existing ASMs

80% of patients will experience an AE after starting an ASM[1]

$GABA_A$ pathway activated by other ASMs is associated with AEs such as somnolence and dizziness[2]

Several ASMs cause behavioral (irritability, anger, aggression) or psychiatric (depressive mood, anxiety, psychosis) AEs[3,4]

Pooled CNS AEs[a,5]	BHV-7000 MAD Pooled N=17	Xen1101 MAD Pooled N=18
Somnolence	0%	39%
Headache	18%	39%
Balance disorder	0%	17%
Dizziness	0%	17%
Memory impairment	0%	28%
Sensory disturbance	0%	11%
Speech disorder	0%	33%

[a]MedDRA® Preferred Term within the System Organ Class of "Nervous System Disorders"
Data presented is not the result of any head-to-head clinical trials and does not mean or suggest that BHV-7000 is clinically more safe and effective.[5]

Devinsky et al. *Nat Rev Dis Primers*. 2018;4:18024. 2. Abou-Khalil. *Continuum (Minneap Minn)*. 2022;28(2):500-535. 3. Steinhoff et al. *Epilepsy Behav*. 2021;123:108270. 4. Chen et al. *Epilepsy Behav*. 2017;76:24-31. 5. 73rd Annual American Epilepsy Society Meeting 2019, Abstract #3.31. Poster presented November 25, 2019.

AE, adverse event; **ASM**, anti-seizure medication; **CNS**, central nervous system; **GABA**, gamma-aminobutyric acid; **MAD**, multiple ascending dose; **MedDRA**, Medical Dictionary for Regulatory Activities

BHV-7000: Summary and Clinical Program Status

- **Potent, selective activator of Kv7.2/Kv7.3 potassium channels**
- **Structurally/pharmacologically distinct** from other K+ channel activators
- **Designed to "dial out" $GABA_A$ receptor activation**, improve tolerability
- **Potent** in MES epilepsy model without adverse neurobehavior or motor effects
- **Well-tolerated** in Phase 1 SAD/MAD study
- **EEG study**; initial Phase 1 results confirm target engagement at both low and high doses of BHV-7000, full results expected YE 2023
- **Once daily dosing** with extended-release formulation

There is a missing piece in epilepsy treatment for better-tolerated, efficacious anti-seizure medications

CNS, central nervous system; **EEG**, electroencephalography; **GABA**, gamma-aminobutyric acid; **MAD**, multiple ascending dose; **MES**, maximal electroshock seizure; **SAD**, single ascending dose

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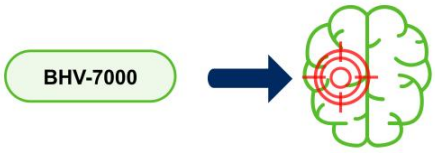
BHV-7000: Phase 1 EEG Study in Healthy Volunteers



Study Objective:

- Demonstrate BHV-7000 target engagement in the cerebral cortex and refine dose selection for Phase 3

Study Measures:

- Continuous EEG monitoring & PK sampling
- Evaluation of changes in EEG spectral power post dose

Study Design

EEG, electroencephalography; **PK**, pharmacokinetics; study ongoing in healthy volunteers

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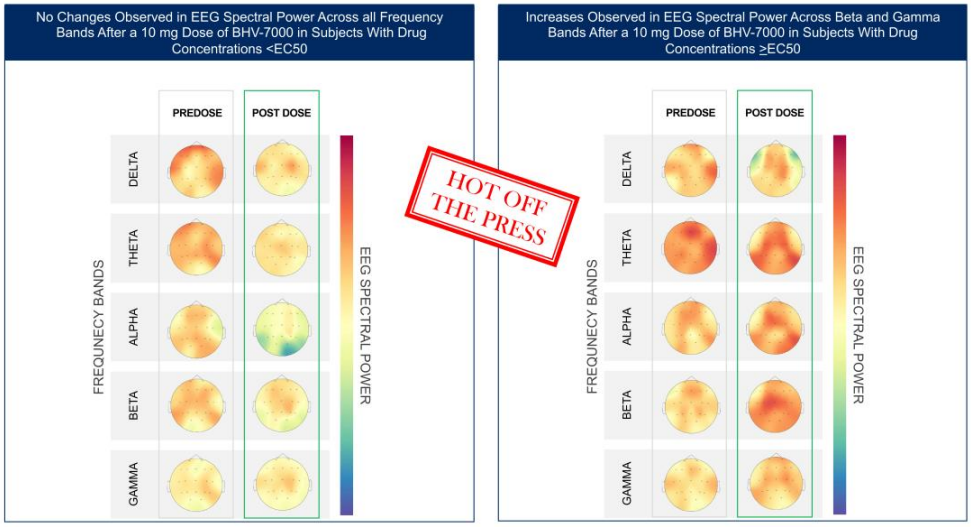
BHV-7000: Spectral Power Changes Observed After 10 mg Dose with Concentrations ≥ EC50



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

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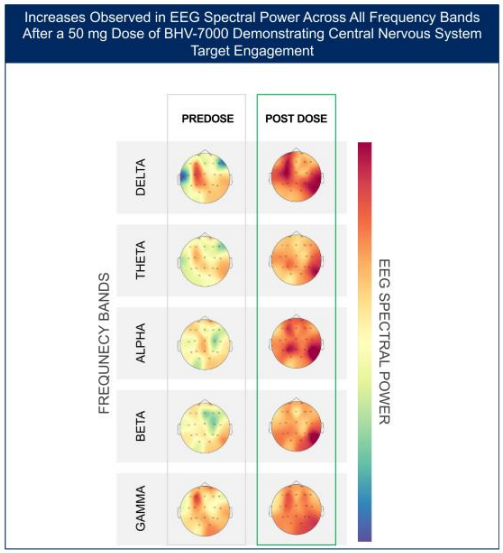
BHV-7000: Increases in Spectral Power Were Observed in all Frequency Bands and all Brain Regions After 50 mg Dose



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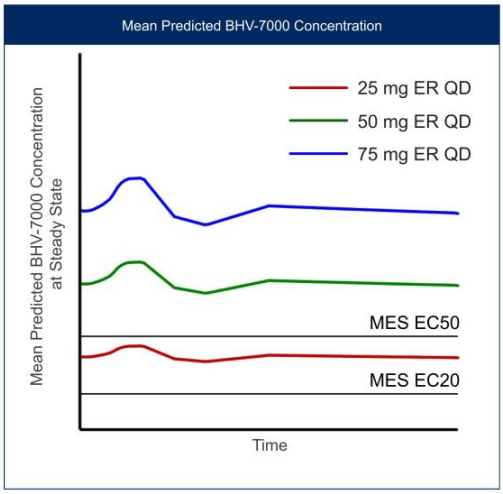
BHV-7000: Mean Predicted Concentration vs. Time Profiles of BHV-7000 Extended Release (ER) For 25 mg ER, 50 mg ER, 75 mg ER Once Daily Dosing at Steady State



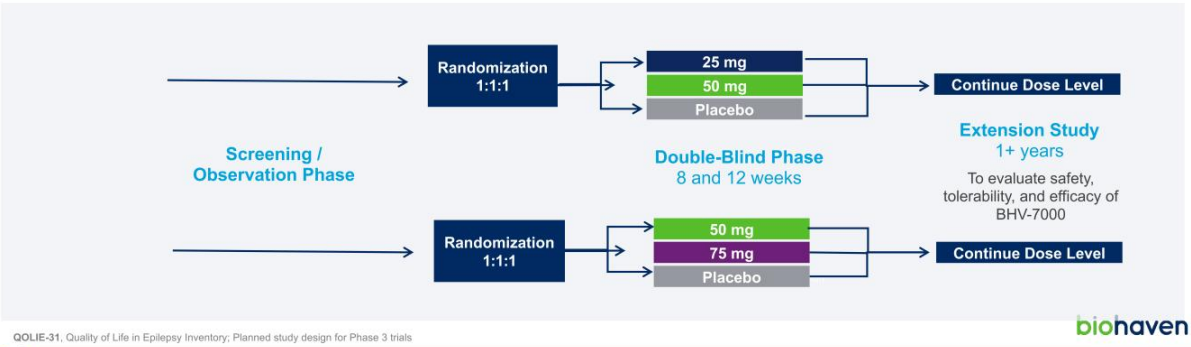
*EC20 and EC50 values from preclinical maximal electroshock seizure (MES) model

BHV-7000: Phase 3 Trials in Focal Epilepsy

Two multicenter, international, placebo-controlled, double-blind studies to evaluate the efficacy of BHV-7000 in adolescents and adults with refractory focal epilepsy

Key Inclusion Criteria:
- 12-75 years old
- Refractory focal epilepsy

Primary Endpoint: median percent change (US), ≥50% responder rate (EU)
Secondary Endpoint: QOLIE-31, Seizure Freedom



QOLIE-31, Quality of Life in Epilepsy Inventory; Planned study design for Phase 3 trials

Kv7 PLATFORM Summary

Proprietary Chemical Library of Novel Kv7 Activators
In-house synthesis with differentiated pharmacological and structural profiles and potential for multiple indications

Kv7.2/7.3 Activation
Clinically validated mechanism of action in epilepsy

BHV-7000: Potential Best-in-Class with Differentiation
Preclinical data suggests wide therapeutic index in the clinic by dialing out GABA risk (*somnolence, sedation, dizziness*)

BHV-7000 Series
COM Patent Protection covered until 2039 (*excl extensions*)

Once-daily, Extended-Release Formulation Identified

Status Update
BHV-7000 well tolerated in Phase 1 SAD/MAD study
CNS target engagement confirmed in EEG biomarker study
Phase 3 study initiation in Epilepsy & Bipolar Disorder expected YE 2023

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Bipolar Disorder Affects 11 Million Adults in the US

While characterized by mania, patients largely suffer from **depression**, yet **few effective options** for BPD and maintenance treatment[1-4]

~50% of patients are **medication nonadherent;** discontinuations commonly due to **poor tolerability**[4,5]

No new mood stabilizer approved in last 20 years excluding antipsychotics[6]

- Lamotrigine - last novel mood stabilizer approved; utility primarily in maintenance, limited efficacy in acute depressive episodes
- **Serious AEs** observed with current mood stabilizers (*thyroid/renal function issues, liver tox, thrombocytopenia, rash, SJS*[3,9])
- **Risks of metabolic dysfunction**, weight gain, and cognitive slowing
- **Adherence issues** lead to ineffective treatment and risk of relapse[5,7,8]

1. Tondo et al *Curr Neuropharmacol*. 2017;15(3):353-358. 2. Miller et al. *J Affect Disord*. 2014;169(Suppl 1):S3-11. 3. Carvalho et al. *N Engl J Med*. 2020;383(1):58-66. 4. McIntyre, Calabrese. *Curr Med Res Opin*. 2019;35(11):1993-2005. 5. Jawad et al. *Ther Adv Psychopharmacol*. 2018;8(12):349-363. 6. Rhee et al. *Am J Psychiatry*. 2020;177(8):706-715. 7. Fung et al. *J Affect Disord*. 2019;257:17-22. 8. Marzani, Neff. *Am Fam Physician*. 2021;103(4):227-239. 9. Bobo. *Mayo Clin Proc*. 2017;92(10):1532-1551.

