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): May 26, 2026

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 May 26, 2026, Biohaven Ltd. (the "Registrant") issued a press release reporting new clinical data in epilepsy with opakalim. A copy of this press release is furnished herewith as Exhibit 99.1 to this Current Report and is incorporated herein by reference.

On May 27, 2026, the Registrant issued a press release reporting positive clinical biomarker and patient data. A copy of this press release is furnished herewith as Exhibit 99.2 to this Current Report and is incorporated herein by reference.

On May 27, 2026, the Registrant made a presentation (the "Presentation") at its annual R&D Day held in conjunction with the Yale Innovation Summit at the Yale School of Management in New Haven, Connecticut. A copy of the Presentation is attached as Exhibit 99.3 to this Current Report on Form 8-K, and is incorporated herein by reference.

The information in this Current Report on Form 8-K, including the information set forth in Exhibits 99.1, 99.2 and 99.3 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	Press Release, Dated May 26, 2026, "Biohaven Reports New Clinical Data in Epilepsy with Opakalim, a Selective Kv7.2/7.3 Activator, Highlighting Seizure Control and Markedly Differentiated Tolerability Profile"
99.2	Press Release, Dated May 27, 2026, "Biohaven Reports Positive Clinical Biomarker and Patient Data: First MoDE and TRAP Extracellular Protein Degraders Achieve Deep, Rapid, Selective Lowering of Disease-Driving Antibodies in Graves' Disease and IgA Nephropathy"
99.3	Investor Presentation, May 2026.
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: May 27, 2026

Biohaven Ltd.

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

Exhibit 99.1

Biohaven Reports New Clinical Data in Epilepsy with Opakalim, a Selective Kv7.2/7.3 Activator, Highlighting Seizure Control and Markedly Differentiated Tolerability Profile

- In a randomized, placebo-controlled, time-to-event trial in idiopathic generalized epilepsy (IGE), the median time to the second day with a generalized tonic-clonic seizure was 141 days in the opakalim 75 mg once-daily treatment group vs. 47 days in the placebo group, representing a 3-fold prolongation.
- In an ongoing open-label extension (OLE) study in focal epilepsy, an updated data analysis shows 54% of patients with focal epilepsy on opakalim 75 mg once-daily achieved a ≥50% reduction in seizure frequency over any consecutive six months of open-label treatment compared to pre-randomization baseline.
- A six-month update of opakalim compassionate use treatment in a Kv7-activation dependent patient with KCNQ2-Developmental and Epileptic Encephalopathy (KCNQ2-DEE) confirms clinical stability and ongoing seizure control. Overnight EEG at 6-months demonstrated a 50% reduction in seizure counts relative to pre-opakalim baseline.
- Opakalim has been well-tolerated across all studies (1000+ subjects to date) with a low incidence of adverse events (AEs) comparing favorably with approved and investigational antiseizure medicines.
    - In the IGE study, the opakalim group reported no cases of somnolence, dizziness, fatigue, or memory impairment; and in the focal epilepsy OLE study, rates of these central nervous system (CNS) AEs were less than or equal to 5% each.
    - Opakalim's tolerability profile is markedly differentiated from that of other investigational Kv7 activators reporting double-digit rates of CNS AEs in OLE studies.
- On track to receive top-line results in 2H 2026 from the first of two pivotal Phase 2/3 randomized, double-blind, placebo-controlled studies in refractory focal epilepsy to support registration.

NEW HAVEN, Conn., May 26, 2026 /PRNewswire/ -- Biohaven Ltd. (NYSE: BHVN), a global clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of life-changing therapies to treat a broad range of rare and common diseases, today reported new data from its selective Kv7.2/7.3 channel activator program, currently in Phase 2/3 studies for the treatment of focal epilepsy, and will present additional updates at its annual R&D Day held in conjunction with the Yale Innovation Summit at the Yale School of Management in New Haven, Connecticut on May 27, 2026. Opakalim is distinguished from other investigational Kv7 activators by its selectivity for Kv7.2/7.3 and lack of GABA receptor activity. Opakalim offers potential for easy-to-use, once-daily, orally-administered treatment without the need for titration to control seizures, and without the burdensome central nervous system (CNS) side effects frequently reported with approved and investigational antiseizure medicines (ASMs).

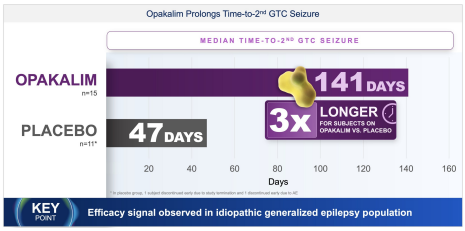


Figure 1: Opakalim 75 mg Once-Daily Prolongs Time-to-2nd Generalized Tonic-Clonic Seizure in Randomized, Double-blind, Placebo-Controlled, Time-to-Event Proof-of-Concept Trial in Idiopathic Generalized Epilepsy with Generalized Tonic-Clonic Seizures

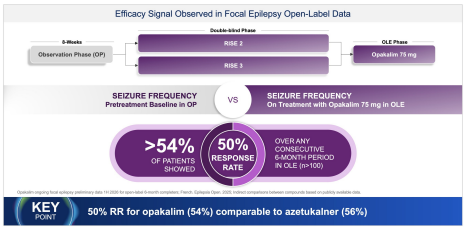
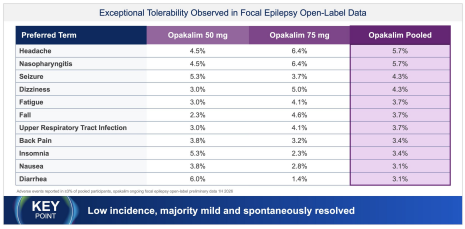


Figure 2: Updated Analysis From the Ongoing Open-Label Extension Study in Focal Epilepsy Shows 54% of Patients on Opakalim 75 mg Once-Daily Achieved a ≥50% Reduction in Seizure Frequency Compared to Pre-Randomization Baseline



Preferred Term	Opakalim 50 mg	Opakalim 75 mg	Opakalim Pooled
Headache	4.5%	6.4%	5.7%
Nasopharyngitis	4.5%	6.4%	5.7%
Seizure	5.3%	3.7%	4.3%
Dizziness	3.0%	5.0%	4.3%
Fatigue	3.0%	4.1%	3.7%
Fall	2.3%	4.6%	3.7%
Upper Respiratory Tract Infection	3.0%	4.1%	3.7%
Back Pain	3.8%	3.2%	3.4%
Insomnia	5.3%	2.3%	3.4%
Nausea	3.8%	2.8%	3.1%
Diarrhea	6.0%	1.4%	3.1%

Figure 3: Updated Safety Data From the Ongoing Open-Label Extension Study in Focal Epilepsy Demonstrates Opakalim Is Well-Tolerated With a Markedly Lower Incidence of Adverse Events Compared to Approved and Investigational Antiseizure Medicines.

The R&D Day presentation will showcase new and updated clinical data from: 1) a randomized, double-blind, placebo-controlled proof-of-concept study in idiopathic generalized epilepsy (IGE); 2) an ongoing

focal epilepsy open-label extension (OLE) study; and 3) a six-month clinical update for a pediatric patient with KCNQ2 Developmental and Epileptic Encephalopathy (KCNQ2-DEE). Together, these emerging data reinforce opakalim's target engagement, differentiated profile and potential to address the unmet need for novel, effective, and well-tolerated ASMs.

Jason Lerner, M.D., Medical Director, Research & Development and Epilepsy Development Lead at Biohaven, commented, "The opakalim data across IGE, focal epilepsy and KCNQ2-DEE are consistent and compelling. What stands out is not just that opakalim controls seizures — it's that it does so without the burdensome side effects that compromise quality of life and adherence for people with epilepsy. Dizziness, somnolence, fatigue, and memory impairment are reported in meaningful proportions of patients on existing and investigational ASMs. Opakalim's zero rates of somnolence, dizziness, fatigue, and memory impairment in our small IGE proof-of-concept study, and single-digit rates of CNS adverse events in our focal epilepsy program suggest that selective Kv7.2/7.3 activation is a fundamentally different and cleaner mechanism. I believe opakalim can offer people with epilepsy real seizure control without asking them to compromise their quality of life."

Efficacy Signal in Highly Treatment-resistant IGE Population

Biohaven to present results from a randomized, double-blind, placebo-controlled, time-to-event proof-of-concept study evaluating opakalim 75 mg once-daily in subjects with IGE with intractable GTC seizures (NCT06425159). The study's prespecified primary outcome measure was defined as the time to the second day with a GTC seizure during the 24-week double-blind treatment period. The study enrolled a total of 27 subjects (15 in the opakalim arm and 12 in the placebo arm). Formal statistical testing is not provided, as this proof-of-concept study was closed prior to reaching the study's prespecified sample size, due to enrollment challenges and strategic portfolio prioritization. The observed efficacy and tolerability signals are consistent with opakalim's mechanism and broader clinical dataset.

Key Findings:

- Median time to second GTC seizure during the 24-week double-blind treatment period: 141 days on opakalim vs. 47 days on placebo, a 3-fold prolongation of time to second seizure event (Figure 1).
- 33% of opakalim-treated subjects completed the 24-week double-blind phase without a second GTC seizure vs. 0% of placebo subjects.
- 20% of opakalim-treated subjects completed the 24-week double-blind phase seizure-free vs. 0% of placebo subjects.
- Opakalim was well-tolerated with remarkably low rates of nervous system adverse events (AEs) including somnolence, dizziness, and fatigue — AEs that collectively occur in more than one-third of patients on competitor investigational Kv7 activator in long-term studies, and at even higher rates with approved ASMs.

Efficacy Signal and Differentiated Safety Profile in Focal Epilepsy OLE

Biohaven to also report updates from its focal epilepsy program, including a recent data analysis from the ongoing open-label extension study of opakalim in subjects with refractory focal epilepsy (NCT06443463). As of 1H 2026, the double-blind study completion rates were 95%; and rollover rates in the optional open-label extension were 95%, reflecting subject and investigator confidence in opakalim.

Key Findings:

- In the opakalim 75 mg once-daily, six-month completers cohort (n>100), 54% of subjects achieved a ≥50% reduction in seizure frequency over any consecutive six months of OLE treatment compared to pretreatment baseline prior to randomization (Figure 2). This result is on par with the ≥50% responder rate reported for the investigational Kv7 activator azetukalner (56%), but opakalim achieves this comparable level of seizure control with a substantially lower burden of CNS AEs, including markedly lower rates of dizziness, somnolence, fatigue, and memory impairment.
- The AE profile was favorable and consistent with prior data, with a markedly lower incidence of AEs compared to approved and investigational ASMs (Figure 3). For example, in opakalim-treated subjects (75 mg), dizziness was reported in only 5.0% of subjects. By contrast, published long-term data from a competitor's Kv7 activator shows its open-label extension study reported dizziness in 25%, somnolence in 17%, memory impairment in 11%, and falls in 15% of subjects. These data suggest opakalim's selective Kv7.2/7.3 activation without GABA effects may translate into a meaningfully cleaner CNS tolerability profile than other ASMs.

Clinical Stability and Ongoing Seizure Control in Kv7-Dependent KCNQ2-DEE Patient

Biohaven to further provide a six-month update for the 9 year-old boy with refractory epilepsy due to KCNQ2-DEE being treated with compassionate use opakalim. The patient had a history of daily tonic seizures despite three concurrent ASMs, including a first-generation Kv7 activator, with prior attempts to taper first-generation Kv7 resulting in status epilepticus, ICU admission, and developmental regression. Following compassionate use authorization under a single-patient IND approved by the FDA, he was transitioned to opakalim at exposures calibrated to match the 75 mg dose being studied in the pivotal focal epilepsy trials.

Key Finding:

- Now at the six-month mark, the patient remains clinically stable. Overnight EEG at six-months demonstrated a 50% reduction in seizure counts relative to pre-opakalim baseline. Opakalim has been well-tolerated over the six-month treatment period.

Biohaven is on track to announce in 2H 2026 top-line results from the first of two pivotal Phase 2/3 randomized, double-blind, placebo-controlled studies in refractory focal epilepsy to support registration.

About Opakalim

Opakalim (BHV-7000) is Biohaven's next-generation, selective Kv7.2/7.3 potassium channel activator that targets a clinically validated mechanism of action for the treatment of epilepsy. Opakalim is differentiated from both first- and second-generation Kv7 activators by its selectivity: it preferentially activates the Kv7.2/7.3 heteromeric channels that are the predominant regulators of neuronal excitability, with substantially less activity at GABA receptors. This selectivity profile is hypothesized to underlie opakalim's favorable tolerability, including the low rates of somnolence, dizziness, and fatigue observed in clinical studies to date. Opakalim has been studied in more than 1,000 subjects across multiple clinical trials, consistently demonstrating a favorable tolerability profile. Biohaven is currently conducting two Phase 2/3 randomized, double-blind, placebo-controlled studies (NCT06132893 and NCT06309966) comparing the efficacy of opakalim to placebo as an adjunctive therapy for refractory focal onset epilepsy, as well as an open-label extension study (NCT06443463) to evaluate the long-term efficacy and safety of opakalim.

About Biohaven

Biohaven is a biopharmaceutical company focused on the discovery, development, and commercialization of life-changing treatments in key therapeutic areas, including immunology, neuroscience, and oncology. Biohaven is advancing its innovative portfolio of therapeutics, leveraging its proven drug development experience and multiple proprietary drug development platforms. Biohaven's extensive clinical and preclinical programs include Kv7 ion channel modulation for epilepsy; MoDE™ and TRAP™ extracellular protein degradation for immunological diseases; and myostatin inhibition for neuromuscular and metabolic diseases, including obesity. For more information, visit www.biohavenpharma.com.

Forward-Looking Statements

This news release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The use of certain words, including "continue", "plan", "will", "believe", "may", "expect", "potentially", "groundbreaking" 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 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, including the studies of opakalim; the timing of planned interactions and filings with the FDA; the timing and outcome of expected regulatory filings; complying with applicable US regulatory requirements; the potential commercialization of Biohaven's product candidates; and the effectiveness and safety of Biohaven's product candidates. Additional important factors to be considered in connection with forward-looking statements are described in Biohaven'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 news release, 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.

MoDE and TRAP are trademarks of Biohaven Therapeutics Ltd.

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Exhibit 99.2

Biohaven Reports Positive Clinical Biomarker and Patient Data: First MoDE and TRAP Extracellular Protein Degraders Achieve Deep, Rapid, Selective Lowering of Disease-Driving Antibodies in Graves' Disease and IgA Nephropathy

- BHV-1300 demonstrated deep, rapid, and sustained lowering of pathogenic TSHR autoantibodies (TSHR-IgG1) in patients with Graves' hyperthyroidism receiving 1000 mg SC weekly, with mean reductions in TSHR-IgG1exceeding >80% over the 12-week study.
    - Participants with Graves' overt hyperthyroidism, confirmed by elevated baseline thyroid tests despite being treated with anti-thyroid drug therapy (ATD), experienced normalization of thyroid hormones within weeks; T4 normalization occurring at a median of 3 weeks and T3 at a median of 5 weeks after the first administration of BHV-1300.
    - These preliminary patient data from an ongoing Phase 1b study highlight deep lowering of TSHR-IgG1 with BHV-1300 as a potentially disease-modifying approach to Graves' disease.
- BHV-1400 achieved rapid, deep, selective, and sustained lowering of Gd-IgA1 in patients with IgA nephropathy (IgAN), differentiating Biohaven's leading TRAP degrader from the complement and BAFF/APRIL inhibitor competition.
    - Participants with IgAN administered BHV-1400 showed a rapid, > 60% mean reduction of Gd-IgA1 within hours, and a 70% mean reduction of within the first one-month of dosing. Observed reductions in Gd-IgA1 were deeper than has been reported with BAFF/APRIL inhibitors, APRIL-inhibitors, and CD38 inhibitors at these early time points.
    - Preliminary observations also demonstrated an increase in eGFR, decrease in spot UPCR, and a decrease in hematuria with one month or less of dosing.
    - BHV-1400 brings precision immunology to the treatment landscape of IgAN as it was rationally designed to selectively remove galactose-deficient IgA1 (Gd-IgA1), the pathogenic antibody driver of the disease while sparing healthy antibodies IgA, IgG, IgE, and IgM.
    - Designed to target the disease driver while preserving healthy immunoglobulins, the complement system, and cell-mediated and humoral immunity, BHV-1400 offers a differentiated approach to current immunosuppressive therapies approved or in development.
- Both BHV-1300 and BHV-1400 continue to demonstrate the paradigm shifting potential of its extracellular degrader platform to target pathogenic antibodies causing disease. BHV-1300 and BHV-1400 show a differentiated safety profile with no clinically significant increases in cholesterol, decreases in albumin, or increases in ALT, AST, or bilirubin. Most AEs were mild and self-resolving, there were no drug discontinuations throughout the patient studies, and no serious or severe AEs.
- Pivotal Phase 3 trials in Graves' Disease and IgA Nephropathy to initiate in the coming weeks by mid-2026. Both trials use a patient friendly, simple to self-administer autoinjector for BHV-1300 and BHV-1400.

NEW HAVEN, Conn., May 27, 2026 /PRNewswire/ – Biohaven Ltd. (NYSE: BHVN) (“Biohaven”) a global clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of life-changing therapies with the potential to transform autoimmune diseases today reported compelling results regarding its proprietary extracellular MoDE™ (BHV-1300) and TRAP™ (BHV-1400) degrader platform. The new patient data from its BHV-1300 MoDE degrader for Graves' disease and BHV-1400 TRAP degrader for IgA nephropathy is being presented today at Biohaven's R&D and Analyst Day as part of the 2026 Yale Innovation Summit at the Yale School of Management in New Haven, Connecticut.

Tova Gardin, M.D., Chief Translational Officer of Biohaven, commented, "These new data in patients with Graves' disease and IgAN bridge scientific insights and Phase 1 findings – including pharmacodynamics and safety – to advance the programs into the upcoming Phase 3 studies planned for this summer. We continue to make good on our promise to translate the best of immunoscience into meaningful solutions for patients. Through focused innovation and execution, we have advanced the first MoDE and TRAP extracellular protein degraders, demonstrated their ability to rapidly and deeply reduce the antibodies that drive disease, and are encouraged by the biomarker data as well as early improvements in clinical outcomes noted by patients and investigators. As we enter pivotal trials in 2026 and continue to innovate with breakthrough science and precision tools, these data represent just the beginning of the impact we plan to deliver with our Biohaven proprietary extracellular degrader platform."

Dr. Coric continued, "Additionally, our first-in-class FGFR3-directed ADC, BHV-1530, continues dose escalation with no dose-limiting toxicities observed to date, and we have begun an expansion cohort in advanced endometrial cancer with our next-generation TROP-2 directed ADC BHV-1510 in combination with Libtayo. We are also excited about progress with our TYK2/JAK1 inhibitor for early Parkinson's disease and continue to advance enrollment in this trial. Finally, our thought leadership in neurology was on display last month at AAN, where we notably delivered a total of 5 oral presentations and posters highlighting our differentiated neuroscience and immunoscience portfolio. Though our approach has been marked by a disciplined and careful management of resources, we are pleased with progress achieved in recent months and look forward to sharing more detailed and robust updates across our portfolio at our annual R&D Day at the Yale Innovation Summit on May 27, 2026 in New Haven, Connecticut."

Key Highlights from the Phase 1b Graves' Disease Patient Experience with BHV-1300:

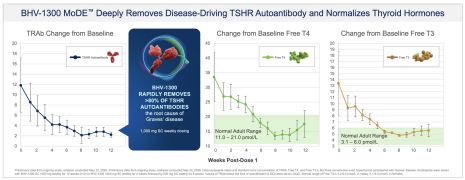
- Weekly administration of BHV-1300 1000 mg achieved mean reductions of pathogenic TSHR-IgG1 of >80% by week 12 in patients with Graves' hyperthyroidism (see Figure 1), a deeper reduction in pathogenic TSHR-IgG1 than has been demonstrated with the FcRn inhibitor competition.
- Patients with elevated thyroid hormones experienced a normalization of free T4 at a median of 3 weeks and a normalization of free T3 within a median of 5 weeks (see Figure 2). Patients reported improvements in classic symptoms of hyperthyroidism including palpitations, fatigue, diarrhea, diaphoresis, tremor, and mood.
- BHV-1300 has been safe and well-tolerated through 12 weeks of dosing. Most AE's have been mild and self-resolving, there have been no drug-discontinuations, and no serious or severe AEs. There have been no clinically significant increases in cholesterol, decreases in albumin, or increases in ALT, AST or bilirubin. Critically, BHV-1300 preserved IgG3 and demonstrated no clinically significant reductions in IgG3, IgA, IgE, or IgM relative to baseline, maintaining the immune protection that FcRn inhibitors — which lower all IgG subclasses including IgG3 — have not demonstrated.