AE, adverse event; **BD**, bipolar disorder

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Compelling Evidence for Kv7 Activation in Bipolar Disorder Treatment

Overlapping molecular, cellular mechanism in bipolar disorder

- ✓ ANK-3: highly implicated gene in bipolar disorder; codes for a protein that anchors Kv7 channels to the cell membrane[1]
- ✓ Kv7.2/7.3 channels among most dysregulated proteins in bipolar brain tissue[2]
- ✓ Bipolar patients exhibit several relevant epigenetic changes linked to Kv7[3]

Preclinical evidence for manic and depressive poles

- ✓ Mice who upregulate Kv7 are resilient to stress-induced depressive effects[4]
- ✓ Kv7 activators reverse & prevent pathologic hyperactivity in depression and mania models[5,6]
- ✓ Kv7 mutations cause transdiagnostic mood disturbances including hyperactivity, insomnia, anxiety, and cognitive dysfunction[1]

1. Judy et al. *Front Genet.* 2013;4:87. 2. Kristensen et al. *J Neurochem.* 2012;3:373-382. 3. Kaminsky et al. *Bipolar Disord.* 2015;2:150-159. 4. Friedman et al. *Nat Commun.* 2016;24(7):11671. 5. Dencker et al. *Behav Brain Res.* 2010;1:78-83. 6. Redrobe et al. *Behav Brain Res.* 2009;198(2):481-485.
ANK-3, ankyrin 3

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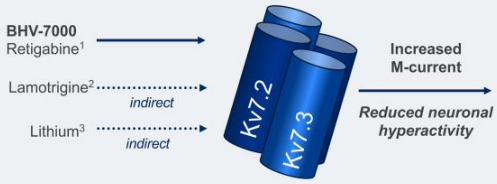
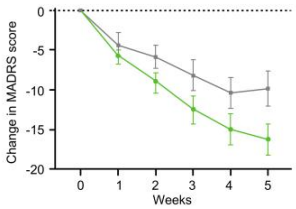
BHV-7000: Demonstrates Potential for Clinical Translation of Kv7 Activation in Bipolar Disorder

BHV-7000 shares mechanistic overlap with cornerstone bipolar treatments

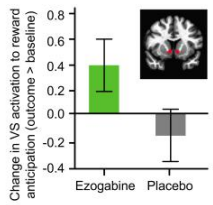


Robust Preliminary Acute Efficacy in MDD Likely To Translate to Bipolar Disorder

Retigabine vs placebo; MDD measured via MADRS and fMRI[4,5]



~7 decrease vs placebo with retigabine in depression improvement



fMRI study: Retigabine effects mediated by the limbic system

Medications such as antipsychotics and lithium have established efficacy in unipolar and bipolar depression

1. Friedman et al. *Nat Commun*. 2016; 24;7:11671, 2. Friedman et al. *Science*. 2014;344(6181):313-319. 3. Kristensen et al. *J Neurochem*. 2012;3:373-382. 4. Amann et al. *J Clin Psychopharmacol*. 2006;26(5):534-536. 5. Costi et al. *Am J Psychiatry*. 2021;178(5):437-446.
fMRI, functional magnetic resonance imaging; **GSK3B**, Glycogen Synthase Kinase 3 Beta; **MADRS**, Montgomery-Åsberg Depression Rating Scale; **MDD**, major depressive disorder

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BHV-7000: Potentially Addresses Key Unmet Needs in Bipolar Disorder by Reducing Stress-Related Hyperactivity While Enhancing Resilience

Currently Approved Products	BHV-7000
• **Minimal efficacy** • **Widely prescribed antidepressants carry "switching" risk**	✓ Novel mechanism - **potential for robust antidepressant effects** without "switching" risk
• **Patients change / discontinue medication** after ~2 months • **>50% of patients discontinue** at 6 months due to intolerance[1]	✓ **Favorable safety and tolerability** over current mood stabilizers and antipsychotics
• **1st line mood stabilizers require titration or frequent laboratory monitoring,** burdening both prescribers and patients[3]	✓ **No titration / safety laboratory monitoring** anticipated

1. Jawad et al. *Ther Adv Psychopharmacol.* 2018;8(12):349-363. 2. Vieta et al. *Nat Rev Dis Primers.* 2018;4:18008. 3. Yatham et al. *Bipolar Disord.* 2018;20(2):97-170.

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BHV-7000: Potential to Overcome Challenges With Existing Therapies

Potential for best-in-category tolerability and safety

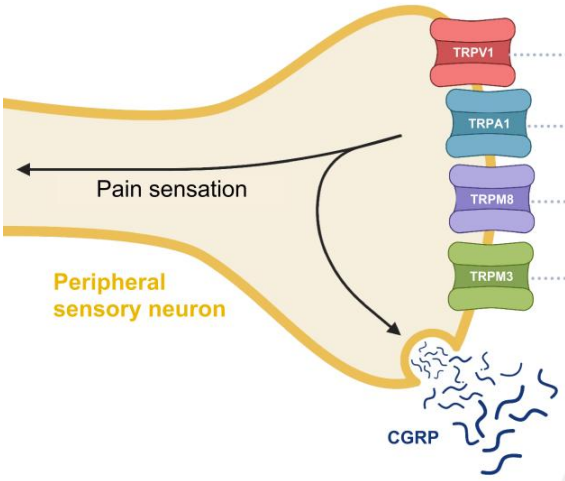
- Low burden to patients and providers, enabling safer, easier long-term treatment
- No expected long-term metabolic side effects, no “switching” risk, no titration, and no drug monitoring

	Lithium	Valproate	SSRI	Antipsychotics	Lamotrigine
Metabolic AEs				●	
Hepatic AEs		●			
Renal AEs	●				
Rash / SJS					●
Sexual SE			●		
Sedation / Cognitive AE	●	●		●	
Drug monitoring	●	●			
Switching risk			●	●	
Titration	●	●			●

● Patient Burden

SJS, Stevens-Johnson Syndrome

TRPM3: A Novel Peripheral Target for Neuropathic Pain



- X — **Oral class terminated for hyperthermia**
  No new molecules in this class despite promising
- ? — **Multiple TRPA1 programs terminated**
- ? — **Conflicting data for pro- and anti-nociceptive role;** remains in active drug development
- **Promising as a novel target:** broader expression than TRPV1 and TRPA1 in peripheral neurons; unlikely to affect body temperature homeostasis

2021: Nobel Prize in Physiology or Medicine awarded to David Julius and Ardem Patapoutian for their discovery of the cellular sensors of temperature and pressure

See Koivisto et al. *Nat Rev Drug Discov*. 2022;21(1):41-59 for background on TRP channel drug development.

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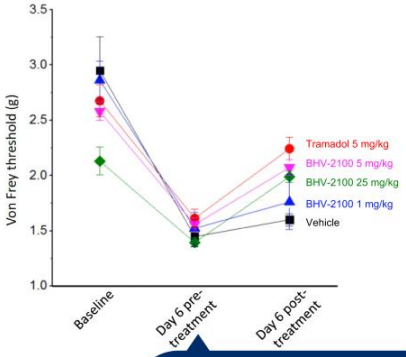
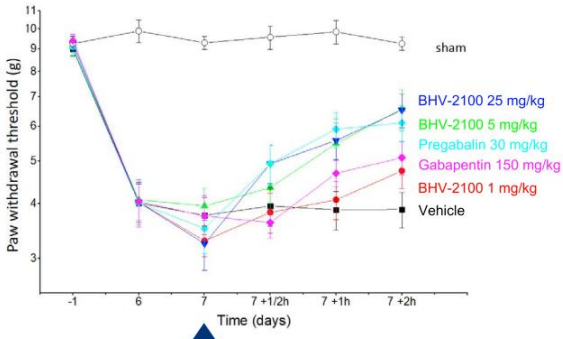
TRPM3 (BHV-2100) Reduces Pain in Preclinical Models of Chemotherapy and Diabetic Neuropathy

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



Drug administered 6 days after oxaliplatin in mice



Drug administered 7 days after diabetic induction with STZ in rats

Source: Biohaven data on file

BHV-2100: A Versatile Agent for Treatment of Multiple Pain Conditions

Unmet Need in Neuropathic Pain Disorders

>50% of patients with common neuropathic pain disorders (e.g., diabetic peripheral neuropathy) are **inadequately controlled even with 2+ medications** to attempt to control pain

Selective and Potent

Selective and potent inhibition of TRPM3 provides a **novel, non-opioid approach** to neuropathic pain treatment

Selectivity within TRP family, **avoids** potential class liabilities such as **hyperthermia**

Preclinical Data

Preclinical data shows potent **reversal of pain** in multiple translatable animal models

Molecular Characteristics

Molecular characteristics predict **convenient, safe** molecule with optimal target product profile for a **daily oral medicine**

Investigational New Drug filing planned for 2H 2023

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TYK2 (BHV-8000) Overview

First-in-Class Oral Brain-Penetrant TYK2/JAK1 Inhibitor
Uniquely potent, TYK2/JAK1 selective, brain penetrant inhibitor

Breaks the Cycle of Neuroinflammation
Reduces inflammatory impacts of microglia, astrocytes, & infiltrating T-lymphocytes

Potential in Multiple Neuroinflammatory Disorders
Strong evidence supports efficacy in Parkinson's disease, Alzheimer's disease, Multiple Sclerosis and other neuroinflammatory diseases

BHV-8000 Series
COM Patent Protection covered until 2037 (*excl extensions*)

Favorable PK/PD and Selectivity Profile
Avoids class risks associated with JAK2/3 inhibition

Encouraging Results from Ongoing FIH Phase 1 Clinical Trial
Multiple cohorts dosed in SAD portion of SAD/MAD study
Projected therapeutic concentrations achieved
BHV-8000 well tolerated, only mild adverse events reported

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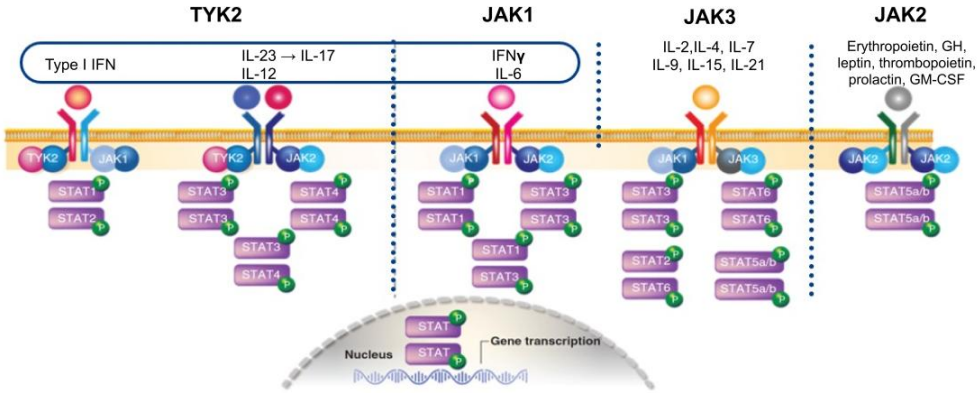
BHV-8000: TYK2/JAK1 in Neuroinflammatory Disease

- Dual inhibition of TYK2 and JAK1 can effectively block Th17 cell generation, Type I IFN signaling, and inflammation
- JAK inhibitors are more efficacious anti-inflammatory agents than anti-TNFs



Adapted from Gonciarz et al. *Immunotherapy* 2021;13(13):1135-1150.
GH, growth hormone; **GM-CSF**, granulocyte macrophage colony stimulating factor; **IFN**, interferon; **IL**, interleukin; **JAK**, Janus kinase; **STAT**, signal transducer and activator of transcription proteins; **Th**, T helper cell; **TNF**, tumor necrosis factor; **TYK**, tyrosine kinase

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Cellular Drivers In Neuroinflammation: Predominant TYK2/JAK1 Effects

Microglia

- **IFN-γ**

- IL-β
- TNF downstream of IFN-γ
- IL-8
- GM-CSF, MCP-1

Microglia are the resident macrophages of the CNS, playing an important role in neuroinflammation, repair and maintenance

Astrocytes

- **IFN-γ**
- **IL-12**

- TNF
- IL-8

Abnormal astrocytic activity may exacerbate inflammatory reactions and contribute to tissue damage

Lymphocytes, other leukocytes

- **IL-23**
- **IL-17 downstream of IL-23**

- IL-2, IL-4

Strong evidence for Th17 lymphocyte involvement in the pathogenesis of multiple sclerosis and Parkinson's disease

TYK2/JAK1 cytokines

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BHV-8000: Summary

Selectivity is a differentiator

- Selective inhibition of TYK2/JAK1 provides potential for best-in-class immunomodulation in neuroinflammatory disorders
- Selectivity for TYK2/JAK1 mitigates non-selective JAK class liabilities, largely related to JAK2 and JAK3 inhibition, and offers potential to improve benefit-risk for the highly selective BHV-8000 dual kinase inhibitor

Potential in multiple neuroinflammatory disorders

- Complements other approaches directly addressing neurodegeneration such as amyloid, α-synuclein, tau, and mitochondrial targeting therapies
- Strong evidence supports potential efficacy in Parkinson's disease, Alzheimer's disease, and further neuroinflammatory diseases

Clinical trials underway and anticipated in 2024

- Phase 1 initiated May 2023; multiple cohorts dosed in SAD portion of SAD/MAD study
- Phase 2 in Parkinson's disease anticipated to begin in 2024
- Partner (HighlightII Pharmaceuticals) anticipates initiating a study in Alzheimer's disease in China in 2024

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Properties of TYK2/JAK1 Selective Inhibitors Ideal for Treatment of Neuroinflammation

Brain penetrance

- Biologics are not brain penetrant
- Requires specially designed small molecule to reach site of action
- Existing agents exclude all lymphocytes from the CNS
  - TYK2/JAK1 inhibitor expected to selectively deplete CD4+ Th17 cells at the site of action

Dose-limiting tolerability issues of JAK2 and JAK3 inhibition minimized

- Serious cardiovascular events
- Severe immunosuppression
- Anemia, cancer, death

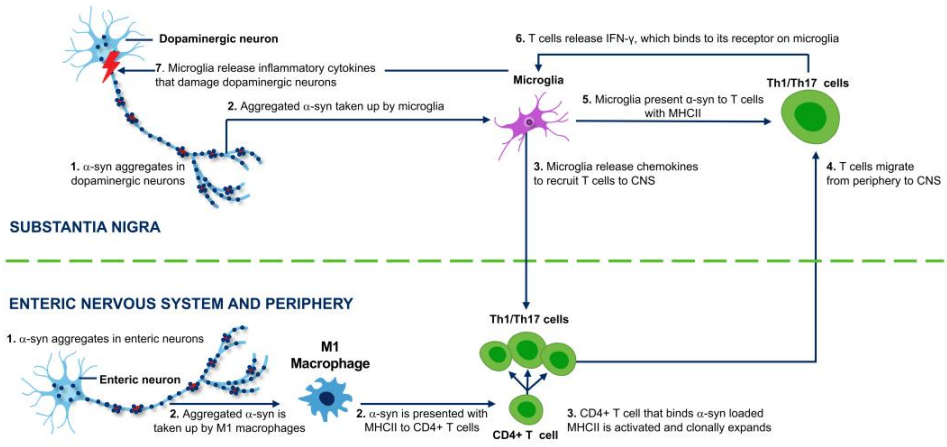
Small molecules allow convenient at-home, daily oral administration

Potential adverse events of central immunomodulation rapidly addressed following withdrawal vs. long exposure of biologics

BHV-8000: Targets Both Axes of Neuroinflammation in Parkinson's Disease

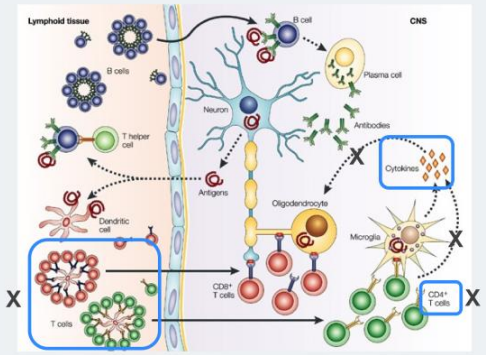
TYK2/JAK2 INHIBITION OF PARKINSON'S NEUROINFLAMMATORY CASCADE

TYK2/JAK1 inhibitors reduce Th17 cell activation and expansion by inhibiting IL-23 signaling and reduce microglial activation by inhibiting IFN-γ signaling triggered by pathogenic α-synuclein aggregates[1,2]



1. Allen Reish, Standaert. *J Parkinsons Dis.* 2015;5(1):1-19. 2. Fu et al. *J Neuroinflammation.* 2022;19(1):98.
α-syn, alpha-synuclein; **CD4**, cluster of differentiation 4; **CNS**, central nervous system; **IFN-γ**, interferon-gamma; **IL**, interleukin; **JAK**, Janus kinase; **M1**, classically activated; **MHC**, major histocompatibility complex; **Th**, T helper cell; **TYK**, tyrosine kinase

TYK2/JAK1 Inflammatory Pathways in Multiple Sclerosis



- Multiple sclerosis is an inflammatory disease in which humoral immune and cell-mediated immune responses target CNS antigens
- IL-17A-defective mice are highly resistant to induction of EAE
- PKM2 activators mediate potent inhibitory effects in EAE model due to Th17 cell effects
- In a meta-analyses of literature, TNF-α, IL-15, IL-12, IL-23/IL-17, and IFNγ were elevated in or predictors of MS patients vs. controls
- Secukinemab (IL-17A) demonstrates an effect in relapsing remitting MS
- Brain penetrant TYK2/JAK1 kinase inhibitors reduce **Th17 cells (IL-17 and IL-23)** and target IL-12 signal transduction
  - BHV-8000 is ideally suited to reducing **neuroinflammation** in MS

McGinley et al, Immunity 52:342-356, Palle et al, *Med Sci*, 5:23, 2017; Bai et al, *Frontiers in Neuroscience*, 10.3389, Oct 4, 2019, Havrdova, *Multiple Sclerosis Journal*, 18_509, 2012; Figure from *Nat Rev Neurosci.* 2002 Apr;3(4):291-301. doi: 10.1038/nrn784.

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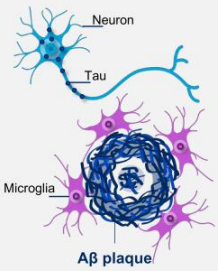
TYK2/JAK1 Inhibition Reduces Several Key Cytokines Driving Alzheimer's Disease (AD) Pathology

Neuroinflammation is a key event in AD pathogenesis, suggesting that a combination of anti-amyloid β (Aβ)/tau and anti-inflammation therapies is necessary[1,2]

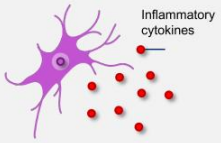
Neuroinflammation

- Cytokines and chemokines affect tau phosphorylation and amyloid β (Aβ) deposition

Aβ plaque deposition + tau accumulation



Microglia activation and release of cytokines



- Cytokines released include IL-1b, IL-6, TNF-α, and IFN- γ
- Aβ deposition also induces expression TYK2 and JAK1
- TYK2 is the most prominent gene altered by Aβ[3]

Synapse removal + cognitive decline

- Concomitant presence of Aβ, tau, and microglial activation abnormalities dramatically increases odds of cognitive symptoms[2]

Adapted from Neher. *Immunity*. 2022;55(5):821-823.

1. Domingues et al. *Curr Alzheimer Res*. 2017;14(8):870-882. 2. Pascoal et al. *Nat Med*. 2021;27(9):1592-1599. 3. Nevado-I et al. *Cells*. 2019;8:825.