Malini Gupta, M.D., ECNU, FACE, Director of G2Endo- Endocrinology in Memphis, the 2025 AACE Thyroid Chair and investigator in the BHV-1300 study, commented, "We are excited by these initial data in patients with Graves' disease, which demonstrate BHV-1300's ability to profoundly reduce TSHR autoantibodies and to normalize thyroid function in patients who have limited options today." Dr. Gupta added, "The strong link between TSHR-IgG1 lowering and clinical response positions BHV-1300 as a potential first-and-best-in-class therapy for Graves' disease. We see substantial unmet need in this population with no current disease modifying therapy and are excited for our patients to participate in the BHV-1300 pivotal Phase 3 study this year."

The positive Phase1b results in patients with Graves' disease who were hyperthyroid despite concurrent treatment with ATDs build on the observed dose-response relationship of BHV-1300 and literature that suggests deeper TSHR-IgG1 reductions are known to drive meaningfully higher efficacy compared to more

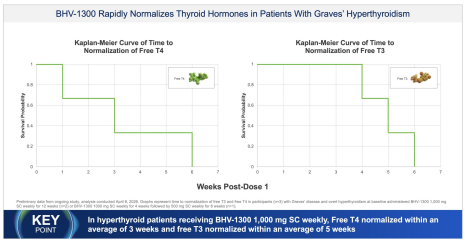
modest lowering. Additional biomarker and pharmacokinetic data (n=8) regarding Graves' patients who were and were not hyperthyroid at baseline will be presented at the Biohaven R&D Day and will be available on the company's website. Based upon the pharmacokinetic and biomarker results with BHV-1300 in this Phase 1b study, Biohaven is advancing to a pivotal trial in Graves' disease in the coming weeks. The planned study design is a double-blind placebo-controlled study in adults with Graves' hyperthyroidism evaluating normalization of T3, T4, and TSH at 26 weeks absent an antithyroid drug.

Figure 1: BHV-1300 rapidly and robustly reduced TSHR autoantibodies and normalized free T4 and free T3 in consecutively treated hyperthyroid patients (n=3) who were already on ATDs



BHV-1300 MoDE™ Deeply Removes Disease-Driving TSHR Autoantibody and Normalizes Thyroid Hormones

Figure 2: Time to normalization of thyroid hormones after treatment with BHV-1300 in consecutively treated patients (n=3) with hyperthyroidism at baseline despite concurrent use of antithyroid drugs.



BHV-1300 Rapidly Normalizes Thyroid Hormones in Patients With Graves' Hyperthyroidism

Key Highlights from the Phase 1b IgA Nephropathy Disease Patient Experience with BHV-1400:

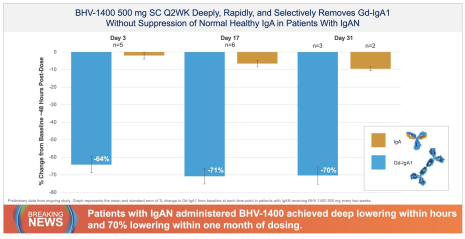
- Administration of BHV-1400, the Company's first TRAP, galactose-deficient IgA1 (Gd-IgA1) TRAP degrader for the treatment of IgA nephropathy (IgAN) achieved deep, rapid, and sustained mean reductions of pathogenic Gd-IgA1 of >60% within 48 hours of subcutaneous administration and 70% within the one month of dosing in patients with IgAN (see Figure 3). These reductions

are deeper than those demonstrated by BAFF-APRIL inhibitors, APRIL inhibitors, and CD38 inhibitors at this early time point.

- Reductions in Gd-IgA1 were associated with resolution of hematuria, decreases in spot UPCR, and increases in eGFR (see Figures 4-6). Participants also subjectively reported improvements in fatigue.
- BHV-1400 has been safe and well-tolerated throughout one month of dosing. Most AE's have been mild and self-resolving, there have been no drug-discontinuations, and no serious or severe AEs. There have been no clinically significant increases in ALT, AST or bilirubin, and no clinically significant reductions in other immunoglobulins relative to baseline.
- Effects were selective, with no clinically significant reductions observed in other immunoglobulins: IgA, IgG, IgE, or IgM.

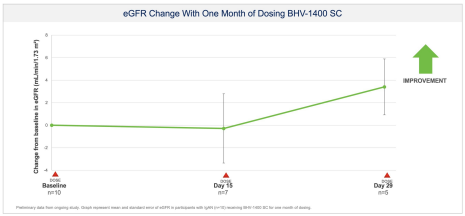
Dr. Jonathan Barratt, the Mayer Professor of Renal Medicine at University of Leicester and leading expert in the treatment of IgAN, commented on the new Phase 1b patient data, "These new data, which include data from my own patients, represent the next frontier of innovation for patients with IgA nephropathy. Currently approved treatments broadly suppress the immune system, and disease recurs upon their cessation, necessitating long term, potentially life long, treatment. There is a need for rapid acting and safe and rapid therapies that can be utilized throughout a patient's lifetime. The data I presented today show consistency between Phase 1 healthy subjects and patients with IgAN in BHV-1400's ability to deeply remove pathogenic Gd-IgA1. This reduction in Gd-IgA1 is associated with an immediate impact on patient outcomes rapidly without immunosuppression. I remain excited about BHV-1400, based on the Phase 1 patient data, as it rapidly and specifically targeted the fundamental abnormality in IgA nephropathy while sparing the rest of the immune system. It has the potential to take away the major driver for immune complex formation while leaving other antibodies unaffected, which means it potentially has efficacy with unrivaled safety."

Figure 3: BHV-1400 rapidly and robustly reduced Gd-IgA1 in patient with IgAN.



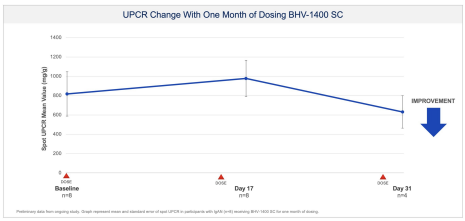
BHV-1400 500 mg SC Q2WK Deeply, Rapidly, and Selectively Removes Gd-IgA1 Without Suppression of Normal Healthy IgA in Patients With IgAN

Figure 4: Associated changes to eGFR in IgAN patients administered one month of treatment with BHV-1400.



eGFR Change With One Month of Dosing BHV-1400 SC

Figure 5: Associated changes to UPCR in IgAN patients administered one month of treatment with BHV-1400.



UPCR Change With One Month of Dosing BHV-1400 SC

About Graves' Disease

Graves' disease is the most common cause of hyperthyroidism, driven by autoantibodies stimulating the TSH receptor. A relapsing and remitting condition, Graves' disease affects 1% of the global population.

Driven by an autoantibody (TSHR-IgG1) that binds the TSH receptor, Graves' disease causes multi-organ symptoms and is complicated by associated TSHR-IgG1 driven conditions: thyroid eye disease, neonatal Graves' disease, and pretibial myxedema. Current treatment options are limited to thyroid organ removal or ablation or anti-thyroid drugs, none of which target the underlying autoantibody driving the disease. Standard ATDs do not target the underlying driver of disease and leave patients still symptomatic and at risk for development of thyroid eye disease and pretibial myxedema. Among patients with Graves' disease recently exposed to antithyroid drugs, 93% report multiple ongoing symptoms, with 72% reporting five or more persistent symptoms. With no new FDA approved therapy in over seventy years, there is a high unmet need for a novel therapy targeting the root cause of disease.

Biohaven's Lead MoDE degrader, BHV-1300, is poised to advance into its pivotal trial in Graves' disease mid-2026.

The presentation slides from Biohaven's R&D Day for the TRAP and MoDE degraders and its other platforms will be available on the Events and Presentations page of the Biohaven website just prior to their presentations.

About BHV-1300

BHV-1300, first MoDE, is a small molecule, extracellular IgG degrader, rationally designed to leverage the body's natural hepatic clearance mechanisms to selectively target and remove IgG1, IgG2, and IgG4, the underlying cause of many immune-mediated diseases. BHV-1300 is mechanistically differentiated from FcRn inhibitors in multiple important ways: first, it selectively targets the disease-causing IgG subclasses (IgG1, IgG2, IgG4) while sparing IgG3, which mediates protection against bacteria, viruses, and parasites and which has not been demonstrated with FcRn inhibitors; second, as a small molecule, BHV-1300 does not interact with FcRn and therefore does not accelerate the clearance of co-administered Fc-containing biologic therapies — a meaningful clinical limitation of the FcRn inhibitor class; third, it avoids the off-target effects of cholesterol elevation, albumin reduction, and headache associated with first-generation FcRn inhibitors; and fourth, it is delivered in a convenient self-administered autoinjector.

About IgA Nephropathy

IgA nephropathy is the leading cause of glomerular disease globally and is commonly diagnosed in individuals in their second and third decades of life, with most individuals progressing to renal failure over the ensuing 10-15 years. As a disease of the immune system, IgA nephropathy frequently returns even after renal transplant. While the 2021 Kidney Disease Improving Global Outcomes (KDIGO) treatment guidelines recommended only standard chronic kidney disease treatments, the 2025 guidelines emphasize the importance of treating the underlying immune disease by removing aberrant forms of IgA. "Galactose deficient IgA1 is the fundamental abnormality in IgA nephropathy," Dr. Barratt explained, "It's a group of IgA molecules that have changes to the sugars on the IgA1 hinge region that fundamentally change the way this antibody behaves. It promotes immune complex formation and it's these immune complexes that cause glomerular injury and damage and promote loss of kidney function."

About BHV-1400

BHV-1400, Biohaven's lead TRAP extracellular degrader, rapidly and selectively removes Gd-IgA1, the fundamental abnormality in IgA nephropathy, without adversely affecting any other immunoglobulins or components of protective immunity. BHV-1400's precision approach is differentiated from all existing and investigational therapies for IgAN: complement inhibitors, BAFF/APRIL inhibitors and non-selective inhibitors of IgA all suppress immunity. BHV-1400 has been safe and well-tolerated across the ongoing Phase 1b study in IgAN patients. Most adverse events (AEs) were mild and self-resolving, there were no discontinuations due to AEs related to study drug, and there were no serious or severe AEs related to drug. There were no clinically significant increases in ALT, AST or bilirubin, no clinically significant reductions in albumin and no clinically significant increases in cholesterol relative to placebo over the one month dosing period. There were no clinically significant reductions in other immunoglobulins including IgG, IgA, IgE, or IgM relative to baseline.

About Biohaven

Biohaven is a biopharmaceutical company focused on the discovery, development, and commercialization of life-changing treatments in key therapeutic areas, including immunology, neuroscience, and oncology. The Company is advancing its innovative portfolio of therapeutics, leveraging its proven drug development experience and multiple proprietary drug development platforms. Biohaven's extensive clinical and preclinical programs include Kv7 ion channel modulation for epilepsy; MoDE and TRAP extracellular protein

degradation for immunological diseases; and myostatin inhibition for neuromuscular and metabolic diseases, including obesity. For more information, visit **www.biohavenpharma.com**.

Forward-Looking Statements

This news release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The use of certain words, including "continue", "plan", "will", "believe", "may", "expect", "potentially", "groundbreaking" 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 to and potential marketing approval and commercialization of 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, including the studies of BHV-1300 and BHV-1400; the timing of planned interactions and filings with the FDA; the timing and outcome of expected regulatory filings; complying with applicable US regulatory requirements; the potential commercialization of Biohaven's product candidates; and the effectiveness and safety of Biohaven's product candidates. Additional important factors to be considered in connection with forward-looking statements are described in Biohaven'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 news release, 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.

MoDE and TRAP are trademarks of Biohaven Therapeutics Ltd.

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biohaven®
BHVN
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NYSE
Biohaven R&D Day
May 27, 2026
DAYS
MATTER™
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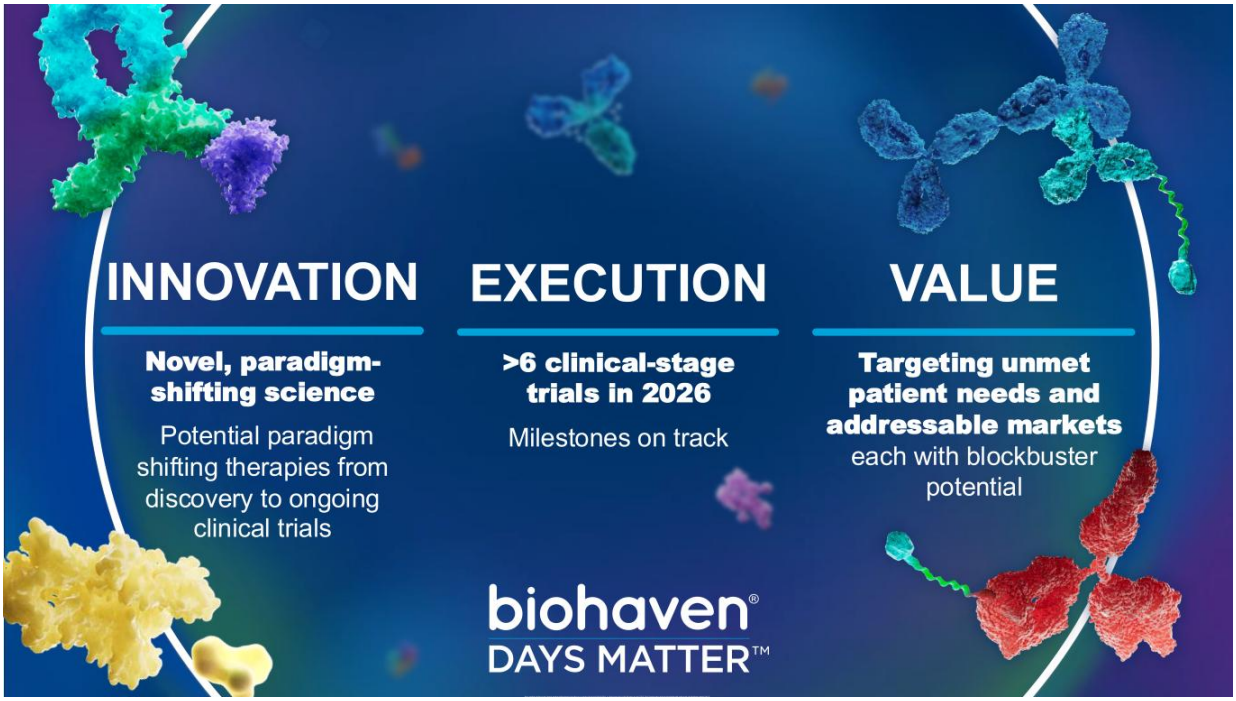
Forward-Looking Statement

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 (including those for our taldefgrobep alfa, opakalim, BHV-2100, BHV-8000, BHV-8100, BHV-1300, BHV-1310, BHV-1400, BHV-1510, BHV-1530 and BHV-1600 development programs), the timing of and the availability of data from our clinical trials, the timing of 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 a s compared to other existing potential treatment options, and the potential advancement of our early phase programs, including BHV-1955, BHV-8200, BHV-2110, BHV-1490, BHV-1420, BHV-1440, BHV-6500 and BHV-1500. The use of certain words, including “continue”, “plan”, “will”, “believe”, “may”, “expect”, “anticipate” “potential first-in-class” 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, including those regarding the resubmission of our new drug application for troriluzole for SCA; the timing and outcome of expected regulatory filings; Biohaven’s compliance with applicable U.S. regulatory requirements; the potential commercialization of Biohaven's product candidates; and the effectiveness and safety of Biohaven's product candidates, including open label clinical data in ongoing studies. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. Additional important factors to be considered in connection with forward-looking statements are described in the Company’s filings with the Securities and Exchange Commission, including within the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations”. This presentation also contains market data and other information based on industry publications, reports by market research firms or published independent sources. Some market data and information are also based on the Company’s good faith estimates, which are derived from management’s knowledge of its industry and such independent sources referred to above.


WELCOME
Vlad Coric, M.D.
Chairman and Chief Executive Officer
biohaven
BHVN
LISTED
NYSE


INNOVATION
Novel, paradigm-shifting science
Potential paradigm shifting therapies from discovery to ongoing clinical trials
EXECUTION
>6 clinical-stage trials in 2026
Milestones on track
VALUE
Targeting unmet patient needs and addressable markets each with blockbuster potential
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DAYS MATTER™


BHV-1400
TRAP™ degrader
First Gd-IgA1 target
IgA nephropathy
First Gd-IgA1 degrader
BHV-1300
MoDE™ degrader
First IgG degrader
Graves' disease
First IgG degrader
Novel brain-penetrant TYK2/JAK1
BHV-8000
First TYK2/JAK1 inhibitor
Brain-penetrant
Parkinson's disease
Ion Channels
BHV-7000
Opakalim
Selective Kv7 activator
Paradigm tolerability
Potential paradigm shifting Kv7 activator
Novel myostatin-activin
Obesity
BHV-2000
Taldefgrobep
Myostatin/activin
High-quality weight loss
Obesity
biohaven®
DAYS MATTER™
INNOVATION
in ACTION
Next-Gen Discovery Targets
Degraders for diabetes, IgG4 diseases and emerging targets
Innovative next-gen molecules
BHV-1955
Potential first-in-clinic
Nasal oxytocin
Tinnitus targets
Oncology
BHV-1530
First FGFR3 ADC
Unique Topoix payload
Oncology
First FGFR3 ADC
First-in-clinic brain-penetrant PKM2
BHV-8100
PKM2 activator
Brain-penetrant
Neurodegenerative disease
Troriluzole
SCA
Continued advocacy
Days Matter™
SCA patients
Pursuing first therapy for SCA


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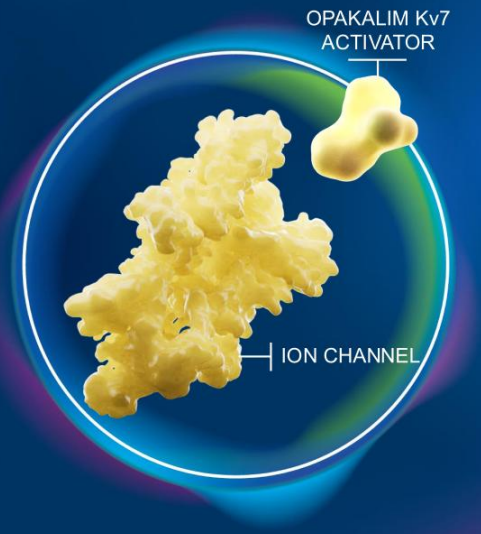
DAYS MATTER™
INNOVATION
in ACTION

biohaven®

ION CHANNEL: OPAKALIM SELECTIVE Kv7 ACTIVATOR

Revolutionizing Epilepsy Treatment With a Modern Kv7 Activator

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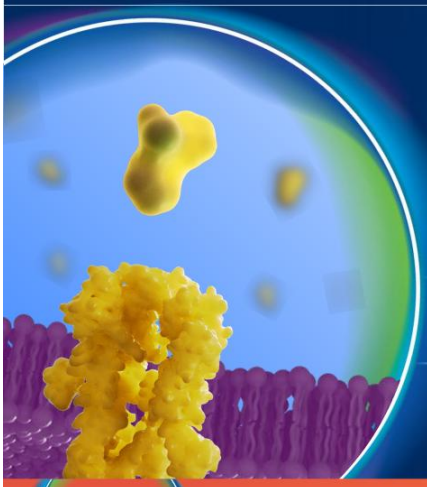
University College London
UCL
Jason Lerner, MD
Medical Director
biohaven
Steven Dworetzky, PhD
Senior Vice President,
Kv7, Strategy & Development
biohaven
Ion Channel
biohaven

An Epilepsy Treatment Designed With Patients and Physicians in Mind

Kv7



Opakalim offers potential for easy-to-use, once-daily treatment with no titration to control seizures without the burdensome side effects frequently reported with approved ASMs and those in development

Selectively activates Kv7.2/7.3 channels—a validated MOA for treating epilepsy—without impacting GABA receptors

Exhibits preliminary efficacy signals in focal epilepsy OLE, KCNQ2-DEE and now idiopathic generalized epilepsy

Demonstrates exceptional safety profile with low rates of CNS adverse events across all trials (1000+ subjects)