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OBSESSIVE COMPULSIVE DISORDER (OCD)

- Compelling mechanistic rationale for cortico-striatal glutamate abnormalities in OCD patients
- Strong PoC in Phase 2
- Well-characterized in 1,000+ patients
- Two Phase 3 studies ongoing; enrollment completion anticipated YE 2023

Troriluzole in OCD: Framing the Unmet Need

OCD Affects

1.2% of the US population, but only 1 in 6 people with OCD are treated with a pharmaceutical medication

SSRIs are the only medication approved for OCD

Take weeks to months to take effect

Often need higher doses than for antidepressants, increasing dose-related side effects / do not work for everyone

Ketamine shown to have short-term efficacy; associated with stigma and undesirable side effects *(e.g., hallucinations, dissociative symptoms)*

Rapastinel also acts on glutamate system, shown in pilot study to reduce symptoms of OCD, anxiety, and depression within hours (*but lasted less than 1 week*)

Limited ongoing investigations in the treatment of OCD, predicting a paucity of new approved agents in the near future

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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

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

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

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Myostatin Platform
TALDEFGROBEP ALFA
BHV-2000

Non-Clinical

- Well characterized in over 20 animal studies for safety and models of disease
- Includes juvenile animals permitting the safety down to 2 years of age

Clinical

- In prior studies, 359 participants received taldefgrobep: 179 healthy participants and 180 participants with Duchenne Muscular Dystrophy 5-12 years old
- Administration by subcutaneous injections in the arm, thigh, and abdomen
- Demonstrated dose-dependent suppression of free serum myostatin
- MRI and DXA data was consistent with a positive beneficial effect on muscle health
- Generally safe and well-tolerated

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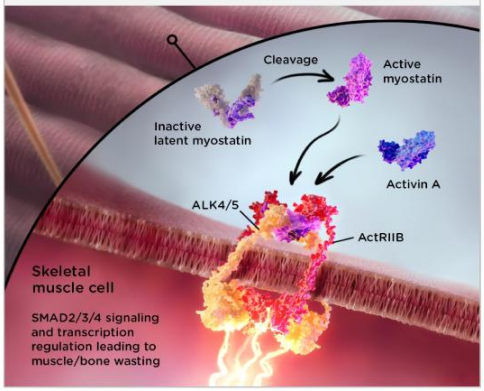
Myostatin and Activin A are Potent Muscle Regulators

Myostatin (GDF-8) is naturally expressed by skeletal muscle and actively inhibits skeletal muscle growth

Myostatin Negatively Regulates Muscle Growth

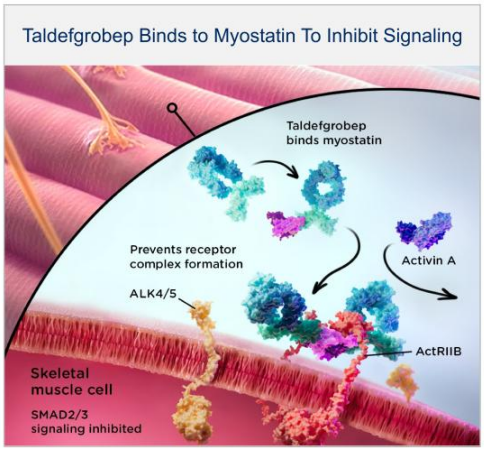


Blocking Myostatin and Activin A Leads to Muscle Hypertrophy

- Myostatin is a secreted protein belonging to the TGF-ß superfamily of signaling molecules
- Myostatin signals by binding initially to the activin type 2 receptors, ActRIIA and ActRIIB, which then engages the activin type 1 receptors, ALK4 and ALK5
- Genetic and pharmacological studies in multiple species, including humans, have shown that myostatin normally acts to block skeletal muscle growth
- The function of myostatin in muscle is partially redundant with that of the related protein activin A

Taldefgrobep Alfa: Differentiated Mechanism of Action

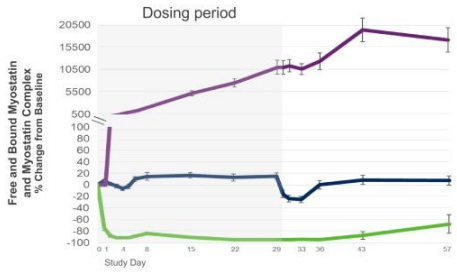
Only agent that reduces free myostatin and blocks receptor signaling



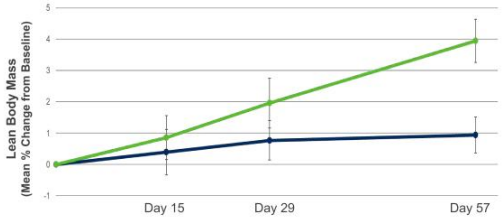
- Taldefgrobep is a fusion protein designed to have optimal affinity for myostatin and not other members of TGF-ß pathway
- Non-clinical studies show that taldefgrobep binds to myostatin at activin Type 1 receptor (ALK4/5) binding site and can inhibit signaling
- The complex taldefgrobep forms with myostatin inhibits both myostatin and activin A signaling in tissue where myostatin is active
- Potential for less off-target blockage of activin Type 2 receptor in non-muscular tissue

Taldefgrobep Alfa: Activity Confirmed in Human Studies

Myostatin Free and Drug Bound Levels



Increased Lean Body Mass



Decrease in Intramuscular Fat

- Healthy volunteers showed dose dependent increases in exposure and lowering of free myostatin when administered subcutaneously on a weekly basis for 4 weeks
- Accumulation of the taldefgrobep/myostatin complex drives competitive inhibition of free myostatin and activin A binding
- Participants demonstrated an increase in lean skeletal tissue (MRI) and increase in lean body mass along with a reduction of intramuscular fat volume (DXA)

Myostatin: Strong Scientific Rationale in Spinal Muscular Atrophy

COMBINATION THERAPY STUDIES OF SMN UPREGULATION IN SMA DISEASE MOUSE MODEL DEMONSTRATED:

- ✓ Improved life span and strength, along with improved muscle function
- ✓ Increased nerve branching, size of post-synaptic area, innervated neuromuscular junctions, enlarged sensory neurons in DRG

- SMA is a neurodegenerative disease; patients retain intact muscle as a target for improvements of function
- Disease modifying therapies approved and widely accessible and effective in SMA patients
- Disease area has well established validated clinical endpoints with proven regulatory path for approval

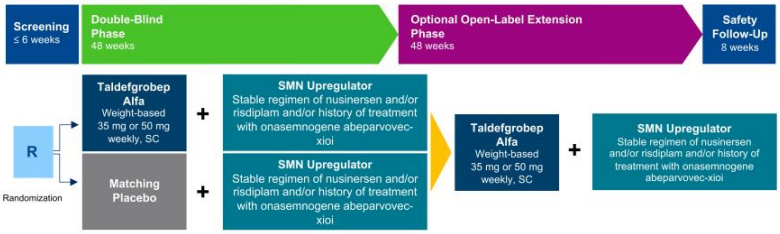
SMN, survival motor neuron; **DRG**, Dorsal root ganglia

Phase 3 RESILIENT Study Overview

RESILIENT Phase 3 Study Design

48-Week, Double-Blind, Placebo-Controlled Study in Pediatric and Adult Participants With Spinal Muscular Atrophy

- Estimated enrollment: 180 participants
- 2:1 randomization: taldefgrobep alfa vs placebo



PRIMARY OBJECTIVE

Change in the 32 item Motor Function Measure (MFM-32) total score between Baseline and Week 48

RESILIENT is a randomized, placebo-controlled trial testing the effectiveness and safety of taldefgrobep as an adjunctive treatment

Taldefgrobep, or a placebo, will be given while the participant is:

- Already taking a stable dose of **nusinersen and/or**
- Already taking a stable dose of **risdiplam and/or**
- Have a history of **onasemnogene abeparvovec-xioi**

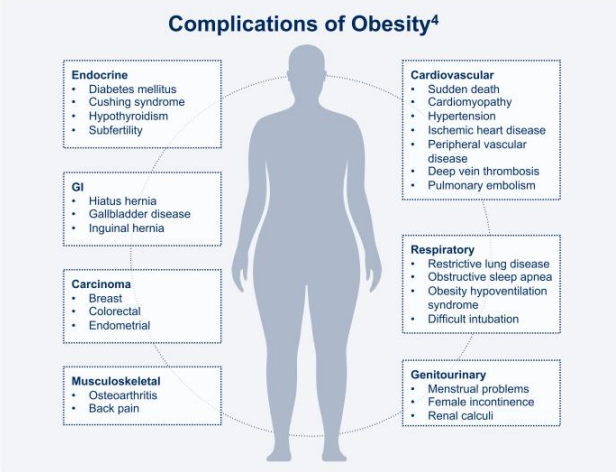
RESILIENT Study Population

- We include a broad population given high unmet need across SMA population, and changing treatment paradigms
- Field has evolved with disease modifying therapies and widespread newborn screening, early treatment, and potentially combinations of therapies
- Shift to focus more on functional status rather than SMA Type; treated patients are achieving milestones they would not have otherwise
- Approximately 180 participants with SMA are expected to enter the treatment phase

RESILIENT is not restricted nor limited to patients based on ambulatory status, background therapy, or classification of SMA

Obesity is a Public Health Crisis

- Obesity is a DISEASE of excess and/or abnormal adipose tissue
  - Cardio-metabolic risk is closely correlated with visceral adiposity
- By 2030, it is estimated that 1 billion people worldwide will be living with obesity, including ~50% of American adults[1]
  - Obesity and related comorbid disease costs the US healthcare system ~175 billion USD annually[2]
  - A small proportion of eligible individuals are currently being treated with anti-obesity medications (AOMs)[3]
- Treatment of obesity is an area of critical unmet medical need



1, The World Obesity Federation. World Obesity Atlas 2022. https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2022; Accessed 17-NOV-2022. 2, CDC. Adult obesity facts. https://www.gov/obesity/data/adult.html; Accessed 13-NOV-2022. 3. Saxon DR, et. al., Antiobesity medication use in 2.2 million adults across eight large health care organizations: 2009-2015. dPrimeau V, Coderre L, Karelis AD, Brochu M, Lavoie ME, Messier V, Sladek R, Rabasa-Lhoret R. Characterizing the profile of obese patients who are metabolically healthy. Int J Obes (Lond). 2011 Jul;35(7):971-81. doi: 10.1038/ijo.2010.216. Epub 2010 Oct 26. PMID: 20975726.