BREAKING NEWS

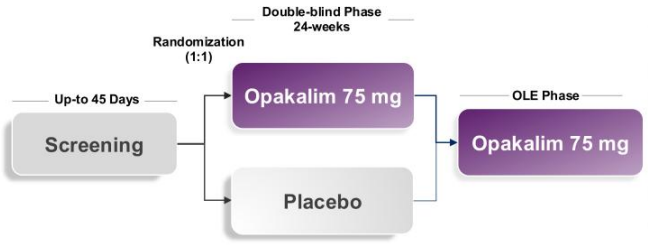
Recent clinical data updates reinforce efficacy and differentiated tolerability

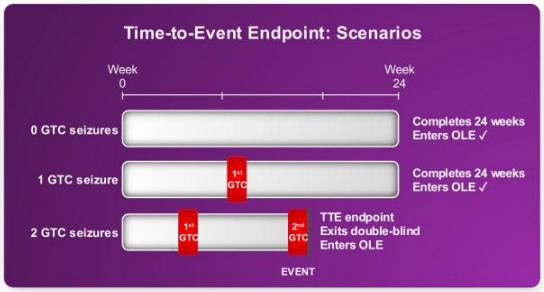

biohaven®
Idiopathic Generalized Epilepsy (IGE)
DAYS MATTER™


Matthias Koepp, MD, PhD
Professor of Neurology
University College London
UCL
Opakalim:
Selective Kv7 Activation for IGE
biohaven

Idiopathic Generalized Epilepsy Time-to-Event Study Design

Kv7





KEY STUDY DETAILS

Study Design: Randomized, double-blind, placebo-controlled, event-driven trial
Endpoint: Primary - Time-to-event (Event = 2nd day with GTC seizure); **Secondary -** GTC seizure freedom
Population: Subjects 18-75 with IGE and intractable GTC seizures
Key Entry Criteria: 3 GTC seizures within the historic 16-week seizure assessment period

Study terminated early due to enrollment and strategic portfolio prioritization; GTC: generalized tonic-clonic; IGE: idiopathic generalized epilepsy; TTE: time-to-event

Demographics and Baseline Disease Characteristics

Kv7

	Opakalim 75 mg n=15	Placebo n=12*
Age (mean)	37	43
Sex (% female)	73%	83%
Region (% US)	47%	25%
BMI (mean)	27	28
Number of epilepsy treatments at screening		
1 to 2	60%	67%
3 to 4	40%	33%
Number of previous and current ASMs		
≤ 6	11 (73%)	10 (83%)
> 6	4 (27%)	2 (17%)
Age at IGE diagnosis (mean)	14	13
Years since IGE diagnosis (mean)	23	30

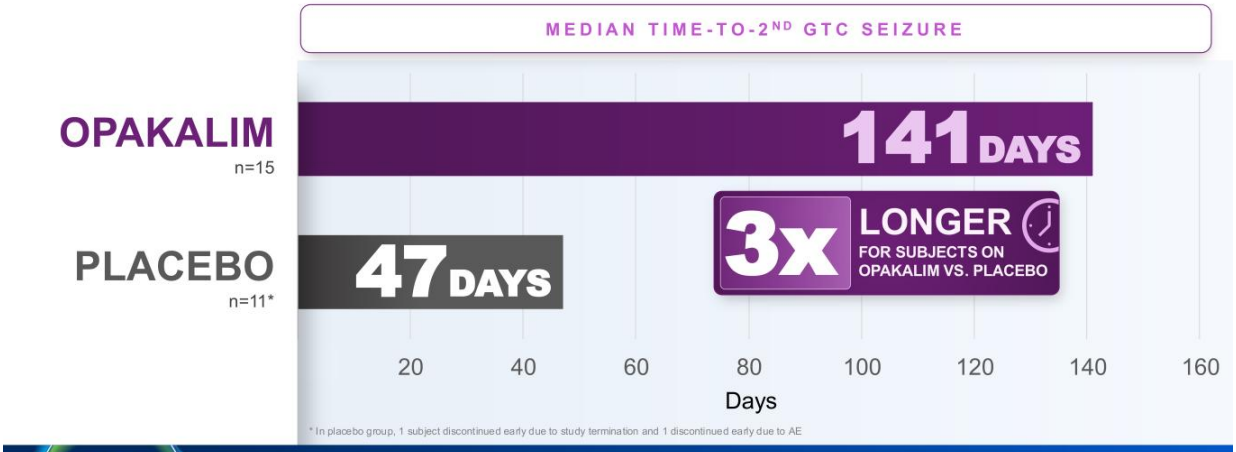
* In placebo group, 1 subject did not have post-dose efficacy data

KEY POINT

Highly treatment-resistant idiopathic generalized epilepsy population

Opakalim Prolongs Time-to-2nd GTC Seizure

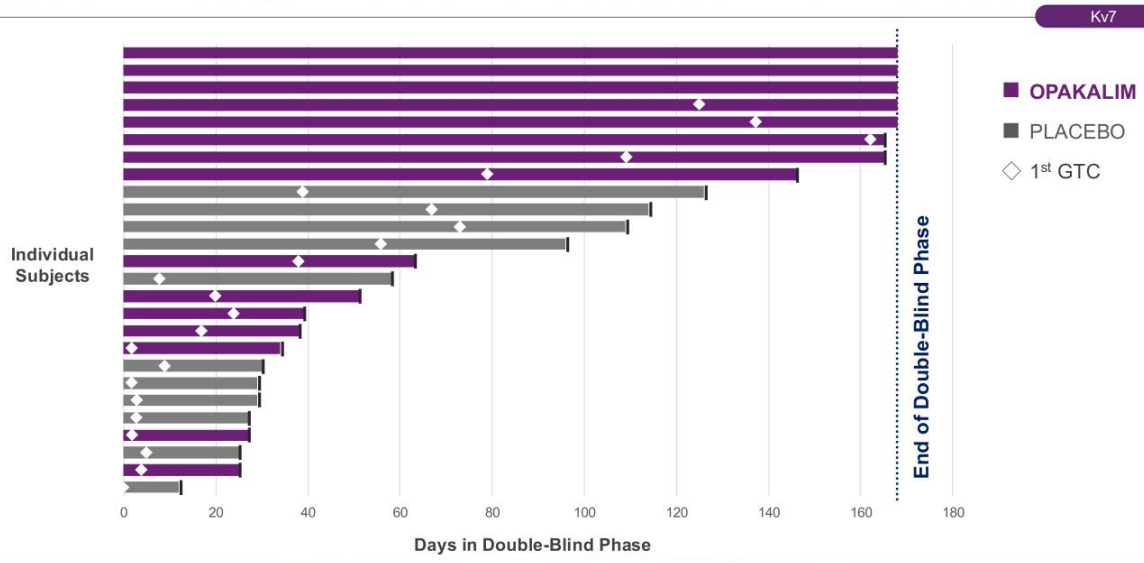
Kv7



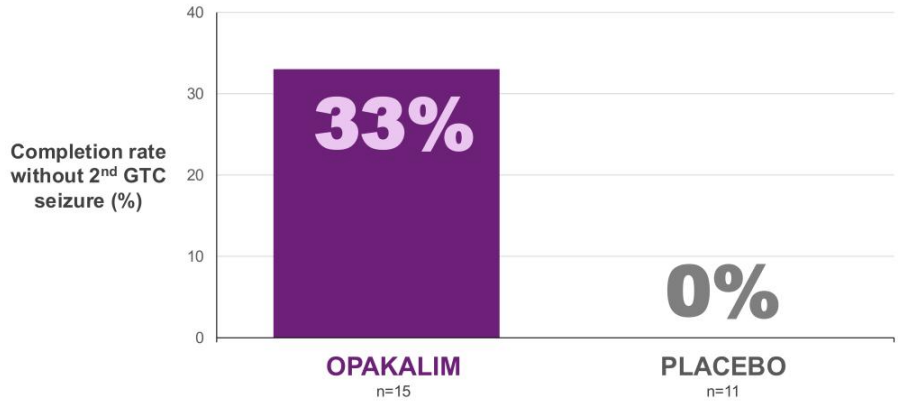
KEY POINT Efficacy signal observed in idiopathic generalized epilepsy population

Opakalim Prolongs Time-to-2nd GTC Seizure & Time in Double-Blind

Kv7

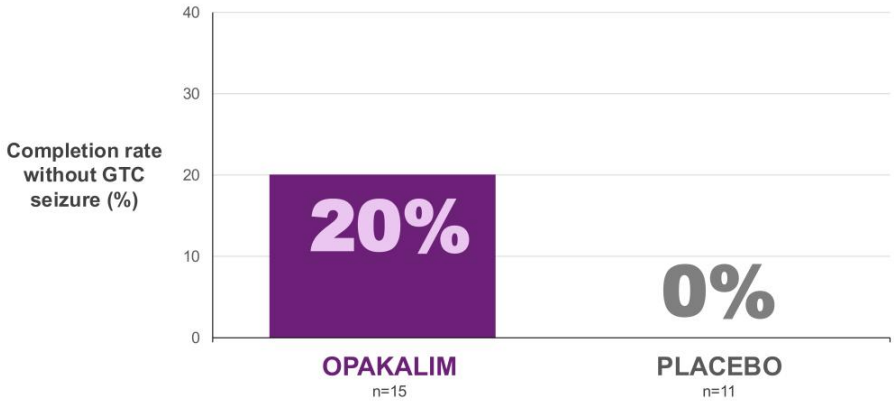


One-Third of Opakalim-Treated Subjects Completed Six-Month Double-Blind Phase Without 2nd GTC



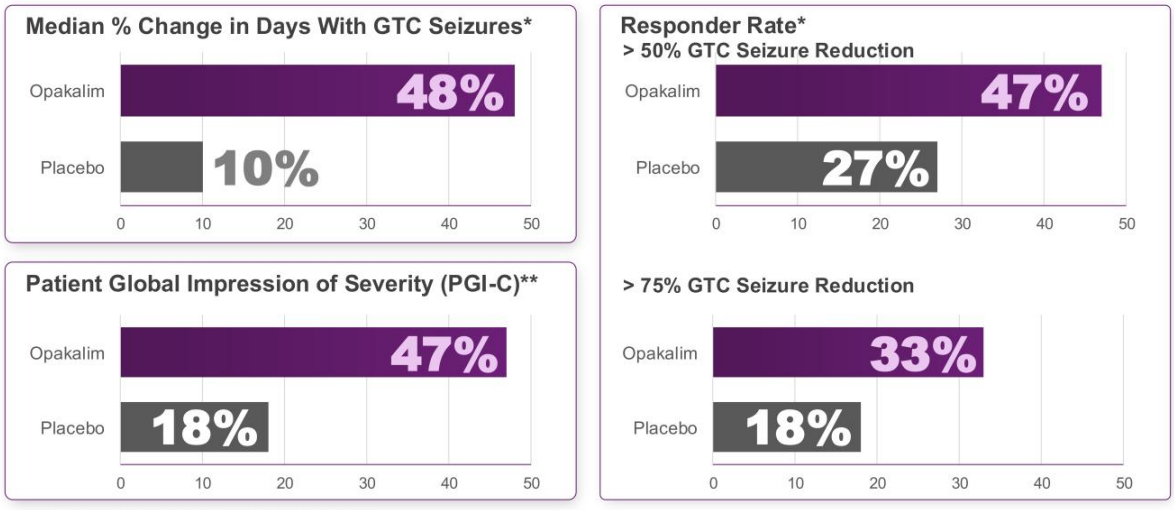
* In placebo group, 1 subject discontinued early due to study termination and 1 discontinued early due to AE

20% of Opakalim-Treated Subjects Completed Six-Month Double-Blind Phase Seizure Free



* In placebo group, 1 subject discontinued early due to study termination and 1 discontinued early due to AE

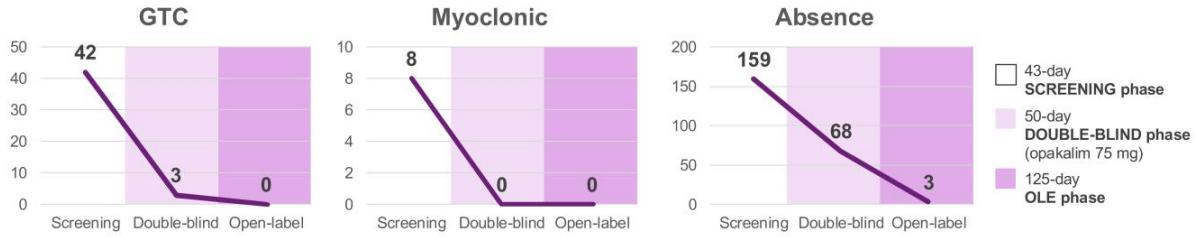
Opakalim-Treated Subjects Showed Improvements on Seizure and Patient Reported Outcomes



*28-day adjusted. **PGI-C – based on last assessment in double-blind phase

Promising Case of Broad-Spectrum Generalized Seizure Efficacy

Our patient has very difficult-to-treat IGE, since entering the opakalim trial she has experienced reduction in all seizure types.



In terms of tolerability, she continues to do very well, with no adverse events.

Opakalim IGE Double-Blind Phase topline data, 1H 2026

KEY POINT

- **50% of subjects with myoclonic seizures became myoclonic seizure free on opakalim**
- **33% of subjects with absence seizures became absence seizure free on opakalim**

Opakalim Exhibits Low Rates of Nervous System Adverse Events

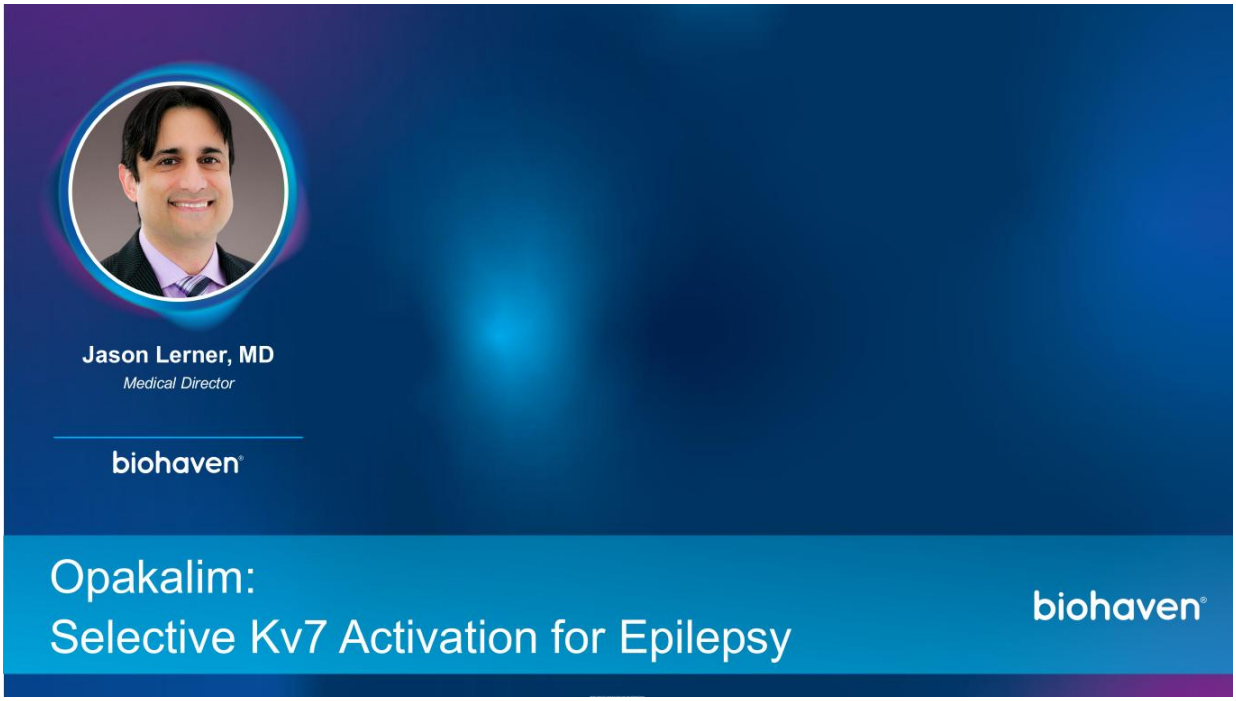
Kv7

Preferred Term	Opakalim (n=15) n (%)	Placebo (n=12) n (%)
Generalized tonic-clonic seizure	1 (6.7)	0
Headache	1 (6.7)	2 (16.7)
Hypotonia	1 (6.7)	0
Paraesthesia	1 (6.7)	0
Presyncope	1 (6.7)	0
Coordination abnormal	0	1 (8.3)
Dysarthria	0	1 (8.3)
Dysgeusia	0	1 (8.3)

Opakalim IGE Double-Blind Phase topline data, 1H 2026

KEY POINT

No somnolence, dizziness, or fatigue


Jason Lerner, MD
Medical Director
biohaven
Opakalim:
Selective Kv7 Activation for Epilepsy
biohaven

Promising Case Reports in Idiopathic Generalized Epilepsy

CASE STUDY #1 • IMPROVED QUALITY OF LIFE

Able to **travel**

Comfortable traveling from Louisiana to California to attend a wedding

33 F | Intractable GTC seizures | Almost daily seizures at baseline | Does not travel

RESPONSE TO OPAKALIM
Decreased GTC seizure frequency with **seizure-free periods lasting weeks** and no side effects

ABLE TO TRAVEL
Traveled to California with her husband, attended a wedding and returned to Louisiana without having a single seizure

CASE STUDY #2 • SEIZURE FREEDOM

425+ DAYS seizure free

Reduced risk of mortality and epilepsy-related comorbidities

60 F | Intractable GTC seizures since age 16 | Frequent seizures at baseline (7 GTC seizures in 30-day screening phase) | Pulmonary and CV comorbidities

RESPONSE TO OPAKALIM
Seizure free in double-blind phase and open-label phase for total of 425+ consecutive days

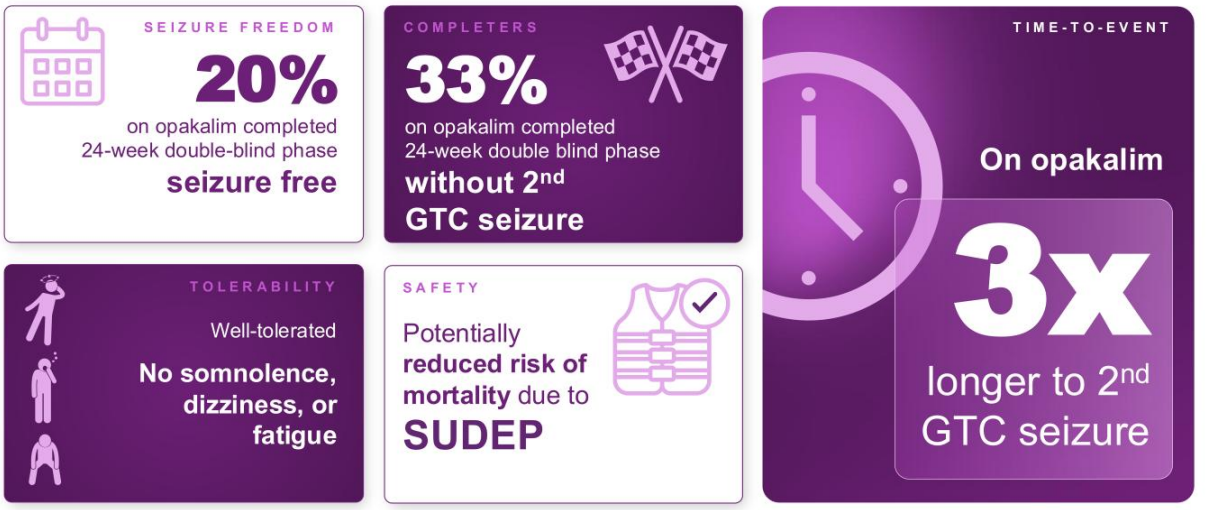
REDUCED RISK OF MORTALITY DUE TO SUDEP
SUDEP-3 Inventory score at baseline **was 3/4 and is now 0/4** on treatment with opakalim indicating reduced risk of SUDEP

Sudden **U**nexpected **D**eath in **EP**ilepsy

- Uncontrolled seizures are a major risk factor
- SUDEP-3 Inventory: validated tool to predict and quantify risk of SUDEP. For each point on the SUDEP-3, odds of SUDEP increase by 180%

Tarighati Rasekhi. Epilepsia. 2021.

Opakalim Demonstrates Antiseizure Efficacy With Favorable Tolerability in Idiopathic Generalized Epilepsy



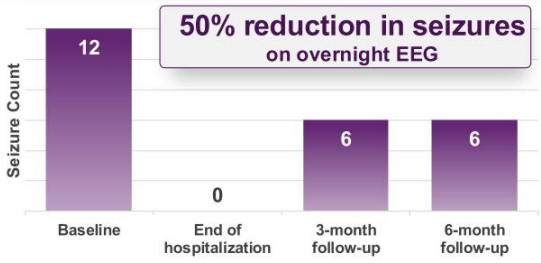

biohaven®
KCNQ2-DEE
DAYS
MATTER™

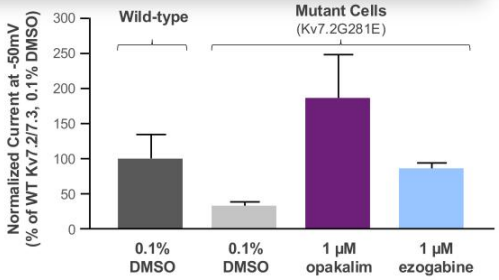
Efficacy Signal Demonstrated in KCNQ2-DEE

Kv7

9-year-old boy with
- **Refractory KCNQ2-DEE**
- **Kv7 activation-dependence**

- Heterozygous for Kv7.2 G281E mutation
- Daily tonic seizures at baseline despite 3 ASMs including 1st gen Kv7 activator
- Prior attempts to taper 1st gen Kv7 activator resulted in **status epilepticus, ICU admission and developmental regression**



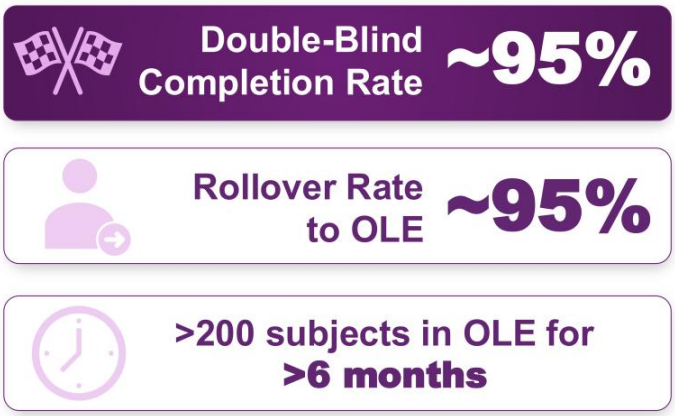


Olson. AAN 2026. Poster #P10 11-002; Equivalent exposures to 75 mg dose in pivotal focal epilepsy studies

KEY POINT **Successfully transitioned from 1st gen Kv7 to opakalim and stable for 6+ months**


biohaven®
Focal Epilepsy
DAYS MATTER™

High Retention and Rollover in Opakalim Focal Epilepsy Trials



Opakalim ongoing focal epilepsy trials preliminary data 1H 2026

Efficacy Signal Observed in Focal Epilepsy Open-Label Data

Kv7

SEIZURE FREQUENCY
Pretreatment Baseline in OP

VS

SEIZURE FREQUENCY
On Treatment with Opakalim 75 mg in OLE

>54% OF PATIENTS SHOWED

50% RESPONSE RATE

OVER ANY CONSECUTIVE 6-MONTH PERIOD IN OLE (n>100)

* RISE 2 Part B: opakalim 75 mg

Opakalim ongoing focal epilepsy preliminary data 1H 2026 for open-label 6-month completers; French, Epilepsia Open, 2025; Indirect comparisons between compounds based on publicly available data.

KEY POINT

50% RR for opakalim (54%) comparable to azetukalner (56%)

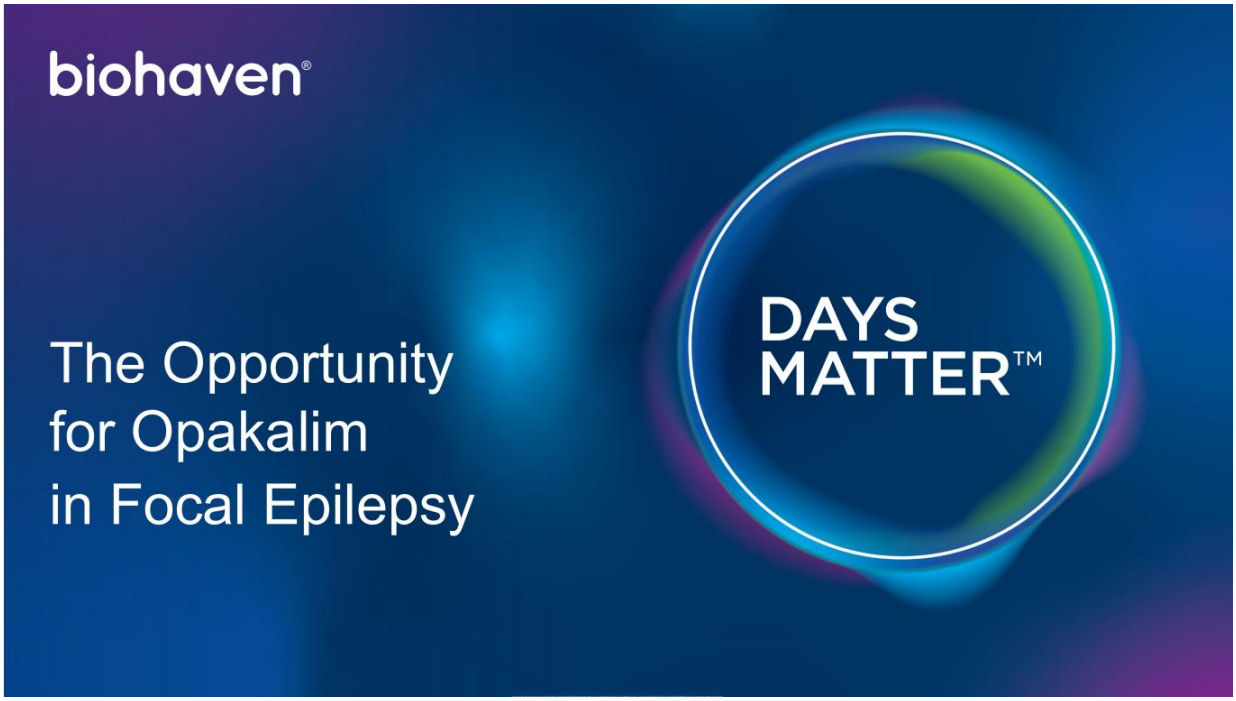
Exceptional Tolerability Observed in Focal Epilepsy Open-Label Data

Kv7

Preferred Term	Opakalim 50 mg	Opakalim 75 mg	Opakalim Pooled
Headache	4.5%	6.4%	5.7%
Nasopharyngitis	4.5%	6.4%	5.7%
Seizure	5.3%	3.7%	4.3%
Dizziness	3.0%	5.0%	4.3%
Fatigue	3.0%	4.1%	3.7%
Fall	2.3%	4.6%	3.7%
Upper Respiratory Tract Infection	3.0%	4.1%	3.7%
Back Pain	3.8%	3.2%	3.4%
Insomnia	5.3%	2.3%	3.4%
Nausea	3.8%	2.8%	3.1%
Diarrhea	6.0%	1.4%	3.1%

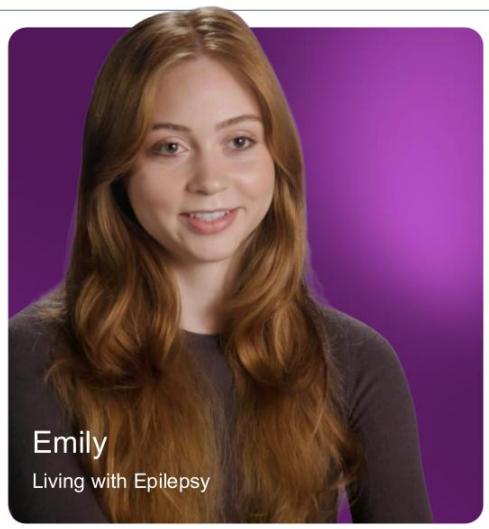
Adverse events reported in ≥3% of pooled participants, opakalim ongoing focal epilepsy open-label preliminary data 1H 2026

KEY POINT Low incidence, majority mild and spontaneously resolved


biohaven®
The Opportunity
for Opakalim
in Focal Epilepsy
DAYS
MATTER™

High Unmet Need Remains for Novel, Well-tolerated and Effective Antiseizure Medicines

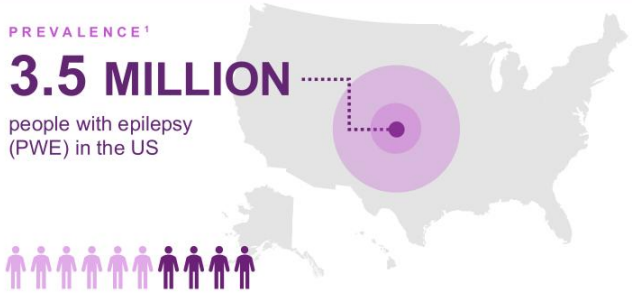
Kv7



PREVALENCE[1]

3.5 MILLION

people with epilepsy (PWE) in the US



REFRACTORY[2]

UP TO 40%

of PWE continue to have seizures despite treatment

HEALTHCARE SPENDING[3]

$24.5 BILLION

annual spending in the US (direct costs)

1. www.cdc.gov/mmwr/volumes/66/wr/mm6631a1.htm. 2. French. Epilepsia. 2007. 3. www.cdc.gov/epilepsy/data-research/facts-stats/index.html#:~:text=Health%20care%20spending

High Unmet Need Remains for Novel, Well-tolerated and Effective Antiseizure Medicines

Kv7

ADVERSE EVENTS[1]

80%
of PWE report AEs after starting an ASM

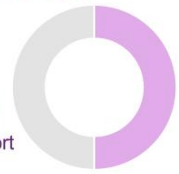
ADHERENCE[2]

UP TO 60%
of PWE report non-adherence to ASMs

COMORBIDITIES[3]

50%
of PWE report at least 1 comorbidity

QUALITY OF LIFE[4]



50%
of PWE report lower QoL

1. Baker. Epilepsia. 1997. 2. Donahue. Neurol Clin Pract. 2025. 3. Bosak. Epilepsy & Behavior. 2025. 4. Strzelczyk. Epilepsy & Behavior. 2023.

Similar Populations in Opakalim and Azetukalner Focal Epilepsy Trials

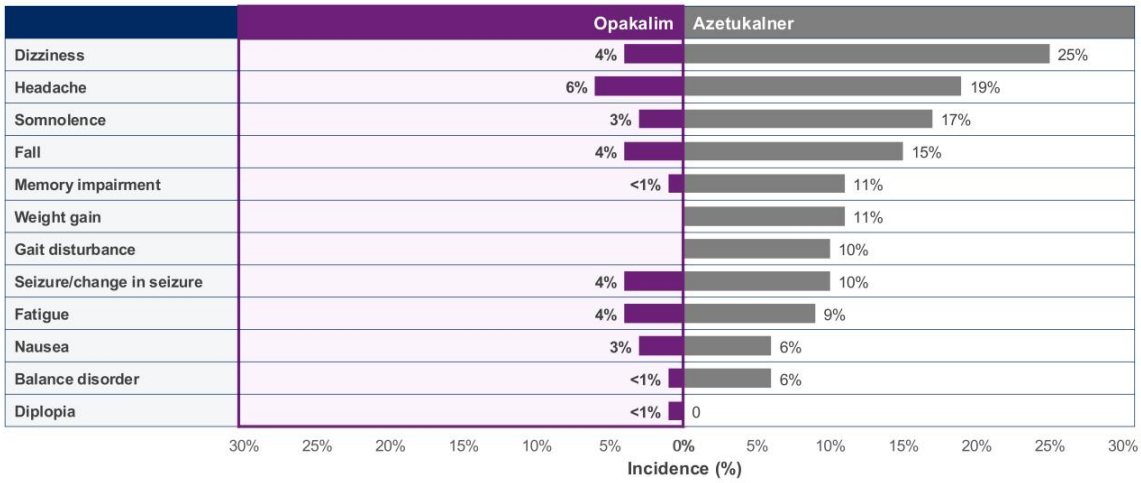
Kv7

	Opakalim	Azetukalner
n	**328**	374
Age (mean)	**39**	40
Sex	**50.4% F**	50.8% F
BMI (mean)	**25.97**	26.8
Baseline Seizure Frequency (median)	**13.00**	12.75
# of concomitant ASMs		
1	**11.4%**	10.2%
2	**36.5%**	38.5%
3	**50.7%**	51.3%
# of ASMs tried and discontinued (median)	**4**	5

Opakalim (all doses) ongoing focal epilepsy open-label preliminary data 1H 2026; Azetukalner (all doses) data from Phase 3 X-TOLE 2 Study: Topline Results, March 9, 2026, xenonpharma.com

Opakalim Demonstrates Favorable Tolerability vs. Azetukalner in Focal Epilepsy Open-Label Trials

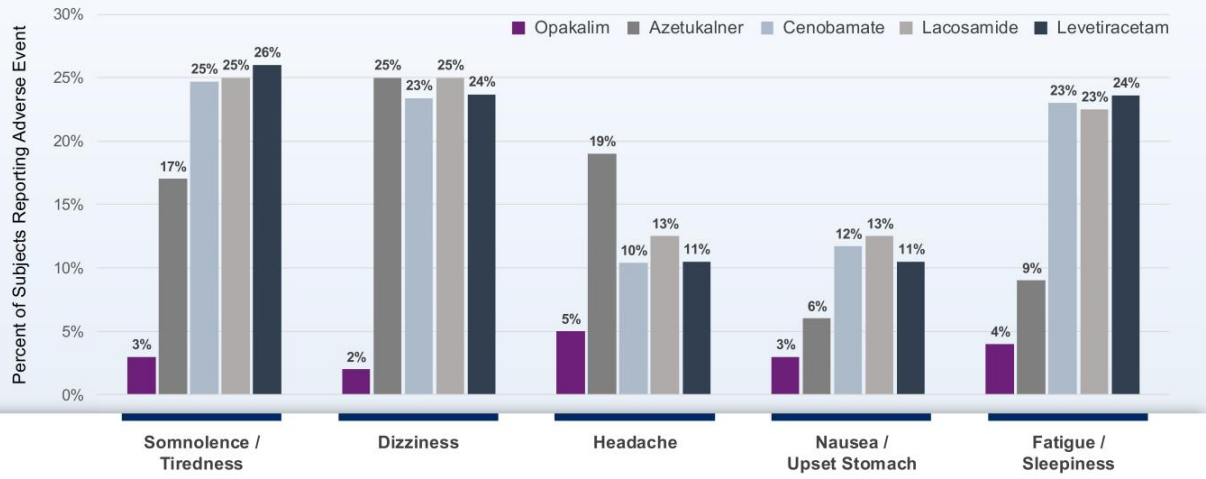
Kv7



Opakalim ongoing focal epilepsy open-label preliminary data 1H 2026; percentages rounded to the nearest whole percent; Azetukalner focal epilepsy data from Open Label Study – French. AES 2025. Poster #3.356.

Opakalim Demonstrates Favorable Tolerability vs. Approved and Investigational ASMs

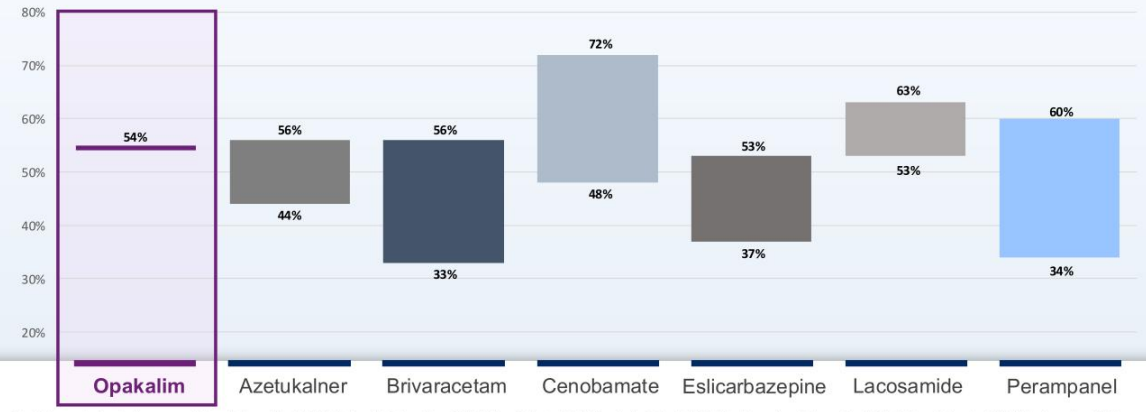
Kv7



Opakalim ongoing focal epilepsy open-label preliminary data 1H 2026; Azetukalner data from Open Label Study – French. AES 2025. Poster #3.356; Cenobamate, lacosamide and levetiracetam data from Winter. CNS Drugs. 2024.

50% Responder Rate in OLE Trials of Several Approved and Investigational ASMs

Kv7



Opakalim ongoing focal epilepsy open-label preliminary data 1H 2026; Hufnagel. Epilepsy Res. 2013; Halász. Epilepsia. 2010; Strzelczyk. Epilepsia. 2021; Ben-Menachem. Epilepsy Res. 2021; O'Brien. Epilepsia. 2020; Klein. Neurology. 2022; Strzelczyk. Expert Rev Clin Pharmacol. 2015; Husain. Epilepsia. 2012; French, J. Epilepsia Open. 2025; Rektor. Epilepsia. 2020.

KEY POINT Opakalim OLE preliminary efficacy outcomes fall within reported range of responder rates for other ASMs in OLE trials

Opakalim Is Easy-to-Use With a Projected Favorable Tolerability Compared to Approved ASMs

Kv7

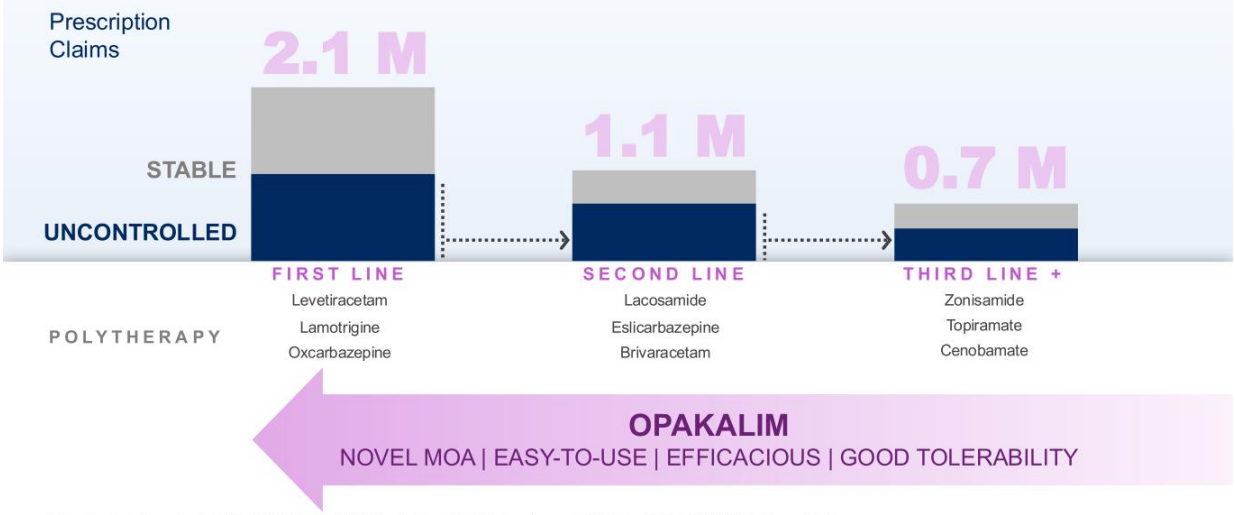
		No titration	Favorable CNS tolerability	Low neuropsychiatric AEs	Low metabolic / electrolyte AEs	Low SJS or DRESS risk
L1	Lamotrigine	✗✗	✓	✓	✓	✗✗
	Levetiracetam	✓	✓	✗	✓	~
	Oxcarbazepine	✗	✗	✓	✗	✗
L2	Lacosamide	✗	✓	✓	✓	✓
	Eslicarbazepine	✗	✗	✓	✗	~
	Brivaracetam	~	✗	✗	✓	✓
L3	Zonisamide	✗	✗	✗	✗	✓
	Cenobamate	✗✗	✗	✓	✓	✗✗
	Topiramate	✗	✗	✗	✗	✓
	Opakalim (Kv7)	✓	✓	✓	✓	✓

✓ Favorable ~ Variable ✗ Unfavorable ✗✗ Very Unfavorable

AE, Adverse Event. **SJS**, Stevens-Johnson Syndrome. **DRESS**, Drug Reaction with Eosinophilia and Systemic Symptoms

Opakalim Offers Potential To Address Unmet Needs in Epilepsy with Attractive Attributes for Epileptologists and General Neurologists

Kv7



OPAKALIM

NOVEL MOA | EASY-TO-USE | EFFICACIOUS | GOOD TOLERABILITY

Forian claims data; diagnosis codes G400, G401, G402; prescribed ASM medications; dataset timeframe January 1, 2016 to June 30, 2022. US KOL Market Research 2026.