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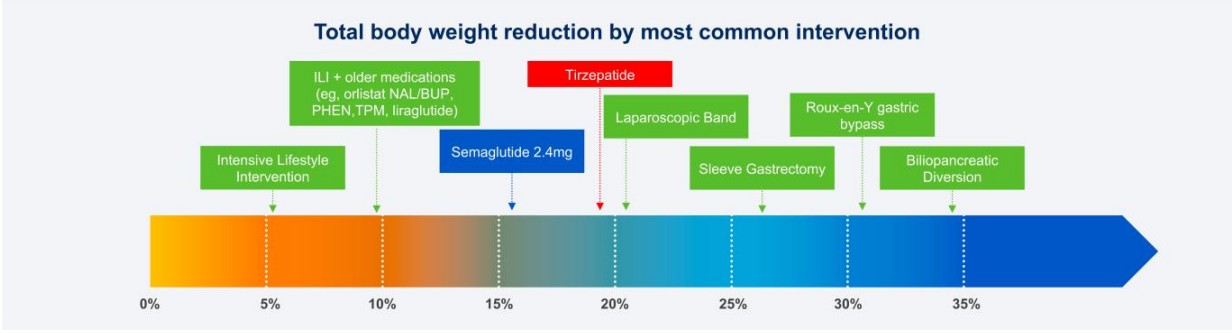
Entering a New Era of Hope and Opportunity for Adults Living with Obesity

- This is a time of rapid change and renewed excitement in the weight management space
- Highly potent anti-obesity medications (AOMs) and combination therapies are approaching efficacy outcomes comparable to bariatric surgery
- Competition in the weight loss space is intensifying but opportunities for disruption exist



Comparative Efficacy Outcomes in Adults Living with Overweight and Obesity

Drug	Dosing	Δ Total Body Weight	Δ Total Fat Mass	Δ Lean Body Mass	Δ A1C
Phentermine/ topiramate n=1,469	PO once daily	-7.8% to -9.8%	NA	NA	-0.4%
Naltrexone/ bupropion n=1,161	1-2 PO twice daily	-5.4%	-11.7%	NA	-0.6%
Bimagrumab n=37	IV Q4W	-6.5%	**-20.5%**	**+3.6%**	-0.76%
Semaglutide 2.4 n=1,306	SC QW	-14.9%	-19.3%	-9.7%	-1.6%
Tirzepatide n=1,896	SC QW	-20.9%	-33.9%	-10.9%	-2.3%
Sleeve Gastrectomy n=85	NA	-26.4%	-40.3%	-16.5% to -19.5%	-2.67%

- In the clinic, anti-myostatin therapies have repeatedly demonstrated the ability to increase lean mass, reduce fat mass, and improve glucose metabolism across diverse patient populations
- Improvements in body composition are optimized by those agents that can target both myostatin and activin A signaling

Qsymia USPI; Greenway FL, et. al. CCR-I. Lancet. 2010(9741):595-605; Contrave USPI (32/650mg); Heymsfield SB, et. al. JAMA. 2021; Wilding JPH, et. al. STEP1. NEJM 2021;384(11):989-1002; Wilding JPH, et. al. STEP 1 Body Composition. J Endocr Soc. 2021;5(1):A16-17; Wegovy USPI (STEP2); Jastreboff AM, et. al. SURMOUNT1. NEJM. 2022;387(3):205-16; Mounjaro USPI (15mg); Sylivris A. et. al. Obes Rev. 2022;23(7):e13422; Maimoun L. et. al. Surg Obes Relat Dis. 2019;15(11):1965-73; Zhang H-W, et. al. Gastric Bypass in Chinese w/ DM and obesity. Ann Transl Med. 2020;8(6):372-82; The Phase 2 bimagrumab study was conducted in adults living with obesity and Type-2 DM, while the Phase 3 phentermine/topiramate, naltrexone/bupropion, semaglutide, and tirzepatide studies were conducted in adults with overweight or obesity but no history of T2DM (unless otherwise specified). The time to analysis varies by asset, phentermine/topiramate (1 year), naltrexone/bupropion (56 weeks), bimagrumab (48 weeks), semaglutide (68 weeks), tirzepatide (72 weeks), sleeve gastrectomy (1 year). Notably, change in HbA1c data have been standardized (all representative of change seen in adults with overweight/obesity plus T2DM). In the tirzepatide (15mg) and semaglutide (1mg) studies, conducted in non-diabetic adults with overweight/obesity, the mean change in HbA1c was -0.52 and -0.52%, respectively; Represents cumulative mean change in fat mass across all tirzepatide dose levels. Abati E, Manni A, Comi GP, et. al. Inhibition of myostatin and related signaling pathways for the treatment of muscle atrophy in motor neuron diseases. Cell Mol Life Sci. 2022;79(7):374; Lee S-J. Targeting the myostatin signaling pathway to treat muscle loss and metabolic dysfunction. J Clin Invest. 2021;131(9):e148372

AM, morning; **BP**, blood pressure; **HDL**, high-density lipoprotein; **LDL**, low-density lipoprotein; **NA**, not available; **PO**, oral; **QW**, once weekly; **TC**, total cholesterol; **TG**, total glucose.

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Inhibiting Myostatin Signaling Demonstrates Important Physical and Metabolic Change

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

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

- Clinically, taldefgrobep has been generally safe and well-tolerated with low rates of GI and musculoskeletal complaints
- In healthy adults, taldefgrobep generated significant improvements in body composition relative to placebo

Advancing Taldefgrobep in Obesity

NOVEL MECHANISM TARGETING BODY COMPOSITION

Potential for combination with GLP-1 class

- Leveraging available pre-clinical and early clinical data allows for significant acceleration of development timelines
- Pre-IND meeting for obesity completed with FDA
- Proof-of-concept trial in adults living with overweight and obesity

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Myostatin Platform
TALDEFGROBEP ALFA
BHV-2000

Novel Mechanism of Blocking Myostatin and Activin A Signaling

- Human data showing potent reduction in free myostatin and accumulation of myostatin-taldefgrobep complex
- Short duration clinical studies demonstrated improvement in lean body mass and loss of adipose tissue

Advanced Development Program

- Large preclinical and clinical safety package licensed from BMS
- Existing database includes pediatric and adult clinical data
- Generally safe and well tolerated in multiple clinical studies

Spinal Muscular Atrophy (SMA)

- Single Pivotal Study launched in mid-2022
- Orphan Drug obtained in the US & EU; Fast-Track Designation in US
- Global Study; Enrollment Completed in 4Q 2023

Development Opportunities

- Attractive opportunity for metabolic disorders including obesity
- Additional neuromuscular, bone, and metabolic indications being evaluated

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A Pipeline of Therapies
Potential to support numerous clinical candidates spanning across a wide range of indications by targeting pathogenic proteins and antibodies

Potential First-in-Class Targeted Protein Degradation MOA
Provides unique advantages, e.g. accelerated path from discovery to clinic

BHV-1300
First-in-human MOA for efficient removal of pathogenic IgG with proven mechanism for autoimmune disorders

Galactose Deficient IgA1 Degradation
Novel antibody-based degrader for treatment of IgA nephropathy

Disease-Specific, Autoantibody-Targeted Degraders
Selective removal of autoantibodies implicated in multiple immune driven degenerative disorders

Highly competitive safety, manufacturable and PD profile

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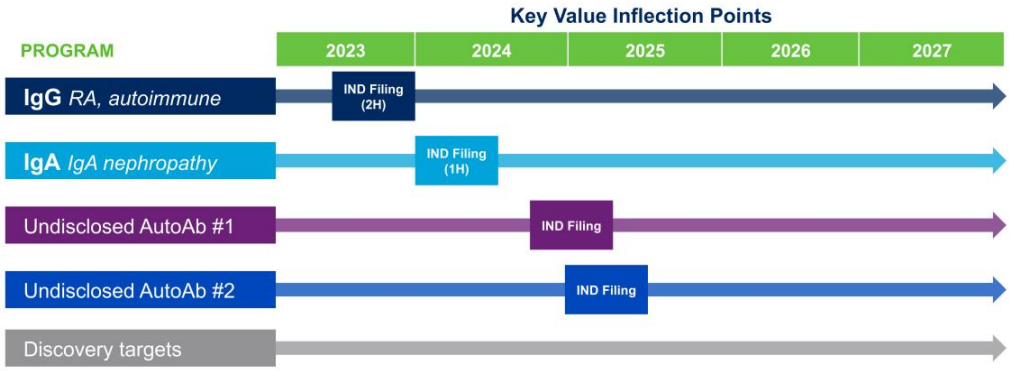
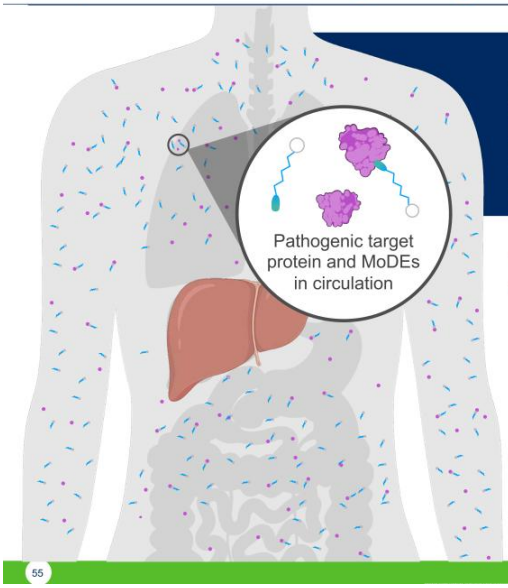
MoDE™ Degraders:
Multiple Asset Opportunities and Efficient Timelines

IgG and IgA antibodies are the first targets for Biohaven's powerful degradation platform



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

Bispecific Platform: IgG Degradation via MoDE™



Molecular Degraders of Extracellular Proteins (MoDE): small molecules bind extracellular target proteins and cause them to be removed from the body ***through the liver***

- Harnesses the body's own machinery for degrading proteins
- Extracellular protein targets are **eliminated** via the asialoglycoprotein receptor (ASGPR)

- Protein targets are degraded via endolysosomal proteolysis

* formerly BH 2640

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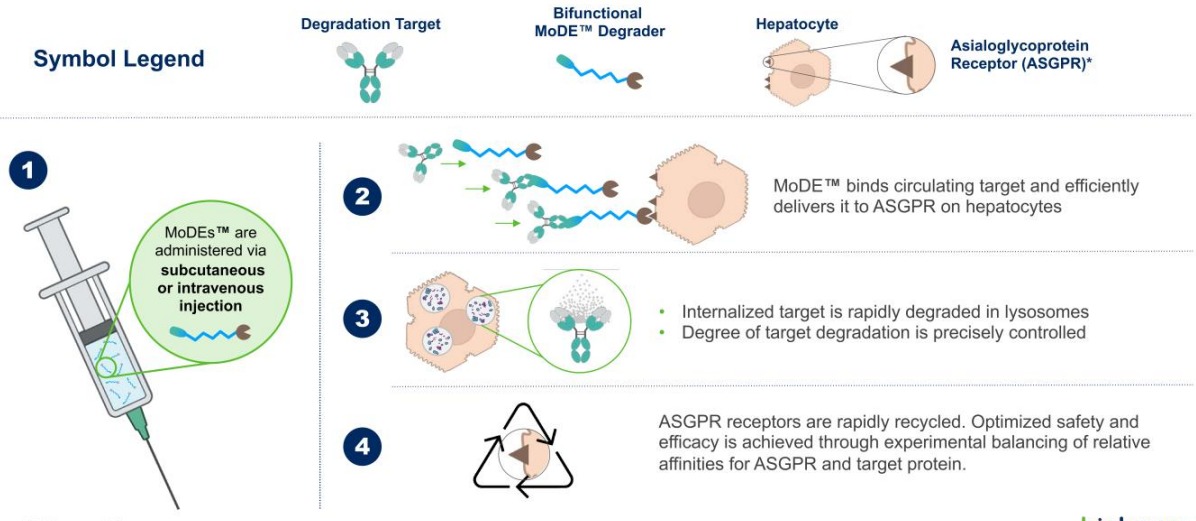
A First-in-Class Mechanism: Hepatic ASGPR Receptor Harnessed for Efficient and Safe Removal of Circulating Pathogenic Targets