Key Opinion Leader Perspective

Kv7

If Opakalim tolerability seen in early studies is maintained, that would be a huge differentiator in clinical practice. That was the case with Keppra – it seemed to be as effective but so much better tolerated than other alternatives.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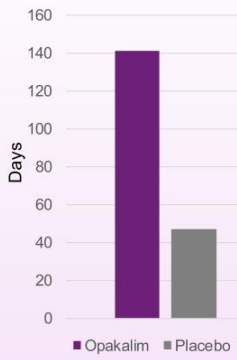
Epilepsy Summary
DAYS MATTER™

Opakalim Continues To Demonstrate Encouraging Results in Epilepsy

Kv7



54% of subjects showed 50% Responder Rate

OVER ANY CONSECUTIVE 6-MONTHS (n>100)

Adverse Event	Opakalim
Headache	5.7%
Nasopharyngitis	5.7%
Seizure	4.3%
Dizziness	4.3%
Fatigue	3.7%
Fall	3.7%
Upper Respiratory Tract Infection	3.7%
Back Pain	3.4%
Insomnia	3.4%
Nausea	3.1%
Diarrhea	3.1%

50% reduction in seizures

IGE RCT

Promising efficacy and safety data in IGE with generalized tonic-clonic seizures

FOCAL EPILEPSY OLE

Efficacy signal observed in focal epilepsy OLE falls within reported range of 50% responder rates for other ASMs in OLE trials

OPAKALIM 75 MG

Continues to be exceptionally well-tolerated in focal epilepsy OLE

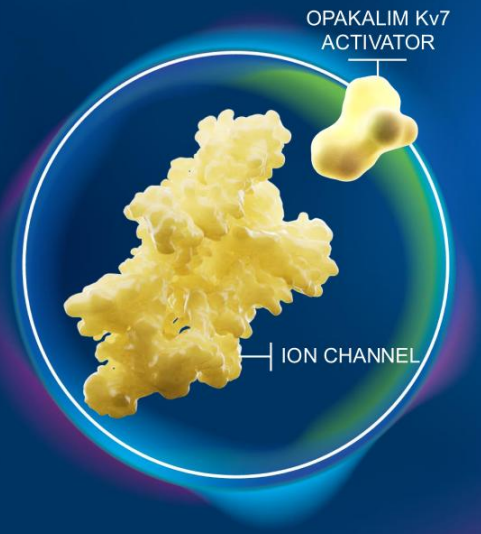
PATIENT WITH KCNQ2-DEE

Transitioned from 1st gen Kv7 to opakalim with clinical stability & ongoing seizure control for 6+ months


Steven Dworetzky, PhD
Senior Vice President,
Kv7, Strategy & Development
biohaven
Opakalim:
Selective Kv7 Activation for Pain and Tinnitus
biohaven

biohaven®

Kv7 Activation for the Treatment of Pain

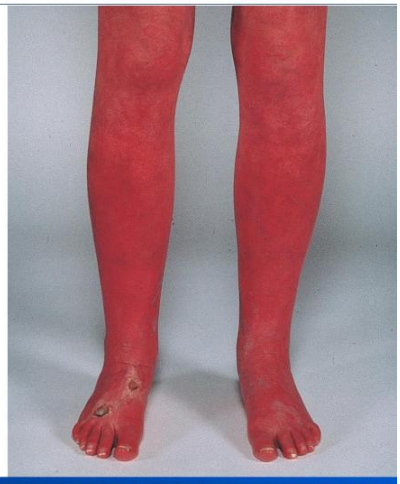


Inherited Erythromelalgia:
Disease Model To Study Opakalim for the Treatment of Neuropathic Pain

INHERITED DISEASE: Caused by gain of function mutations in NaV1.7 channels[1] resulting in hyperexcitability of sensory neurons. Characterized by severe chronic neuropathic pain, episodic pain attacks, skin erythema and sleep disturbances.[1]

GENETIC RESILIENCE MECHANISM: Some individuals with IEM are resilient to pain compared to family members carrying the same mutation. Due to a second GoF mutation in the Kv7.2 or Kv7.3 genes, dampening neuronal hyperexcitability.[2]

THERAPEUTIC HYPOTHESIS: Increased excitability of sensory neurons is key to pathological pain. Kv7.2/7.3 channels control sensory dorsal root ganglion intrinsic excitability. **Opakalim targets neuronal excitability centrally and peripherally.**



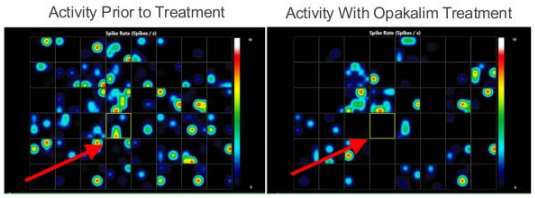
1. McDonnell. Brain. 2016. 2. Yuan. Brain Commun. 2021. 3. Davis. Arch Dermatol. 2000 (image); IEM inherited erythromelalgia; GoF gain of function.

KEY POINT **Human genetics validates Kv7 activation as a "protective" mechanism in IEM and provides rationale for Kv7 activation as a treatment for pain**

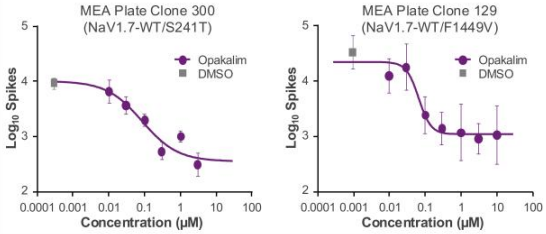
Opakalim Treatment of iPSC-Derived Sensory Neurons From IEM Patients

- Data visualized as color heatmap corresponding to number of spikes detected for each electrode during the preceding second
- Evaluating spontaneous neuronal firing
- The well indicated by a red arrow was exposed to opakalim 1 µM

Microelectrode Array: Real-time Visualization of Neuronal Activity on a 48-Well Plate



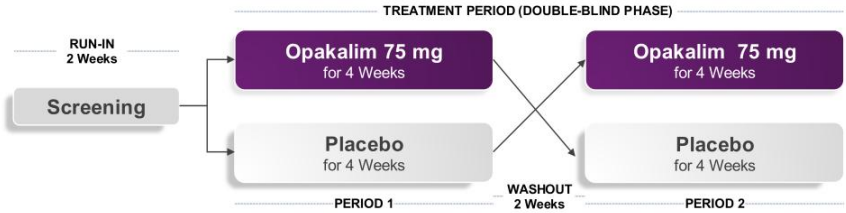
Microelectrode Array: Spike Counts Over 10-Minutes With Varying Concentrations of Opakalim Vehicle: 0.1% DMSO



IASP 2024. Amsterdam, Netherlands 2024.

KEY POINT **Opakalim reduces neuronal spike activity with sub-micromolar IC50s in a "pain in a dish model"**

Pilot Translational Trial of Opakalim in Inherited Erythromelalgia



KEY STUDY DETAILS

Study Design: Randomized, double-blind, placebo-controlled, 2-way crossover design
Population: Participants with IEM, with NaV 1.7 GoF mutations w/o concomitant Kv7 mutations
Sample size: 5 Participants
Endpoints: Area under the curve of pain; frequency, intensity, and duration of pain attacks

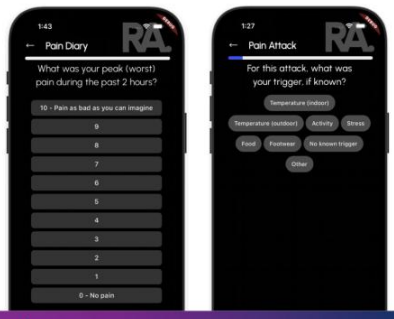
BREAKING NEWS

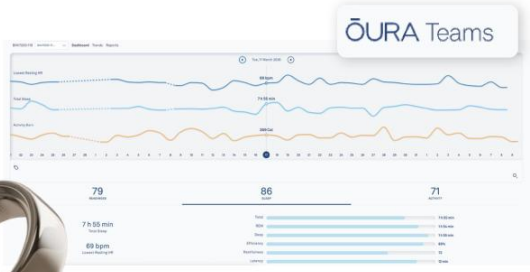
- **Trial initiated in 1Q 2026**
- **Subjects enrolled in the trial were iPSC donors for the in vitro experiments**

Leveraging Innovative Technologies To Monitor IEM Symptoms

Research Ally Phone App

Systematically profiling fluctuating **PAIN** throughout the day





Ōura ring

Monitoring effects of improved pain management on **SLEEP**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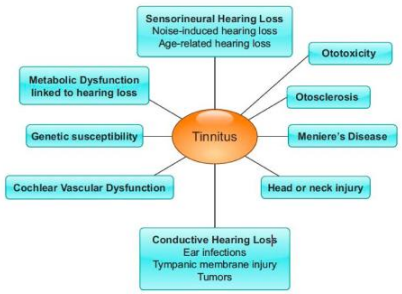
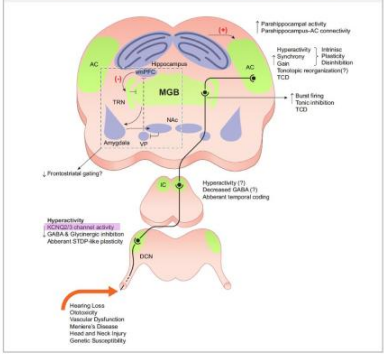
Kv7 Activation for the Treatment of Tinnitus
DAYS MATTER™

Rationale for Kv7 Activation in the Treatment of Tinnitus

Causes of Tinnitus



Changes in Auditory Circuitry Involve Kv7 Channel Activity



- Tinnitus affects **~50 million** Americans
- Driven in part by hyperexcitability in the auditory cortex
- Preclinical models of tinnitus show reduced Kv7.2/7.3 currents

Henton and Tzounopoulou. Physiol Rev. 2021.

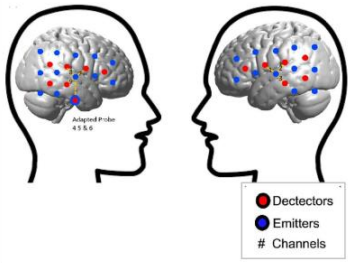
KEY POINT

Kv7 activation reduces hyperexcitability and improves behavioral phenotypes in models of tinnitus

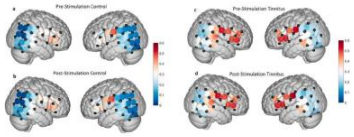
Investigator Sponsored Trial Planned To Test Opakalim for the Treatment of Tinnitus Using Functional Near-Infrared Spectroscopy (fNIRS)

Basura Laboratory at UPitt

Channel Configuration for the Probes



Increased RSFC in the Tinnitus Brain



RSFC, Resting-state functional connectivity. San Juan. Neuroreport. 2021.

KEY POINT

fNIRS uses near-infrared light to measure hemoglobin & hemodynamic changes in brain regions – a validated proxy for neural activity ideal for tinnitus research

Panel

MODERATOR

Tessa Romero
Equity Analyst
J.P.Morgan

PANELISTS

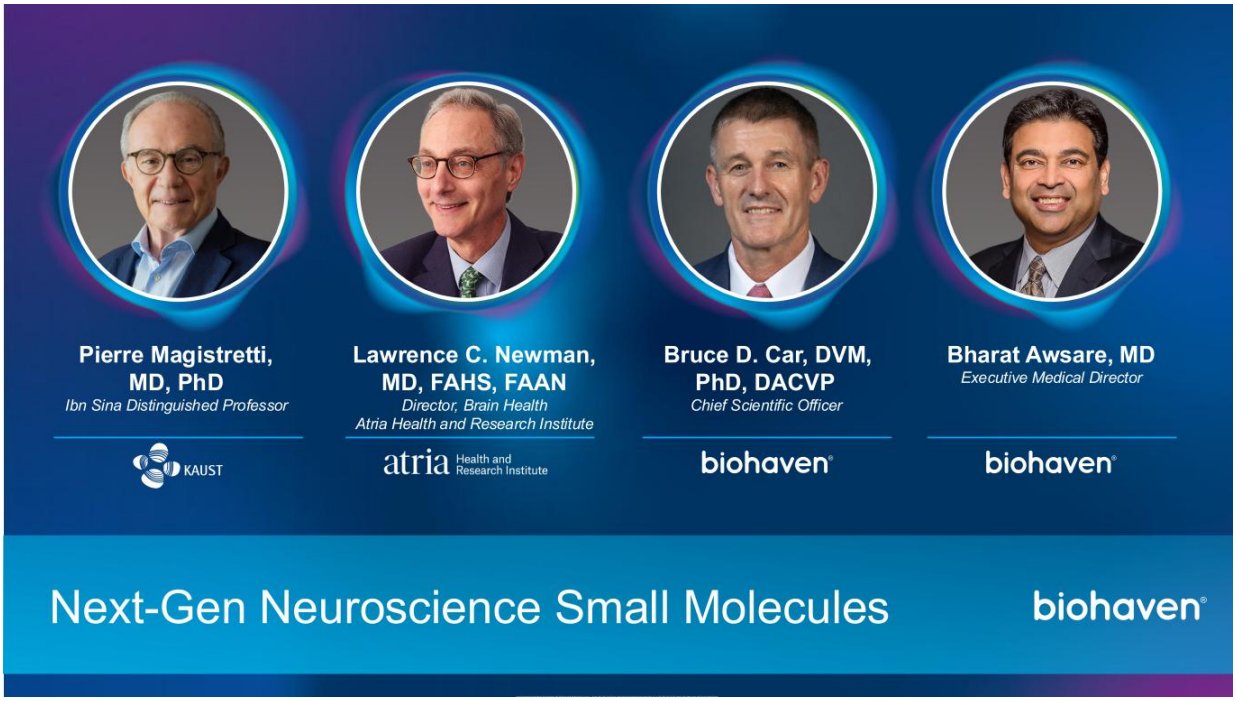
Aline Herlopian, MD
Neurologist and Associate Professor of Neurology
Yale School of Medicine

Matthias Koepp, MD, PhD
Professor of Neurology
University College London

Jason Lerner, MD
Medical Director
Biohaven

Steven Dworetzky, PhD
Senior Vice President, Kv7, Strategy & Development
Biohaven

BHVN
LISTED
NYSE


Pierre Magistretti, MD, PhD
Ibn Sina Distinguished Professor
KAUST
Lawrence C. Newman, MD, FAHS, FAAN
Director, Brain Health
Atria Health and Research Institute
atria Health and Research Institute
Bruce D. Car, DVM, PhD, DACVP
Chief Scientific Officer
biohaven
Bharat Awsare, MD
Executive Medical Director
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Next-Gen Neuroscience Small Molecules
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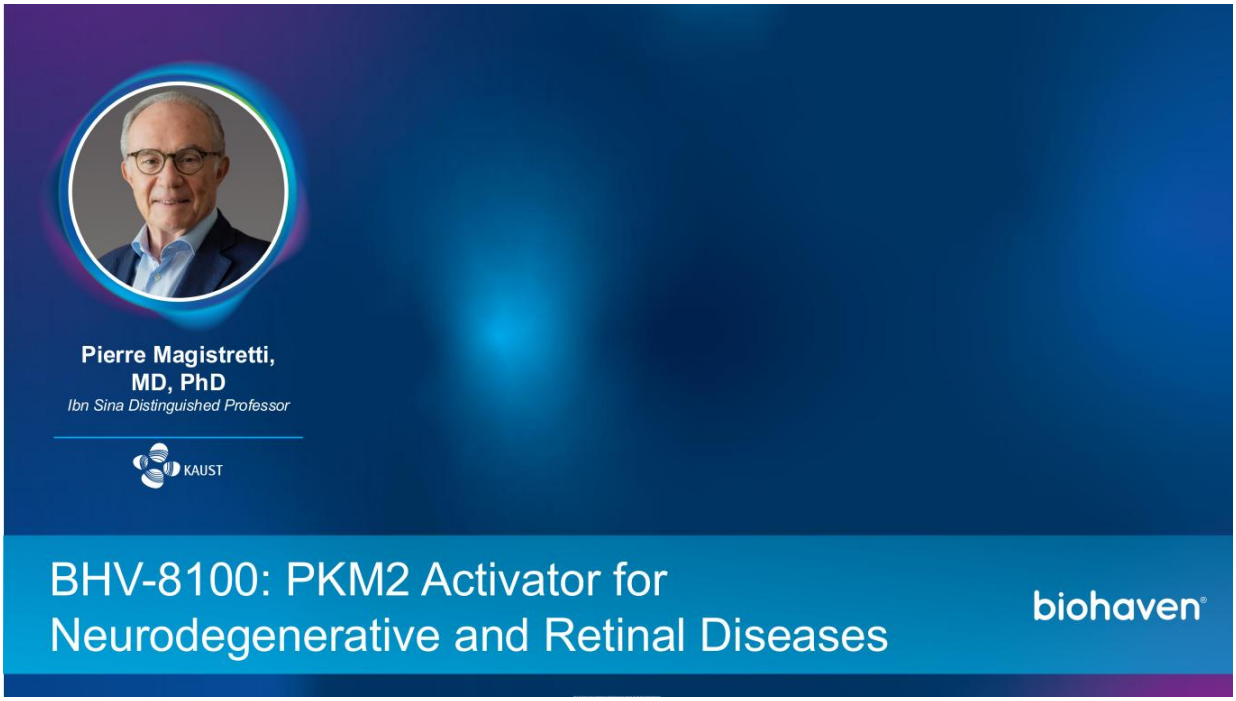
Pierre Magistretti,
MD, PhD
Ibn Sina Distinguished Professor
KAUST
BHV-8100: PKM2 Activator for
Neurodegenerative and Retinal Diseases
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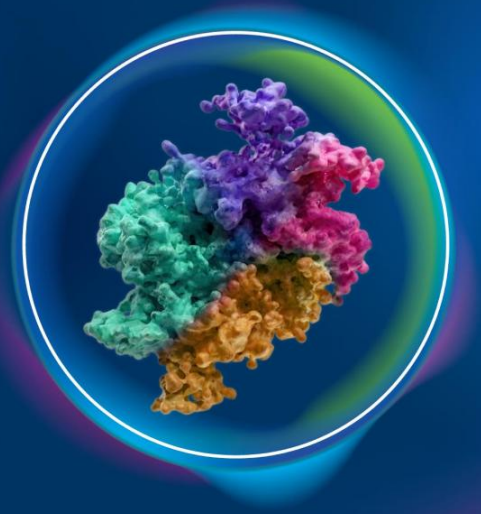
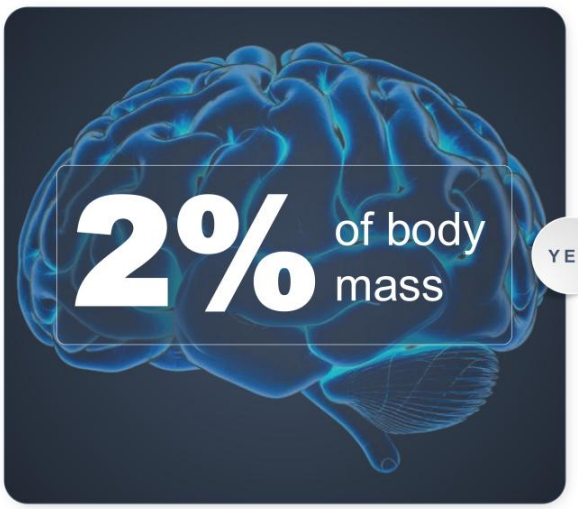
Disease Associated With Brain Metabolism and Aging



The Brain Has Considerable Energetic Requirements

DISCOVERY



YET

15% of **cardiac output**

25% of whole-body **glucose utilization**

20% of **oxygen consumption**

Energetics of Functional Activation in Neural Tissues

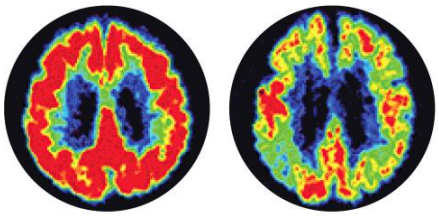
DISCOVERY

Louis Sokoloff

FDG-PET showing areas of cerebral glucose metabolism[1]

Healthy brain

Mild to moderate Alzheimer's disease brain



Normal cerebral glucose metabolism

Diminished cerebral glucose metabolism

Source: Neurochemical Research, Vol. 24, No. 2, 1999, pp. 321-329

1. Small. Proc Nati Acad Sci USA. 2000. Copyright 2013 National Academy of Sciences, U.S.A

Techniques for Functional Brain Imaging

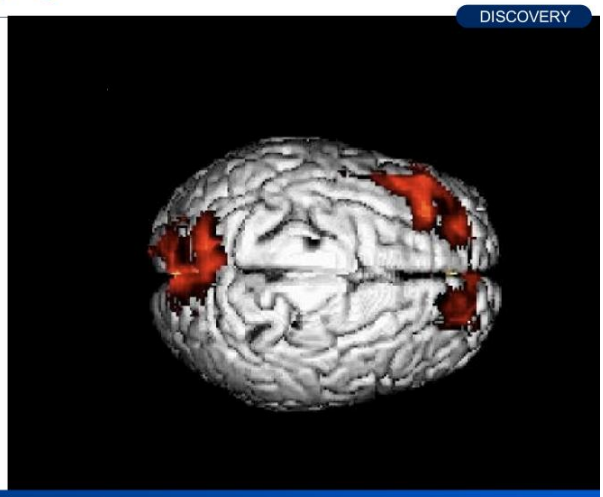
DISCOVERY

Positron Emission Tomography (PET):

- ^{18}F-deoxyglucose
- $^{15}O_2$
- $H_2{}^{15}O_2$

Functional MRI (fMRI):

- Change in the ratio of oxy-/deoxy hemoglobin



KEY POINT

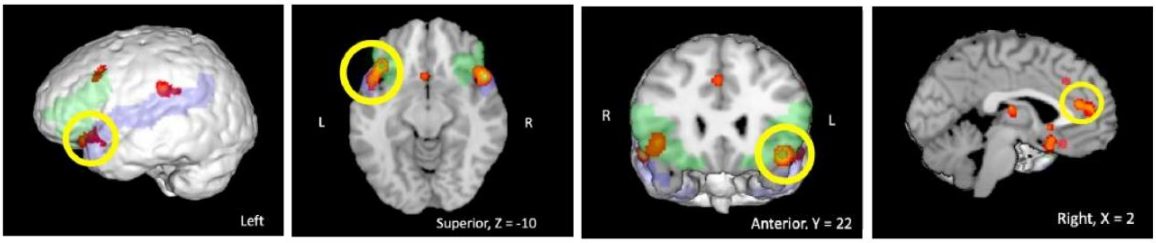
They detect signals related to energy consumption

Brain Aging and Energy Metabolism

DISCOVERY

- Aging leads to **reduction in brain glucose utilization**, i.e., **brain hypometabolism**, as revealed by reduced FDG-PET signal[1]
- Clinical studies showed positive correlation between brain **glucose metabolism** measured with FDG-PET and **cognitive performances**[2, 3]

Meta-Analysis Showing Frontal and Temporal Glucose Hypometabolic Clusters in Aging Individuals
(21 Clinical Studies, Total 911 Participants)[1]

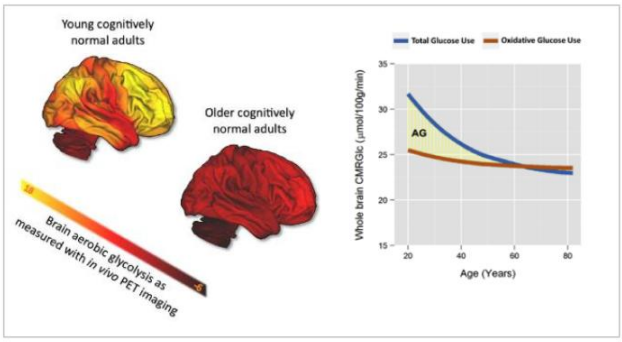


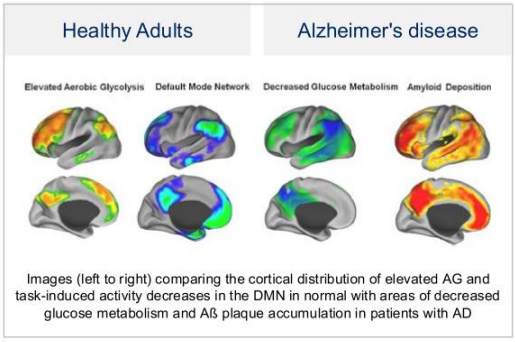
1. Deery. Human Brain Mapp, 2023. 2. Matthews. Alzheimer's Dement. 2021. 3. Matthews. Brain. 2021.

Aerobic Glycolysis Is Reduced in the Aging Brain

DISCOVERY

- **Aerobic glycolysis**, the metabolic process of glucose primarily promoted by astrocytes in the brain, is reduced in the aging brain[1]
- Reduction of aerobic glycolysis is pronounced in frontal and temporal regions[2]

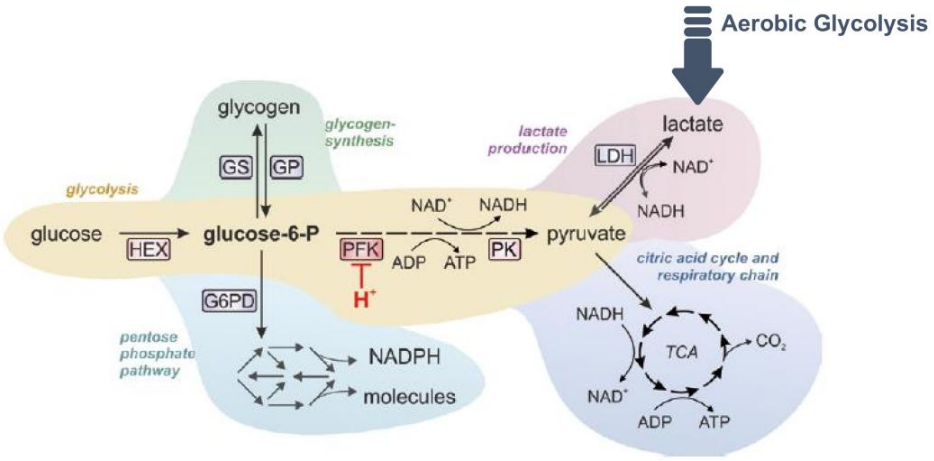




Images (left to right) comparing the cortical distribution of elevated AG and task-induced activity decreases in the DMN in normal with areas of decreased glucose metabolism and Aß plaque accumulation in patients with AD

1. Goyal. Cell Metab. 2017. 2. Vlassenko. Clin Transl Imaging. 2015.

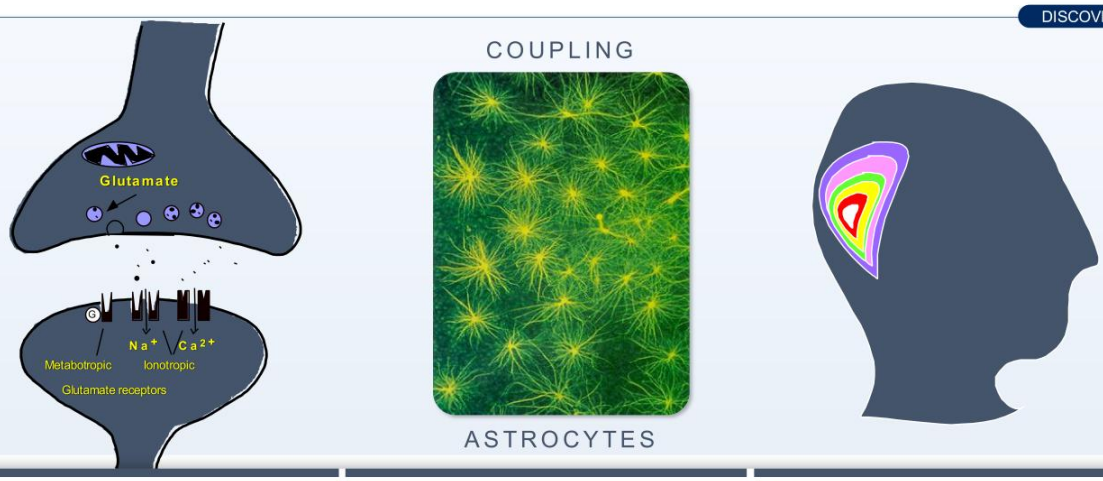
Metabolic Pathways of Glucose



Source: Dietmer. 2017.

Which Are the Cellular and Molecular Mechanisms Underlying the Coupling of Synaptic Activity With Metabolic Responses?

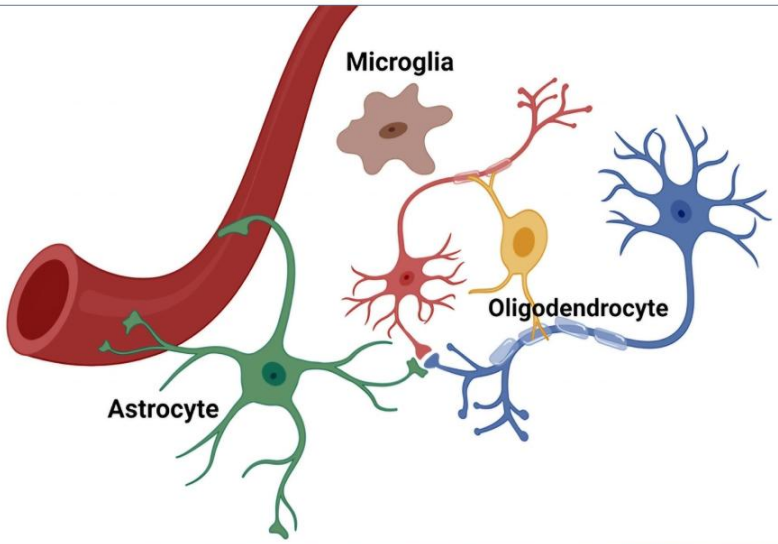
DISCOVERY

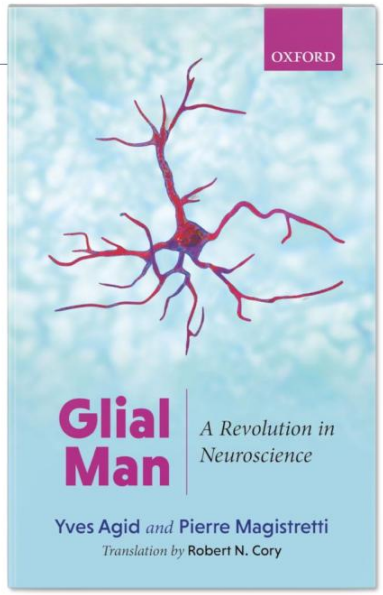


Neuronal Activity ⟷ Metabolic Responses ⇒

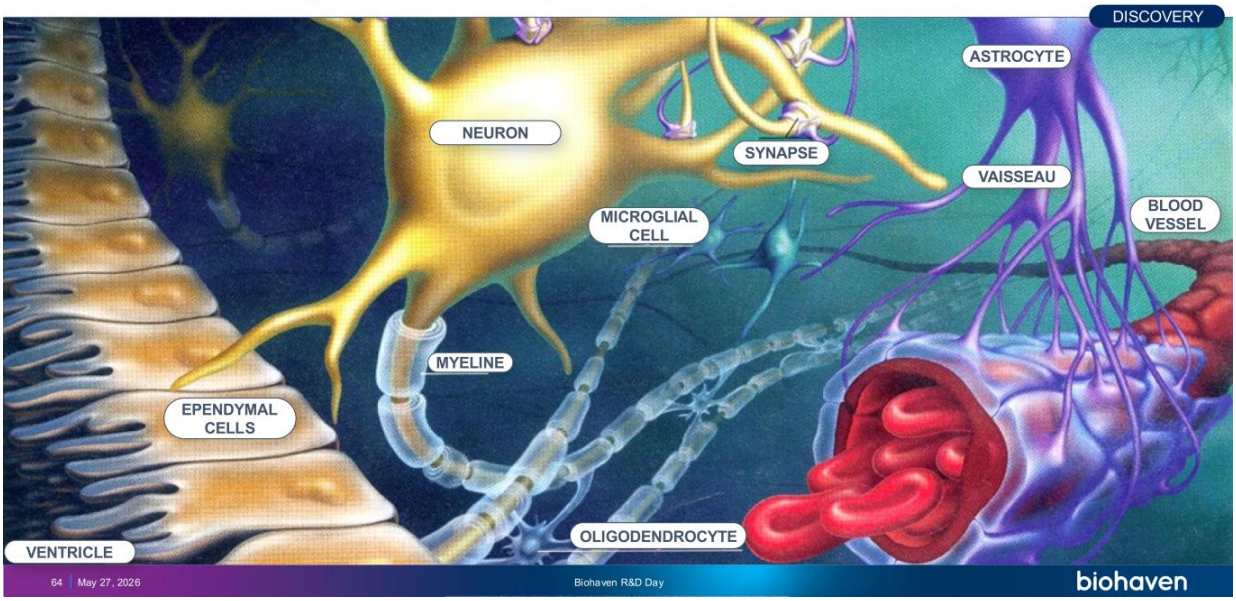
- Functional Imaging
- Synaptic function

Glia: “Glue”

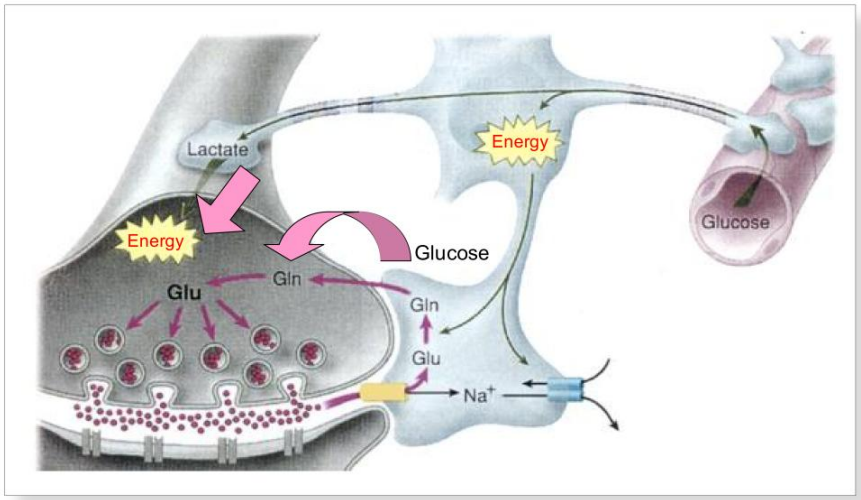

Microglia
Oligodendrocyte
Astrocyte


OXFORD
Glial Man
A Revolution in Neuroscience
Yves Agid and Pierre Magistretti
Translation by Robert N. Cory

Neuron – Astrocyte Relationship



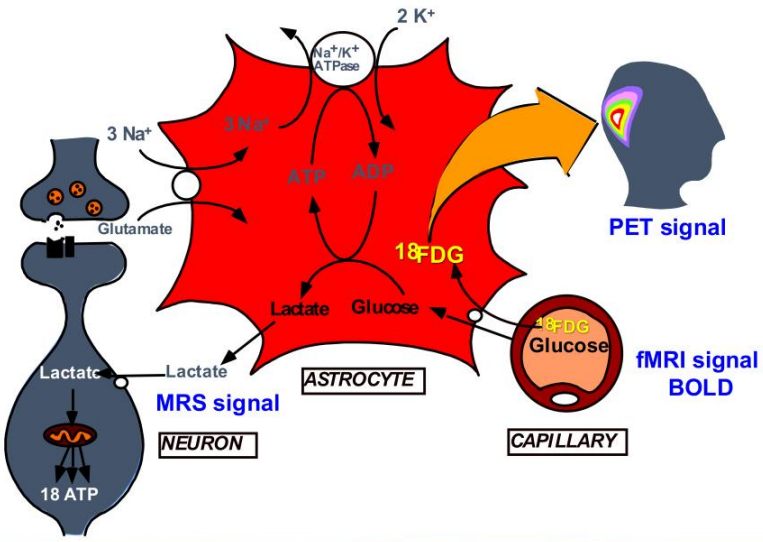
The Astrocyte-Neuron Lactate Shuttle (ANLS)

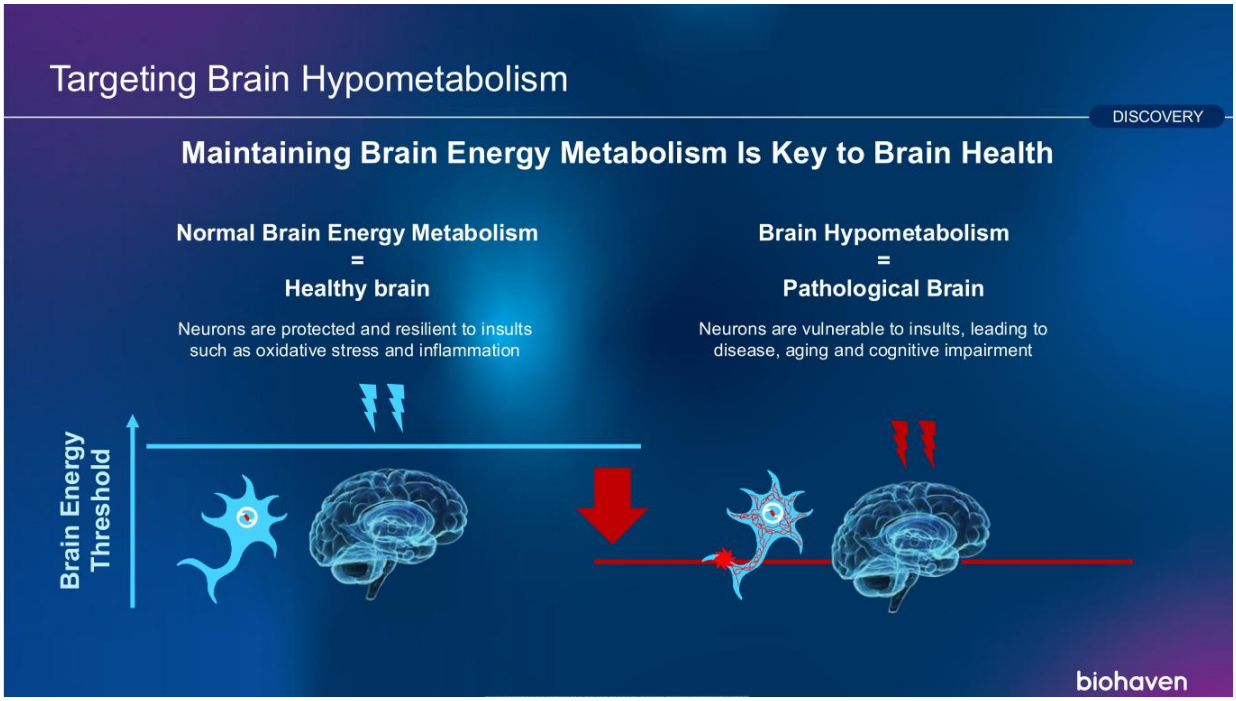


Modified from Magistretti. Science. 1999.