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

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Hepatic ASGPR Receptor Harnessed for Efficient and Safe Removal of Pathogenic Targets

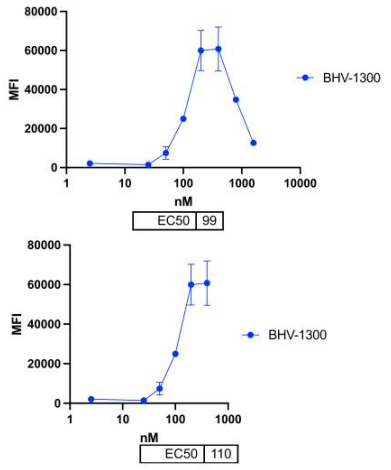
- High capacity ASGPR hepatocellular receptors internalize plasma proteins with specific motifs
- Bispecific ASGPR-binders with target-binder effectively removes pathogenic target from the circulation
- IgG may be more rapidly removed from the circulation than FcRN inhibitory antibody or antibody fragments, without causing hypoalbuminemia or dyslipidemia
  - Improved, dialable potency (deeper IgG/IgA reductions possible)
  - Improved pharmacodynamics (faster onset of action)
  - Improved safety profile (fewer side-effects, rapid drug elimination)

BHV-1300: A highly optimized Biohaven ASGPR binder advancing as drug candidate

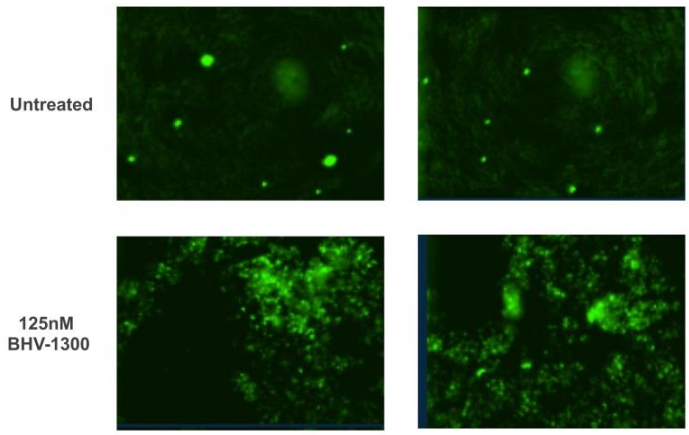
- ✓ Balances liver removal of unbound to target-bound drug
- ✓ Optimizes safety vs efficacy
- ✓ Improves kinetics of target removal
- ✓ Suitable Target Product Profile for a rapid onset medication with weekly or less frequent SC administration

In vitro BHV-1300 Mediates Removal, Uptake and Degradation of IgG

Uptake of IgG in HepG2



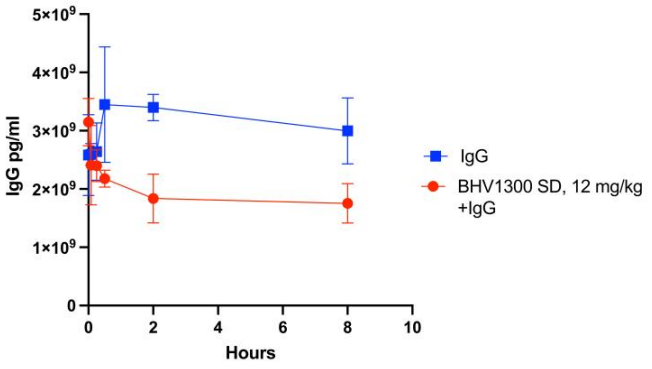
HepG2 cells internalize IgG-BHV-1300 complexes



BHV-1300 Selected for Remarkable Efficiency in Removal of Exogenously Administered Human IgG in Mouse Screen

Approximately 40% IgG removal achieved in 2 hours with a molar ratio of drug-to-target = 1.0

BHV-1300 human IgG depletion in mice, single dose 12 mg/kg



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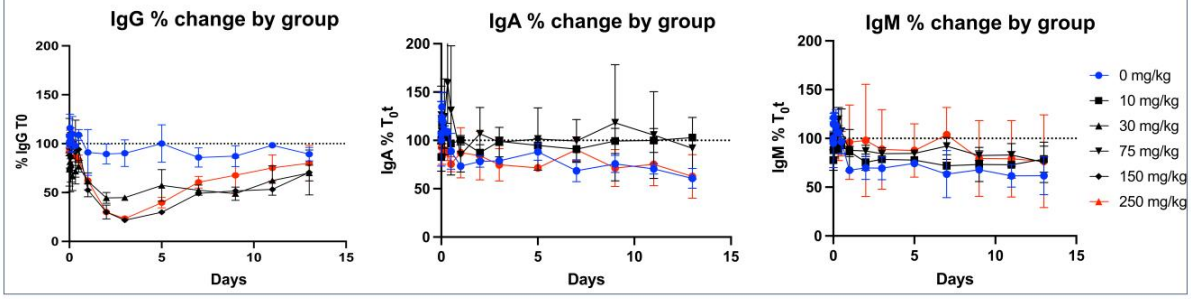
IgG is Specifically Depleted: IgA and IgM Levels Remain Unchanged

BHV-1300 administered IV to cynomolgus macaques



- Preliminary BHVN data and literature consistent with an absence of effects on serum albumin, LDL, HDL or triglycerides, and specificity for targeted IgG species
- Remarkable drug efficiency in mouse given exogenous IgG recapitulated in monkeys with endogenous IgG. Molar ratio of approximately 1.0 allows 60% IgG lowering following a single dose

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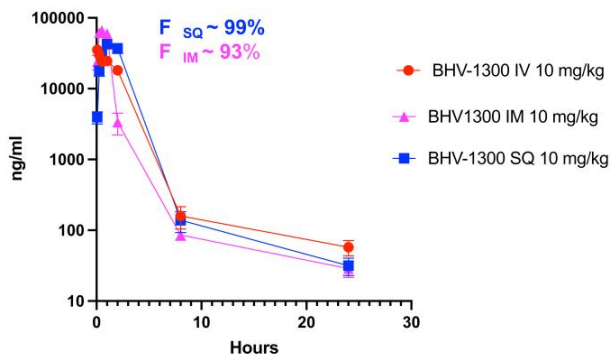
BHV-1300 Administered by SC, IM or IV Routes has Comparable Bioavailability

BHV-1300 levels in plasma after a single dose of 10 mg/kg in the presence of human IgG

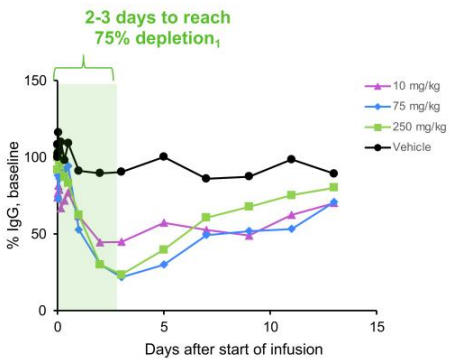


Potentially allows at-home, self administration with subcutaneous injection

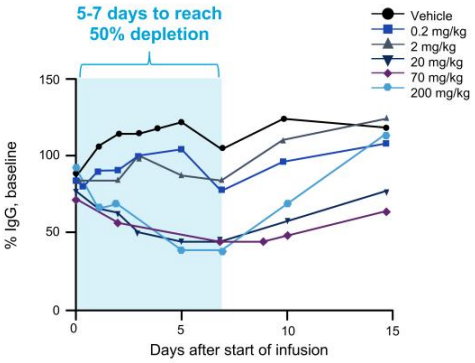
BHV-1300: Shows Potential for Superiority Over SOC (Efgartigimod)

BHV-1300 demonstrated faster depletion of IgG in a non-human primate (NHP) compared to efgartigimod

BHV-1300: NHP Pharmacodynamics



Efgartigimod: NHP Pharmacodynamics



1. deeper reductions (~90%+) possible with multiple dosing

The Journal of Clinical Investigation 2018:128(10):4372-4386. https://doi.org/10.1172/JC197911.
IgG, immunoglobulin G; **NHP**, non-human primate; **SOC**, standard of care

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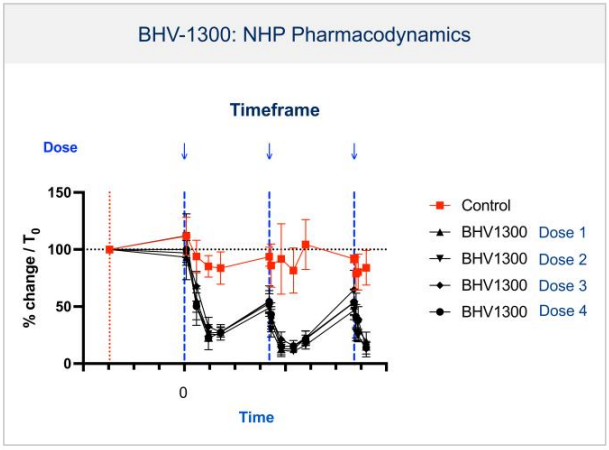
BHV-1300: Repeat dosing allows for deep reductions of over 90%



Combined results of multiple experiments suggests repeat dosing of BHV-1300 in cynomolgus can result in over 90% lowering of IgG

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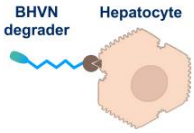
BHV-1300: Specific and Rapid Pathogenic Target Removal



BHV-1300 can specifically remove target IgG from circulation **faster than FcRn inhibitory antibodies, antibody fragments, or immunosuppressants**

- Mechanism not expected to cause hypoalbuminemia or dyslipidemia
- Improved and optimizable potency for target removal
- Deeper target removal when required
- Improved pharmacodynamics with faster onset of action than FcRn inhibition
- Improved safety profile expected (fewer side effects, rapid drug elimination)

FcRn, neonatal Fc receptor; **Ig**, immunoglobulin; **MoDE™**, molecular degrader of extracellular proteins

BHV-1300: Has Potential to Add Significant Value Across Rare And Common Diseases With a Differentiated Profile from FcRn Class

BHV-1300 DIFFERENTIATED FROM COMPETITORS
in FcRn class such as efgartigimod and nipocalimab with a **unique MOA, faster onset, and predicted to have improved safety**

PHASE 2 STUDY
Start in 2024

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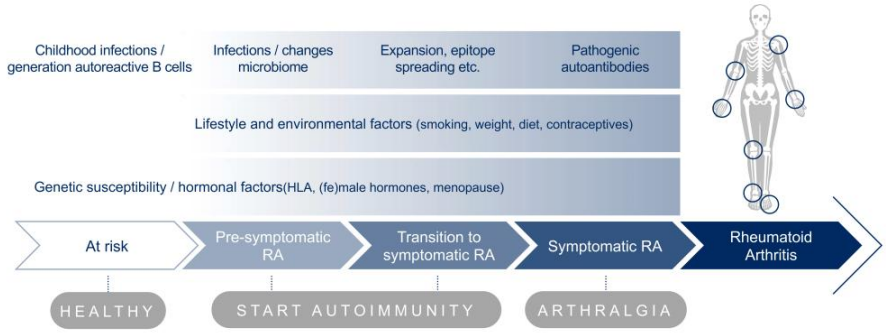
Rheumatoid Arthritis Is a Heterogenous Autoimmune Disorder Marked by Autoantibodies of Various Classes

Autoantibodies can start to accumulate 10 years prior to clinical arthritis[1]

THE ACR/EULAR DIAGNOSTIC CRITERIA INCLUDE[2]:

- 3+ joints involved
- Acute phase biomarkers of inflammation including elevated ESR and CRP
- Symptom duration
- Presence of RF and ACPA

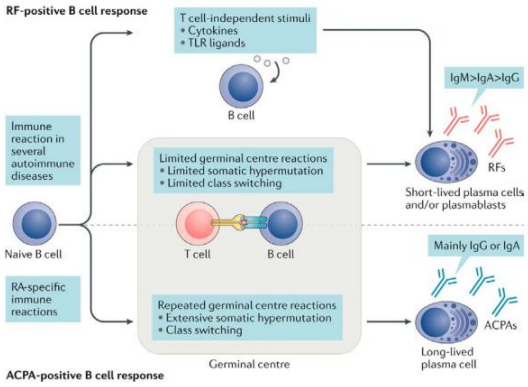
IgG+ ACPA in ~70% of RA population with increasing evidence they may be pathogenic in RA



Without effective and early intervention, inflammation and joint destruction lead to loss of physical function and extremely poor QoL
Additional health risks include elevated risk for cardiovascular disease, osteoporosis, and certain types of cancer (e.g., lymphoma)

1. Adapted from Van Delft and Huizinga, An overview of autoantibodies in rheumatoid arthritis; J *Autoimmun* 2020. 2. UpToDate accessed Jan 2023.

Exact Etiology of RA is Multifactorial With Environmental, Genetic, and T Cell Components, However Autoantibody Presence is a Main Feature



- **Rheumatoid Factor (RF)** antibodies are primarily IgM but form immune complexes with IgG
- **Anti-citrillunated protein antibodies (ACPAs)** including anti-cyclic citrullinated peptide-2 (anti-CCP2) are primarily IgG, but some IgA and IgM species exist
- All **immune complexes** can cause **damage** in joints, connective tissue in many organs, and bone
- **Comorbidities** from cardiovascular to malignancy need to be closely monitored
- In patients who are not in remission, **status every 4-12 weeks needed to tightly control severity** of flares and progression
- **An IgG degrader could remove a major component of these immune complexes without lowering B cell counts**

Figure adapted from Malmstrom and Gronwall, The parallel worlds of ACPA-positive and RF-positive B cells; *Nature Rev Rheum* 2018.

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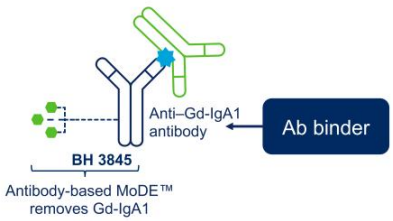
Preclinical Studies Show the Gd-IgA1–Specific MoDE™ Selectively Degrades the Gd-IgA1 Present in IgAN

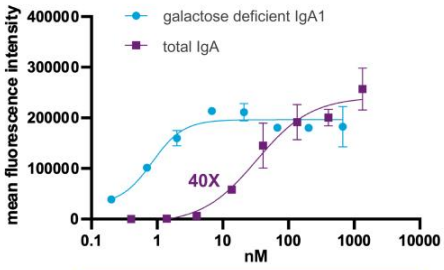
At low concentrations, this Gd-IgA1–specific MoDE™ selectively degrades Gd-IgA1 and spares total IgA, limiting the impact on the immune system

Gd-IgA1–Specific MoDE™



- Reduces only pathogenic Gd-IgA1
- Spares IgA, limiting immune impacts

Gd-IgA1–Specific MoDE™ Selectively Degrades Gd-IgA1



	EC_{50}
Galactose deficient IgA1	0.84
Total IgA	33

Ab, antibody; **EC_{50}**, half maximal effective concentration **Gd**, galactose-deficient; **Ig**, immunoglobulin; **IgAN**, IgA nephropathy; **MoDE™**, molecular degrader of extracellular proteins

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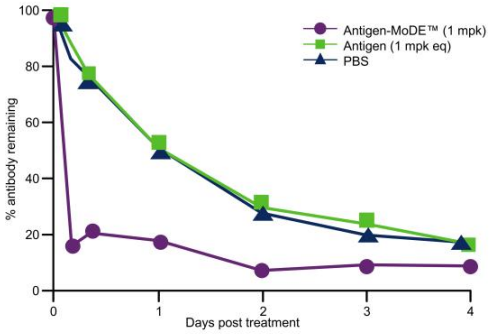
Leveraging Known AutoAb Epitope–MoDE™ Shows Rapid Reduction of Pathogenic AutoAb

Study Design

Greatly Reduced Half-life Compared to Controls	
Treatment	**Half-life (h)**
Antigen-MoDE™	**<2**
Antigen (Neg. Control)	27.5
PBS	29.7

Nearly Complete AutoAb Degradation in 4 Hours



Rapid, potent depletion with antibody half-life reduced by at least 15-fold

AutoAb, autoantibody; **MoDE™**, molecular degrader of extracellular proteins; **PBS**, phosphate-buffered saline

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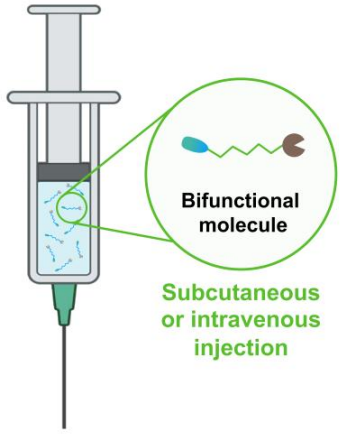
Summary: Biohaven MoDE™ Extracellular Degraders Provide Optionality



- ✓ **Numerous extracellular** and circulating **targets** are involved in pathology and make excellent targets
- ✓ **IND 2H 2023 for lead program BHV-1300** which has "pipeline in a product" potential
  - BHV-1300 has optimized chemistry with differentiated mechanism of action compared to standard of care, as well as to other novel agents in development
- ✓ Additional programs in development exploring targeting specific **autoantibodies** and **Gd-IgA1**
- ✓ **Once a target is identified, approximately ~1 year to degrader candidate**
  - Extracellular degrader as fast as 1.5-3 years to IND versus 6-10 years for typical small molecule program

Select ligand for valid target, conjugate → **Dev, discovery tox combined, pharmacology in parallel**

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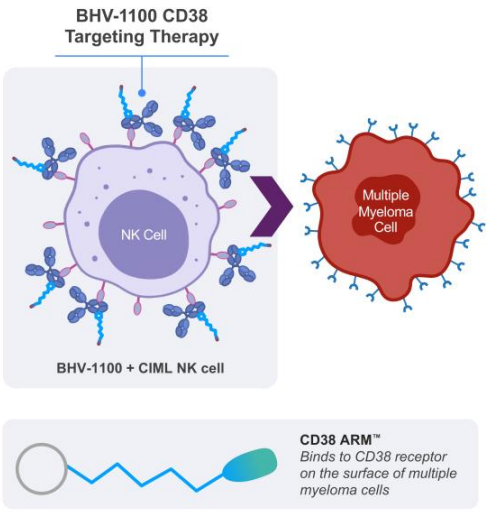
Bispecific Platform:
CD38 Targeted Cell Therapy for Multiple Myeloma

CD38 Antibody Recruiting Molecule (ARM™)

- Modular bispecific molecules with two moieties, each designed for non-covalent binding to a specific target
- Redirect endogenous antibodies to target cancerous or virally infected cells for immune destruction



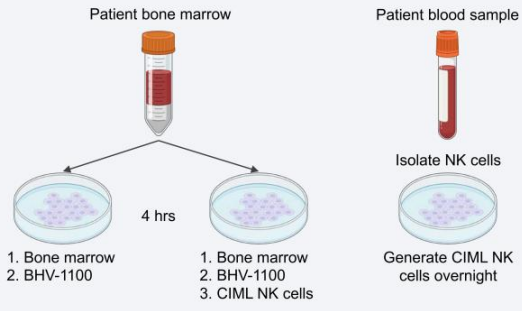
ARM

Key Potential Advantage Over Biologics

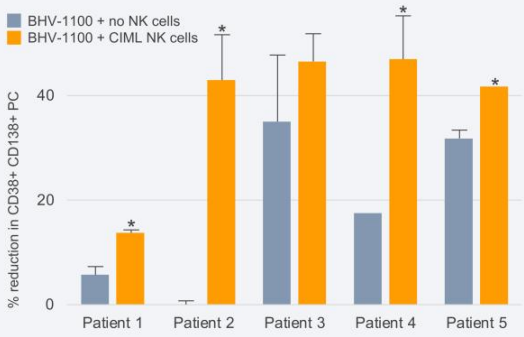
- ✓ Lower manufacturing cost
- ✓ More versatile — smaller and tunable
- ✓ Faster and less expensive to develop
- ✓ Better safety and efficacy
  - Non-immunogenic; better dosing
  - Enhanced PK properties
  - Reduced NK cell fratricide compared to daratumumab

Ex Vivo Patient Study: 4 Out of 5 Patients Showed Reduction in Plasma Cells (Multiple Myeloma)

Using patient bone marrow and a combination therapy



% reduction in plasma cells in patient bone marrow +/- autologous CIML NK cells in presence of BHV-1100



ONGOING CLINICAL STUDY

MRD + post-transplant multiple myeloma patients ongoing at Dana Farber Institute

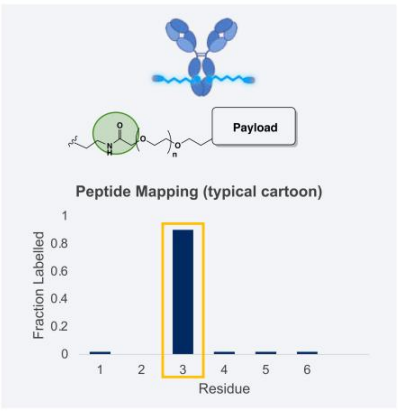
- First patient survival to one year
- Two additional patients randomized

Journal of Clinical Oncology 2020 38:15_suppl, 8523-8523.