Role of Astrocytes in Brain Imaging Signals

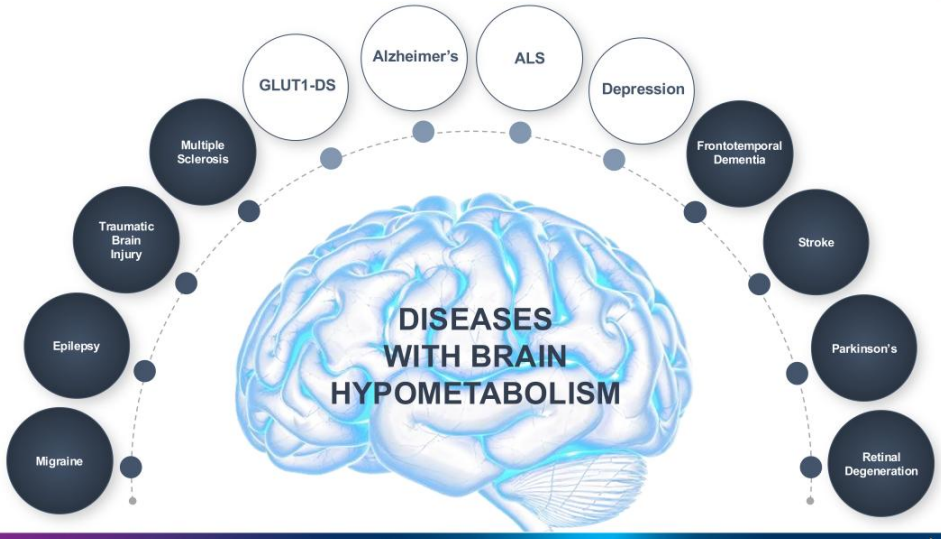
DISCOVERY




Targeting Brain Hypometabolism
DISCOVERY
Maintaining Brain Energy Metabolism Is Key to Brain Health
Normal Brain Energy Metabolism
=
Healthy brain
Neurons are protected and resilient to insults such as oxidative stress and inflammation
Brain Hypometabolism
=
Pathological Brain
Neurons are vulnerable to insults, leading to disease, aging and cognitive impairment
Brain Energy Threshold
biohaven

Targeting Brain Hypometabolism as a Therapeutic Approach

DISCOVERY



Targeting Hypometabolism as a Therapeutic Approach

DISCOVERY

- Astrocytes are the main providers of energy to neurons
- Targeting astrocytic metabolism is a viable therapeutic approach for maintaining cognitive function
- **BHV-8100 provides the first optimized, brain-penetrant clinical candidate and has entered Phase I in 2Q 2026**

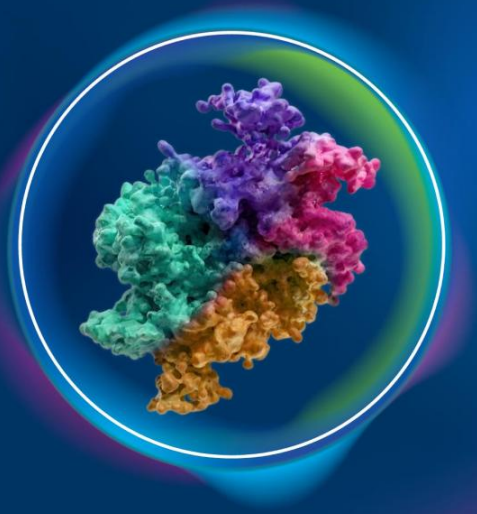

Bruce D. Car, DVM, PhD, DACVP
Chief Scientific Officer
biohaven
Bharat Awsare, MD
Executive Medical Director
biohaven
BHV-8100: Preclinical and Clinic
biohaven

biohaven®

BHV-8100

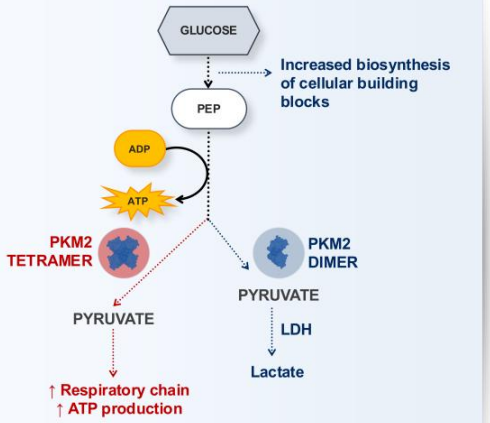
Pyruvate Kinase M2 Activator (PKM2)

Corrects brain hypometabolism

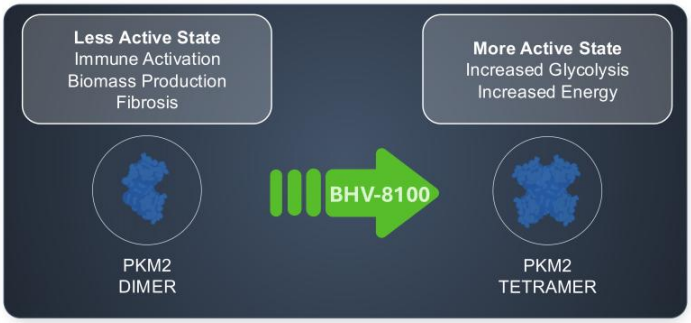


Activation of Pyruvate Kinase Increases Glucose Consumption and ATP Production While Reducing Deleterious Metabolism

DISCOVERY



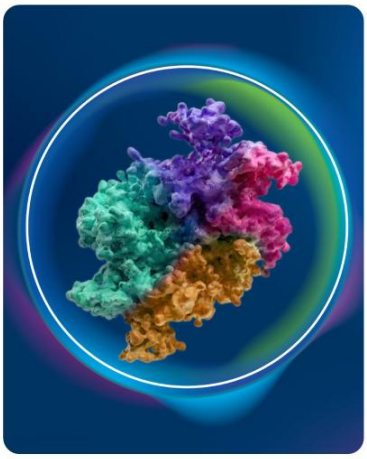
Source: Cancer Letters. 2015.



- BHV-8100 stabilizes enzymatically active tetramer state
- Increased energy in CNS
- Decreased neuroinflammation, angiogenesis and fibrosis
- Reduced deleterious metabolic intermediates

BHV-8100: First Brain-Penetrant PKM2 Activator

DISCOVERY



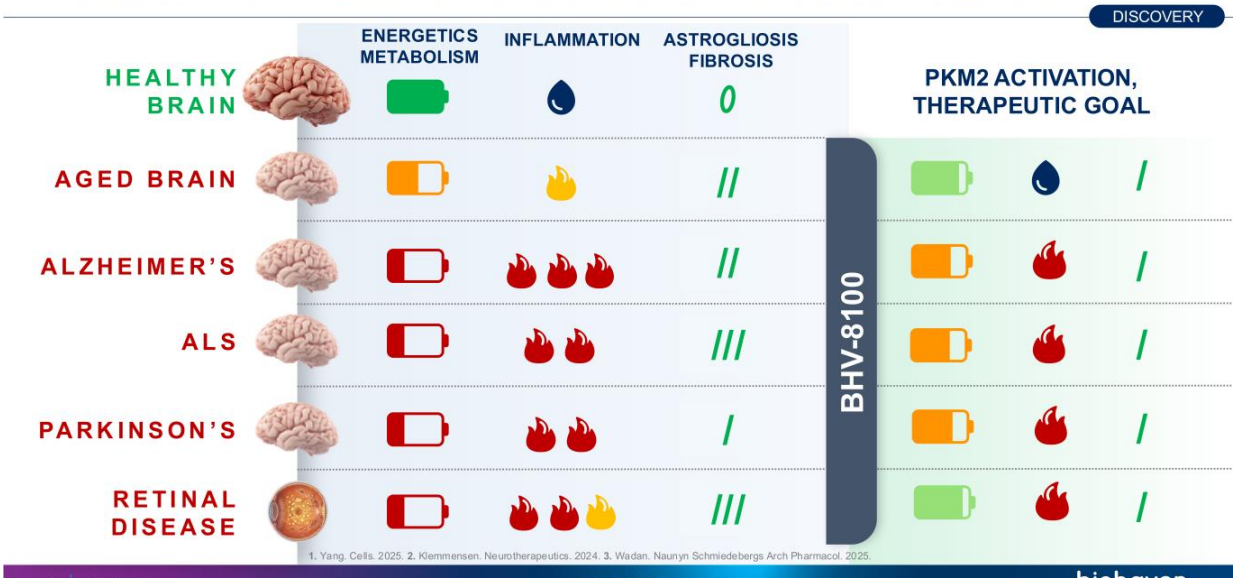
Oral small molecule medicine with multiple potential indications

- Neurodegeneration
- Retinal degeneration and inflammation
- Neuroinflammation
- Age-related changes: Central/Peripheral
- Brain ischemia

KEY POINT First-in-human dosing at pharmacologically relevant doses initiated 2Q 2026

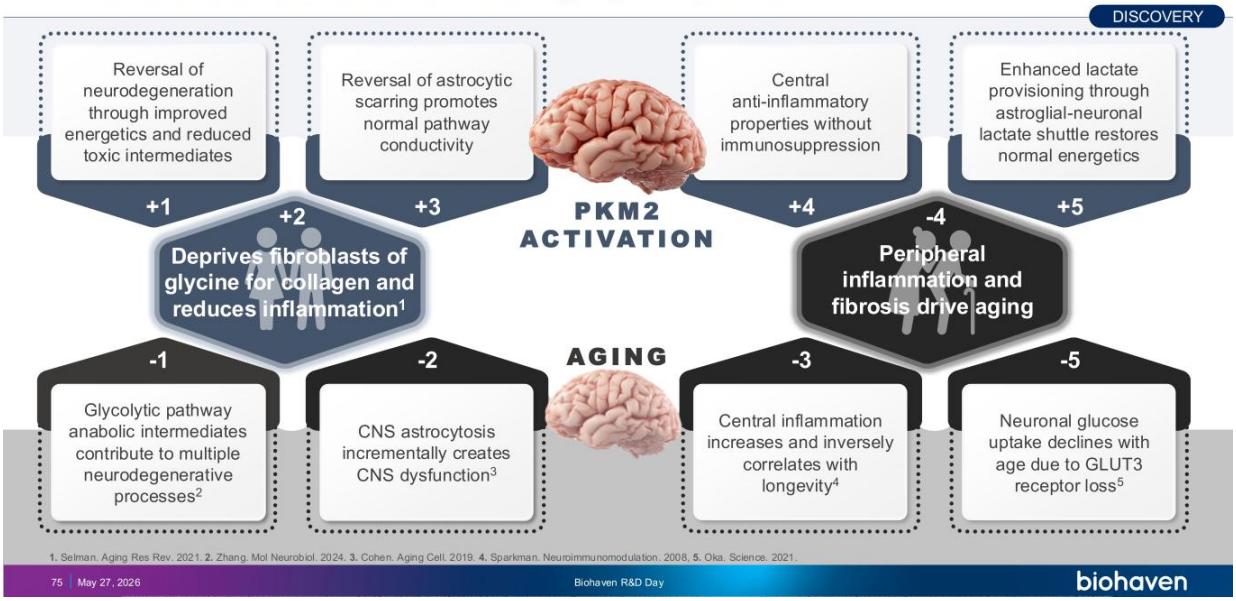
Stimulation of Brain Energetics, Reprogramming Metabolism and Reduced Inflammation Is the Future of CNS Disease Treatment

DISCOVERY



1. Yang. Cells. 2025. 2. Klemmensen. Neurotherapeutics. 2024. 3. Wadan. Naunyn Schmiedebergs Arch Pharmacol. 2025.

Central/Peripheral PKM2 Activation: A Perfect Constellation of Anti-Aging Properties

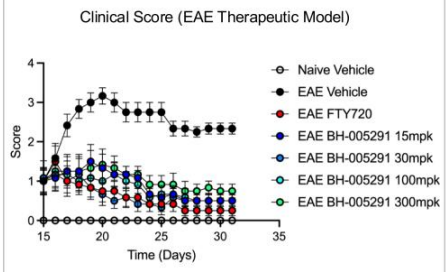


1. Selman. Aging Res Rev. 2021. 2. Zhang. Mol Neurobiol. 2024. 3. Cohen. Aging Cell. 2019. 4. Sparkman. Neuroimmunomodulation. 2008, 5. Oka. Science. 2021.

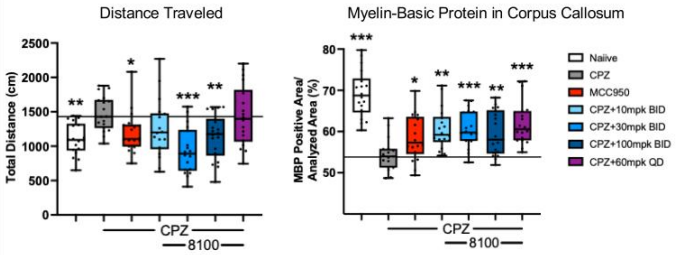
BHV-8100: Experimental Mitigation of Neuroinflammation and Restoration of Energetic Deficiency

DISCOVERY

BHV-8100 Shows Robust Reduction of Disease Burden in EAE



BHV-8100 Demonstrates Striking Efficacy in Cuprizone Model



* p < 0.05, ** p < 0.01, *** p < 0.001 relative to CPZ group, MCC950 is a n NLRP3 inhibitor.

KEY POINT

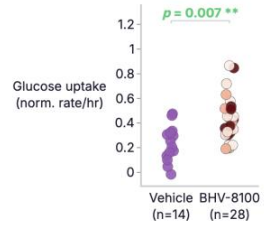
BHV-8100 demonstrates anti-inflammatory efficacy and a strong ability to promote oligodendroglial function in models of EAE

BHV-8100 Demonstrates Sustained Efficacy in Human Brains With Documented Alzheimer's Disease and All-cause Dementia

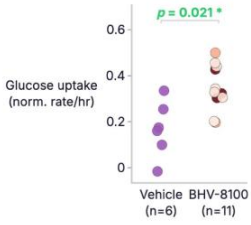
DISCOVERY

Reperfused human brains (Brainex™) allow precise study of brain penetrance, pharmacology, pharmacokinetics, pharmacodynamics and biomarkers in brains with documented diseases

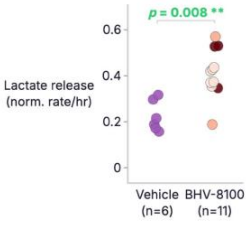
BHV-8100 Increases Glucose Utilization in Brains Across Diverse Dementia Diagnoses



Alzheimer's Disease: BHV-8100 Enhances Glucose Uptake



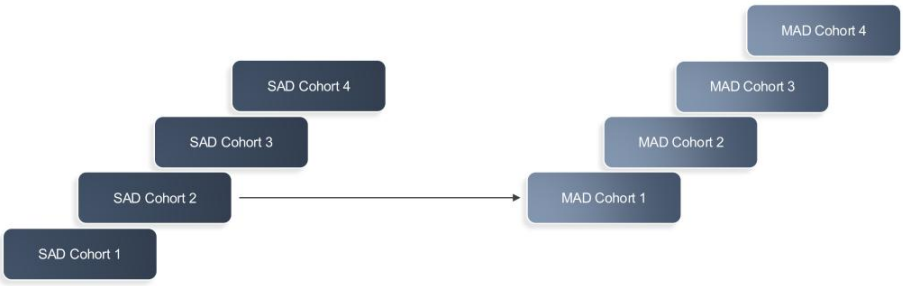
Alzheimer's Disease: BHV-8100 Enhances Lactate Production



KEY POINT Precise determinations of brain penetrance and dose-response pharmacology confirm efficacy and guide human dosage

Open Label, Placebo-Controlled FIH SAD/MAD Study To Evaluate Safety, Tolerability and PK of BHV-8100 in Healthy Adults

DISCOVERY



KEY STUDY DETAILS

Population: Male and non-childbearing female healthy adults

Treatment: BHV-8100 in escalating single and multiple doses vs. matching placebo (6:2 ratio at each cohort)

Key Objectives: PRIMARY: Safety and tolerability; SECONDARY: PK in plasma. CSF concentration (MAD Cohorts only)

*Representative schema

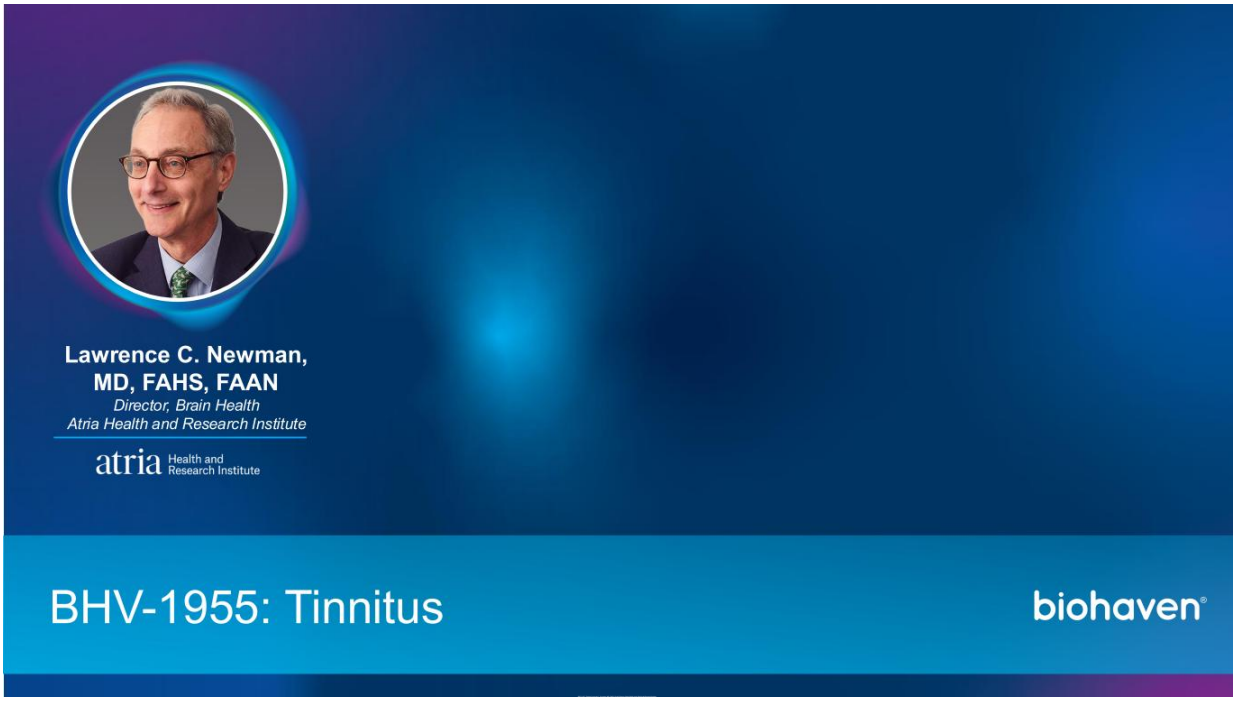
BREAKING NEWS **BHV-8100 achieves clinical milestone with first human dose in SAD/MAD study 2Q 2026**

Early FIH Data of BHV-8100 in SAD Shows Safety and Tolerability in Healthy Participants

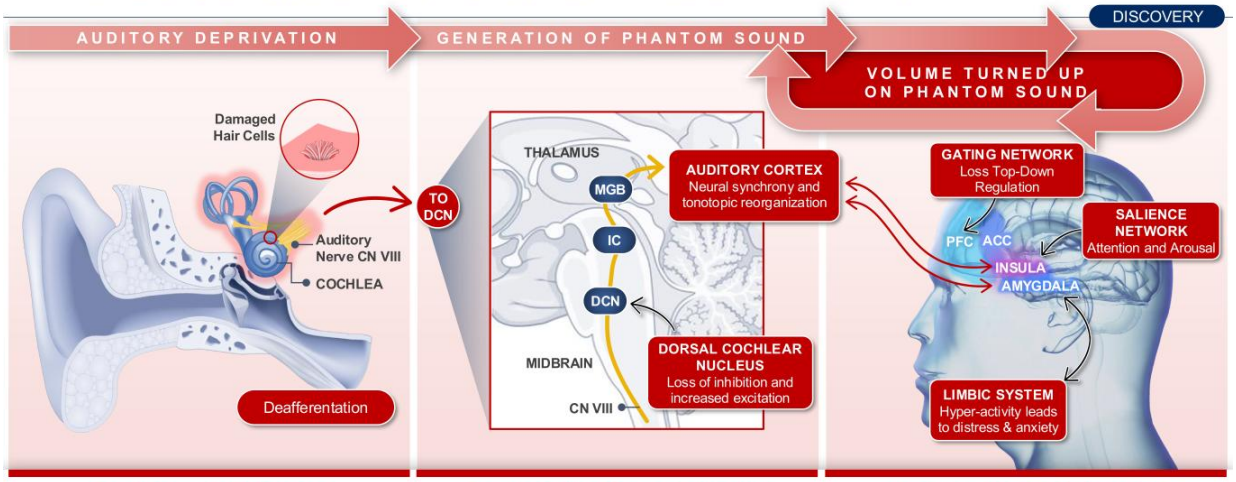
DISCOVERY

- No SAEs or severe AEs
- Most AEs were mild and resolved spontaneously
- No clinically significant changes in ECG
- No clinically significant trends in safety labs including LFTs

Preliminary data from ongoing study as of 22-May-2026.