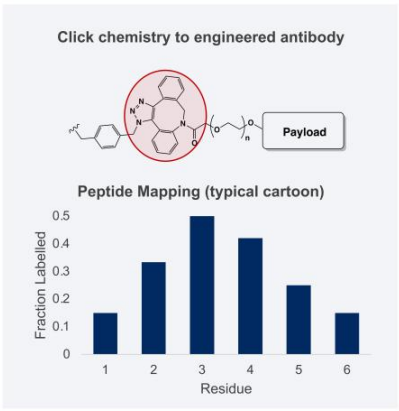
Bispecific Platform: Advancing Next-Generation, Site-Specific Antibody Drug Conjugates (ADCs)

Potential for best-in-class

Biohaven third-generation technology



Second-generation ADC-linker technologies



A single residue per heavy chain is available for conjugation

- **Controlled DAR* ratio is critical to therapeutic index**
- **MATE tech precisely defines DAR***

Improved linker stability should yield wider therapeutic index

- **Improved safety:** less systemic, untargeted payload
- **Improved efficacy:** targeted payload delivered to tumor

Uses native antibody: potentially improved CMC vs. current tech

*DAR = Drug antibody ratio

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Biohaven's Next-Generation Site-Specific ADCs

CONJUGATION CHEMISTRY SUPERIOR TO INDUSTRY STANDARD
maleimide and lipophilic click chemistry

Attachment 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 & 4 and manufacturable: Single step conjugation with predictable good yields, low aggregation
- ✓ **NOVEL IP** filed globally in key markets

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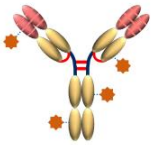
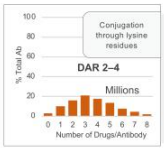
Challenges of Alternate ADC Protein Engineering and Chemistry

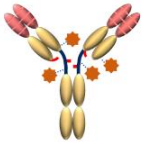
Kadcyla®

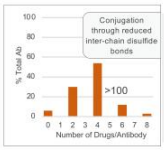




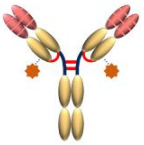
- High DAR species can cause CMC issues like aggregation, *in vivo* instability leading to toxicity
- Heterogeneity complicates CMC, may compromise efficacy

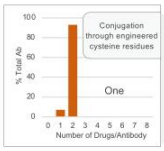
Adcetris®





- Drug linkage can reverse over time, "leaking" free payload





- Nearly all existing methods involve extensive antibody manipulation or engineering
- Potential impact on activity, clearance, immunogenicity, and COGs

DAR, drug antibody ratio

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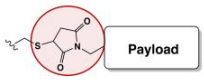
Potential “Best-in-class” Site-specific ADCs

Biohaven chemistry

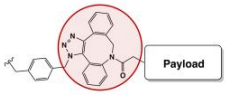
Stable, physicochemically benign amide linkage

Industry standard maleimide



Poorly stable linkage

Click chemistry to engineered antibody



Undesirably large, lipophilic linkage

IMPROVED LINKER STABILITY predicted to improve **therapeutic index**

- ✓ **Improved safety:** Reduced untargeted payload in systemic circulation driving toxicity
- ✓ **Improved efficacy:** Increased targeted payload reaches tumor, higher doses possible

USES NATIVE ANTIBODY

Likely improved CMC vs. current site-specific technologies

ADCs prepared based on Adcetris®

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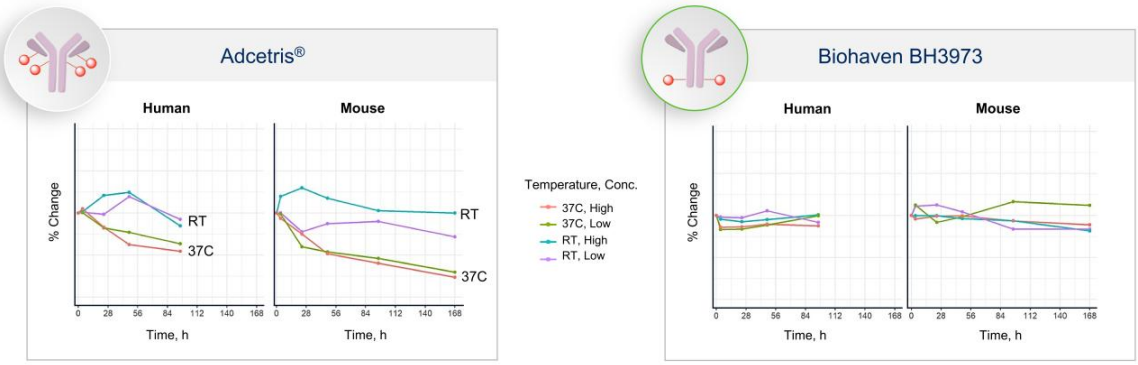
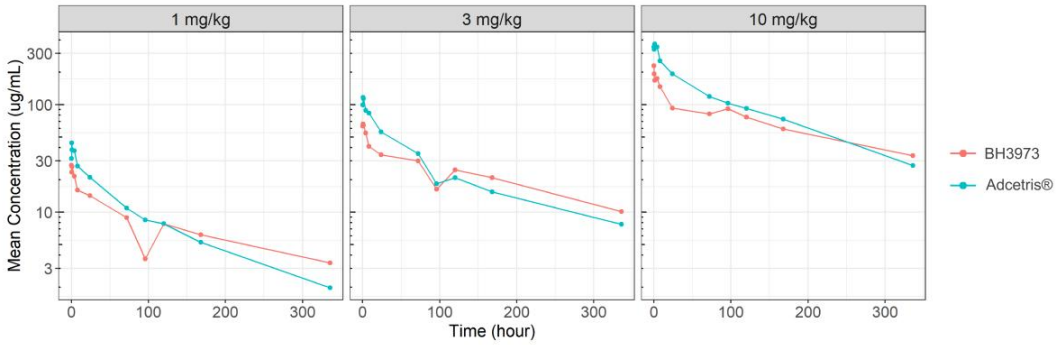
BH3973: Improved Plasma Stability Over Adcetris®



- ADC toxicity/tolerability directly relates to free payload
- Enhanced stability reduces free payload, and potentially allows for higher drug concentration at targeted tumor site for same tolerability

biohaven

Adcetris® and BH3973 Demonstrate Comparable PK



- BH3973 half-life 7-8 days across all doses
- Adcetris® half-life 5-6 days across all doses

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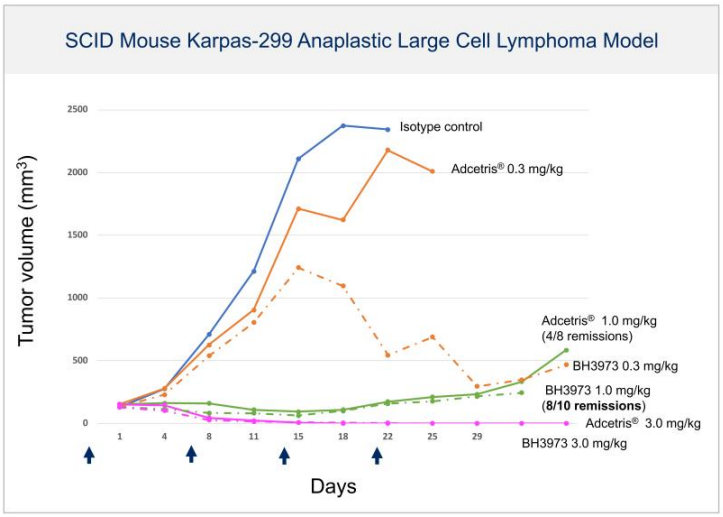
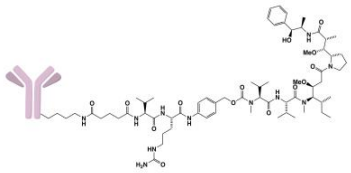
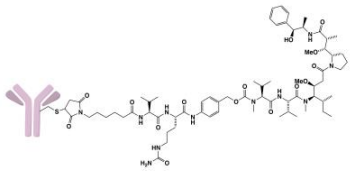
BH3973: Demonstrates Potential for Superior Efficacy to Adcetris®





BH3973 (DAR 2)



Adcetris® (DAR 3.8)

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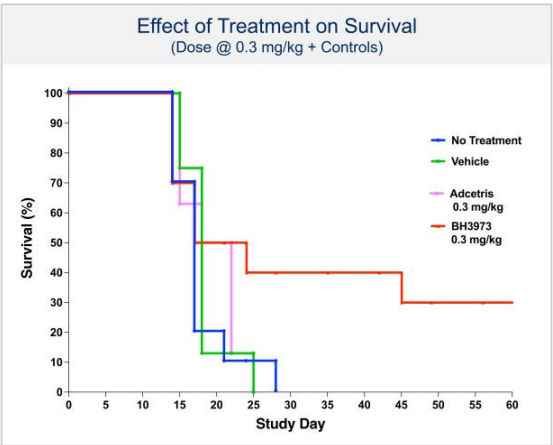
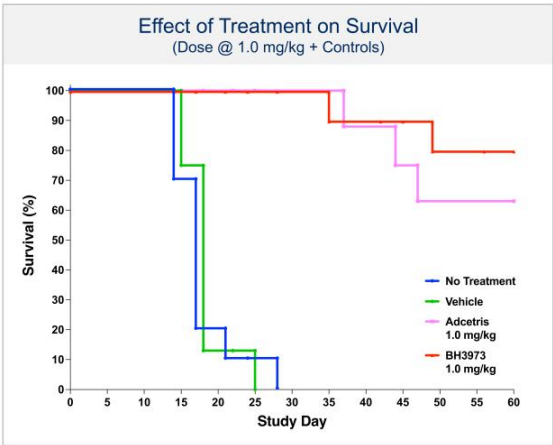
BH3973: Improves Survival in Preclinical Model Compared to Adcetris® With Half the Payload





BH3973: Summary

BIOHAVEN'S ADC TECHNOLOGY IS AN IDEAL ADD-ON TO IN-HOUSE DEVELOPED UNIQUE ANTIBODIES, BISPECIFICS

Even competitor molecules

- ✓ Existing, highly effective ADC formats such as Adcetris® and optimized warheads may potentially be enhanced with improved safety, efficacy, manufacturability and patent life
- ✓ Differentiated *in vivo* efficacy and safety results of BH3973 compared to Adcetris®
- ✓ Broad patent coverage

Capitalization Considerations

1. Excludes outstanding options. 2. As of July 27, 2023. 3. 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.*

Anticipated Near-Term Milestones

Milestone achieved

* Planning in progress | **PD**, Parkinson's disease