Lawrence C. Newman,
MD, FAHS, FAAN
Director, Brain Health
Atria Health and Research Institute
atria Health and Research Institute
BHV-1955: Tinnitus
biohaven

Tinnitus Is a Sound Volume Control Problem in the Brain



Peripheral Pathway
Peripheral Damage

Central Auditory Pathway
Central Gain and Plasticity

Non-Auditory Pathways
Attention and Distress

Tinnitus: There Is No FDA-Approved, Mechanism-Based Pharmacologic Therapy Despite High Prevalence

DISCOVERY

Large Patient Population

- **2 million chronic tinnitus patients** have severe, debilitating disease that requires treatment
- **120 million worldwide**
- **Risk factors:** hearing loss, presbycusis, exposure to loud noises, medications, head and neck injuries, infections

Debilitating Symptoms

- **Phantom noise that can not be ignored**
- **Severe tinnitus has debilitating consequences**: anxiety, difficulty concentrating, sleep impairment, social isolation, cognitive impairment, depression and increased risk of suicide

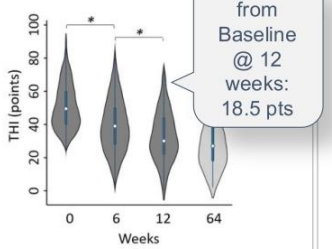
Limited Treatment Options

- **Hearing aides and sound therapy:** exposure to sound to mask phantom sound or reverse neural changes
- **Behavioral Therapy:** improve well being and quality of life
- **Medications:** There are no FDA-approved medications specifically for tinnitus

Clinical Evidence: Oxytocin Receptor Agonism Reduces Tinnitus Severity

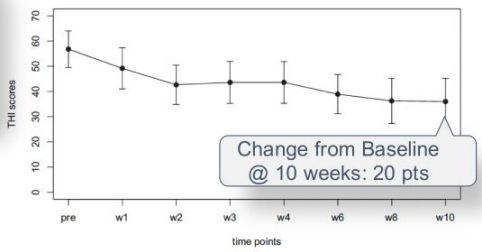
DISCOVERY

Lenire Device[1]



Bimodal stimulation
Only FDA-approved treatment for tinnitus

Low-Dose Oxytocin[2]



8 IU Oxytocin delivered intranasally BID led to similar reductions in the Tinnitus Handicap Index (THI)

High-Dose Oxytocin[3]

CASE STUDIES

	Patient 1	Patient 2
Dose	45 IU	45 IU
Frequency	QID	BID
THI Baseline	96	75
THI after treatment	16	18

Dosing started at 8 IU BID
Increased until tinnitus relief persisted until next dose

1. https://www.nature.com/articles/s41598-022-13875-x. 2. https://pmc.ncbi.nlm.nih.gov/articles/PMC5613090/. 3. NCT04210310 Clinical Research Protocol.

KEY POINT **Increasing dose and frequency of oxytocin extends duration of tinnitus symptom improvement**

Patient Testimonials

DISCOVERY

BAROTRAUMA

My noise was so bad, that for two years I thought I lived on the deck of an aircraft carrier and constantly ideated because of it. I went to 14 ENTs and acupuncturists and cranial sacrals all over the country and nothing worked. Then one day ***Dr. Newman gave me a nose spray, and the sound went to whisper or disappeared on most days, and my life returned to normal.***

IED EXPLOSION IN IRAQ

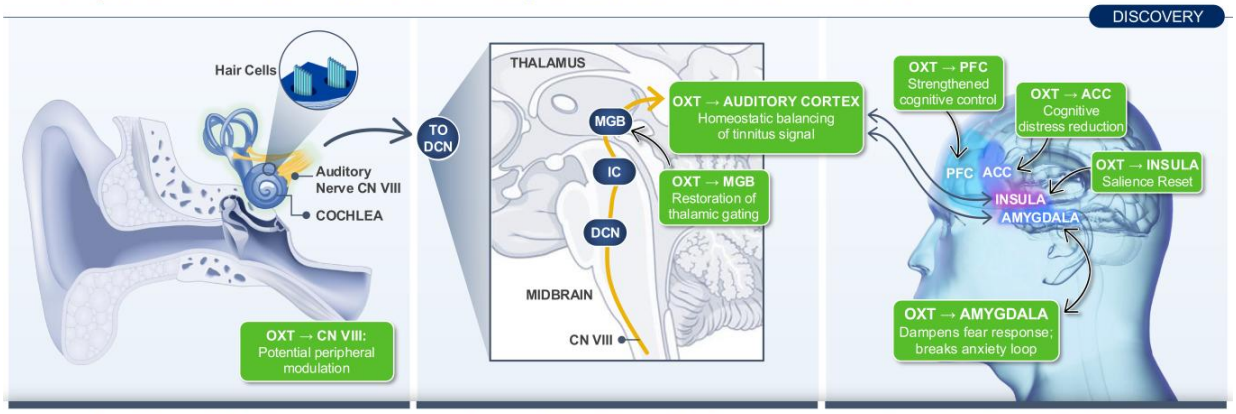
It did help. The spray reduced the high pitch frequency of the tinnitus *and although it did not resolve it completely it made it less obvious to me.*

Ménière's Disease

Despite being a physician and consulting several specialists, my tinnitus remained disabling. After intranasal oxytocin, it no longer does. ***My tinnitus improved rapidly and substantially. The benefit has been sustained, and I have experienced no adverse events.***

Oxytocin Tunes Neuronal Response to Phantom Noise

DISCOVERY

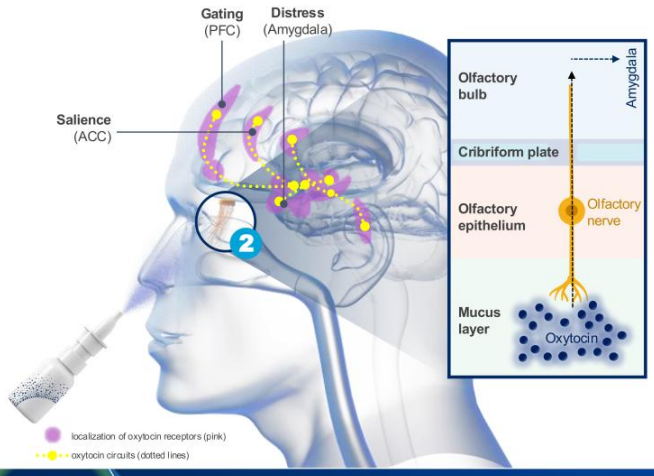


Peripheral Pathway | **Central Auditory Pathway** | **Non-Auditory Pathways**

KEY POINT Oxytocin calms hyperactive pathways in the brain to turn down the volume on the phantom sound

Reformulation Strategy To Deliver High-Dose Oxytocin

DISCOVERY



1. Achieve room temperature stability to eliminate need for refrigeration
2. Ensure efficient deposition to the olfactory epithelium to bypass the blood brain barrier
3. Reduce mucosal clearance and nasal leakage
4. Reduce dosing frequency

KEY POINT BHV-1955 is formulated to deliver oxytocin to brain regions impacted by tinnitus

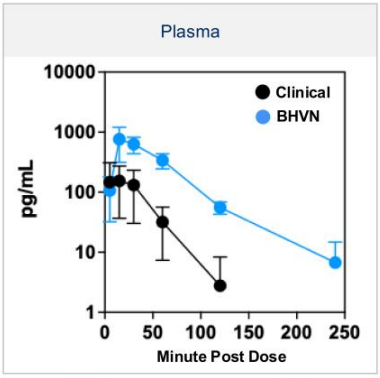
BHV-1955: Improved Exposure in Non-Human Primates Over Clinically Used Formulation

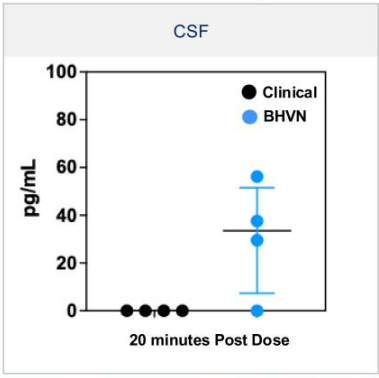
DISCOVERY

STUDY DESIGN

Test Articles and Formulations:
- **Clinical Formulation:** Formulated with mucolox
- **BHVN Formulation**

Dosing: Single dose IN, 48 IU
Subjects: n=4 non-naïve male cynomolgus macaques (7-8 kg)
Blood collection: Up to 4 hours
CSF collection: 20 minutes post dose



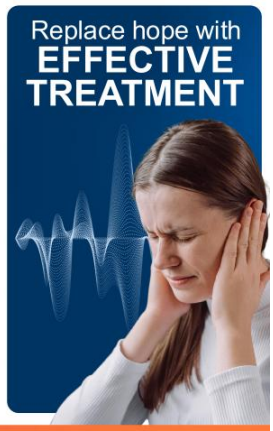


Formulation	Plasma C_{max} (pg/mL)	Plasma AUC_{last} (min*pg/mL)	Plasma T_{max} (min)	Plasma T_{last} (min)	CSF Concentration @ 20 min (pg/mL)
Clinical Formulation	191	12400	33.8	150	0; Detected in 0/4 animals
BHVN Formulation	798	39700	18.8	180	41.1; Detected in 3/4 animals

BHV-1955: Poised To Transform Tinnitus

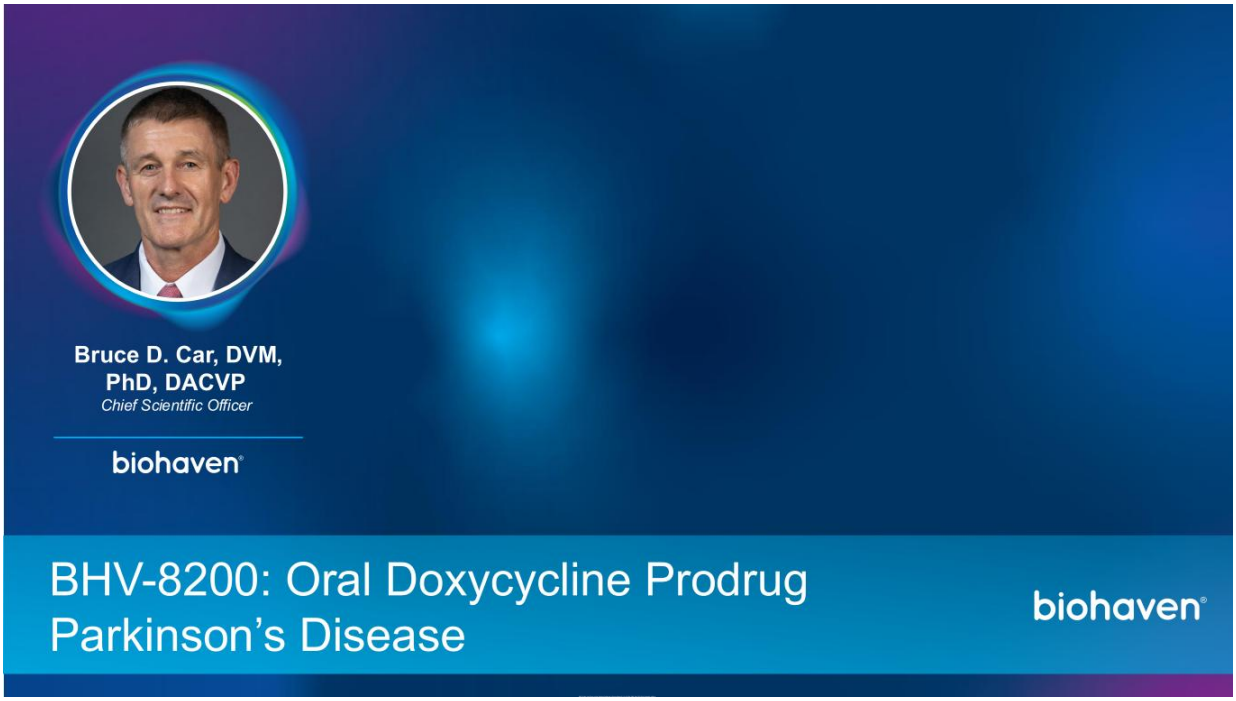
DISCOVERY

MIGRAINE PRE-CGRP (BEFORE 2018) A proven blueprint	THE PARALLEL IS CLEAR		TINNITUS TODAY The Same Landscape-The Same Opportunity
• **~1 billion** people globally • **~39 million** in the US • **~4 million** in the US have chronic migraine	**Massive Unmet Need**		• **749 million** people worldwide have tinnitus • **25-40 million** people in the US experience tinnitus • **2 million** have severe, debilitating disease in the US
• **31%** reluctant to seek help • **~40%** eligible for prevention, only **17%** using it	**Low Treatment-Seeking**		• **~20%** of tinnitus sufferers seek medical help • **~34%** of all tinnitus sufferers plan to seek help
Repurposed drugs included anticonvulsants, beta-blockers, antidepressants, blood pressure drugs	**Disease-Specific Therapies Lacking**	**No FDA-Approved Therapies**	• No approved drug (pharmacotherapy) for tinnitus • Lenire® Device: FDA-authorized neurostimulation
"Believed a doctor could not do anything more"	**Patients Become Resigned to Suffering**		Patients are frequently told "there are no medicines"
Nearly half stopped or modified prevention within 6 months due to poor tolerability or lack of efficacy	**High Discontinuation and Dissatisfaction**	**Limited Support and Access**	Only **~50%** who discuss tinnitus with a physician receive any **treatment recommendation**
CGRP approvals (2018) changes migraineurs lives	**Breakthrough Changed Everything**	**Breakthrough Can Change Everything**	**An effective therapy transforming millions of lives!**



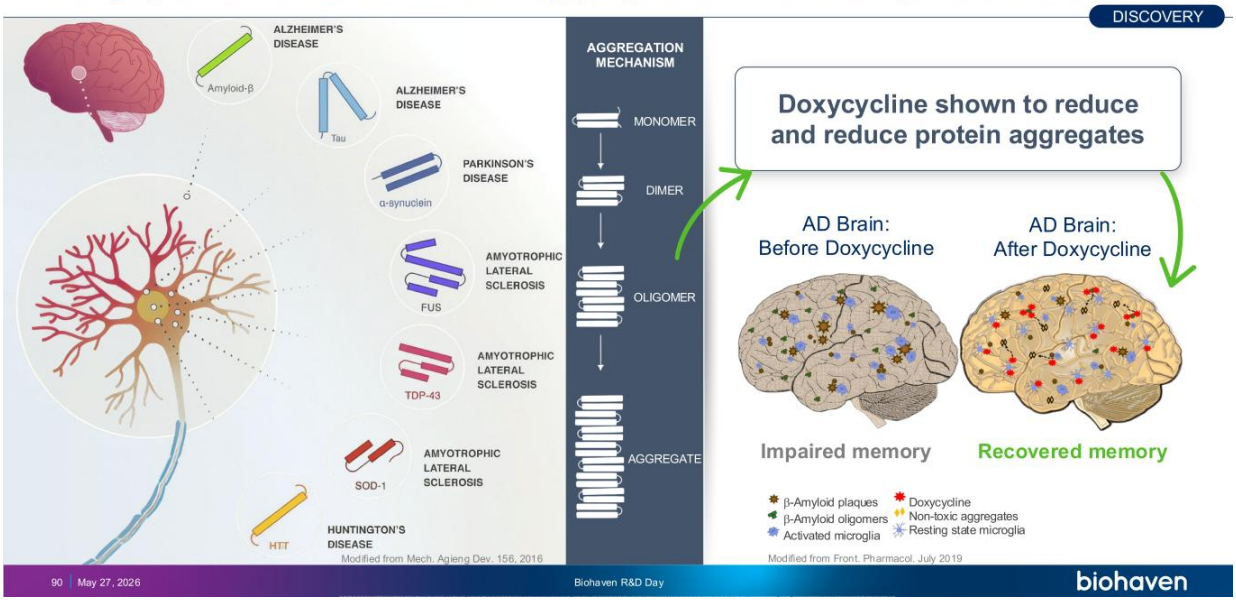
BREAKING NEWS

The tinnitus landscape today mirrors the migraine landscape before CGRP – same scale, same gaps, same opportunity for a breakthrough


Bruce D. Car, DVM,
PhD, DACVP
Chief Scientific Officer
biohaven
BHV-8200: Oral Doxycycline Prodrug
Parkinson's Disease
biohaven

Doxycycline Reduces Protein Aggregates in Neurodegenerative Diseases

DISCOVERY



Refining the Favorable Pharmacology of Doxycycline for Parkinson's Disease Treatment With BHV-8200

DISCOVERY

Abundant evidence exists for doxycycline mitigating Parkinson's disease progression[1,2,3]

• Alpha synuclein aggregation and Lewy body-driven pathology →	• Doxycycline prevents aggregation and disaggregates complexes at relevant concentrations
• Neuroinflammation driven by Th17 hypersensitivity →	• Mitigated Th17-driven neuroinflammation
• Dopaminergic neurodegeneration secondary to neuroinflammation and toxic aggregates →	• Reduced dopaminergic neurodegeneration secondary to toxic aggregates

However, doxycycline has undesirable properties, addressed by BHV-8200

	BHV-8200
• Co-administration with food →	• Eliminates gastric irritation
• Intestinal antibacterial dysbiosis →	• Eliminates antimicrobial activity in the GI
• BID dosing required →	• Exposure suitable for QD administration

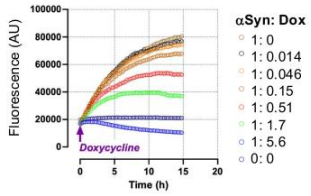
1. La Vitola. Parkinsonism Relat. Disord. 2023. 2. Dominguez-Meijide. Neurobiol. Dis. 2021. 3. Gonzalez-Lizarraga. Sci. Rep. 2017.

Doxycycline Prodrug Optimized for the Treatment of Parkinson's Disease

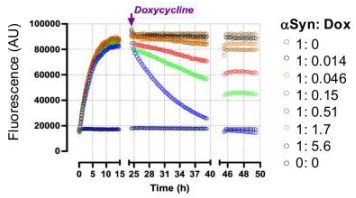
DISCOVERY

- Broad application through inhibition of aggregation:
  - α-synuclein
  - TDP43
  - Amyloid
  - Tau
- BHV-8200 purposefully synthesized to
  - Allow QD delivery
  - Sustain plasma and brain concentrations
  - Removes local (intestinal) anti-bacterial activity
  - Permits 505(b)(2) pathway for registration
- Active agent released by BHV-8200 shown to:
  - Inhibit α-synuclein aggregation
  - Drives disaggregation of preformed aggregates
  - Confirms optimal deliverable
  - Prodrugs show sustained systemic delivery

Inhibition of α-synuclein Aggregation



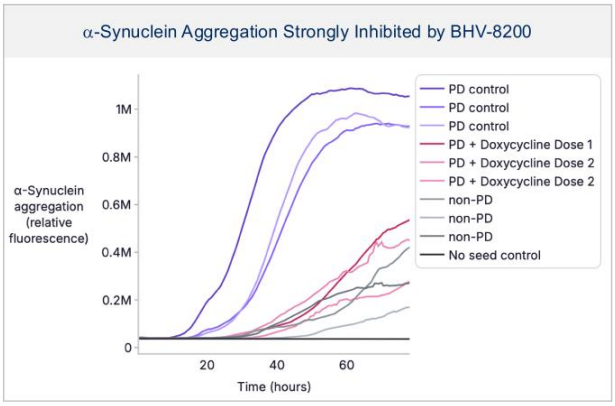
Disaggregation of Preformed of α-synuclein Aggregates

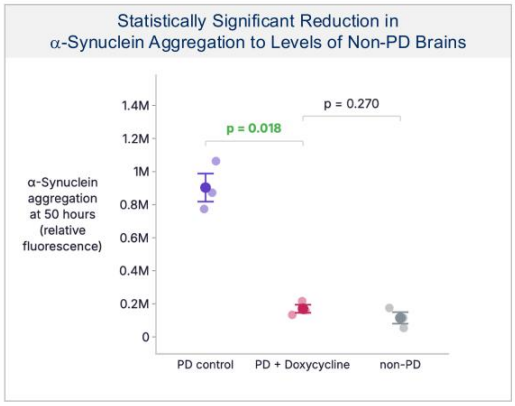


1. La Vitola. Parkinsonism Relat. Disord. 2023. 2. Dominguez-Meijide. Neurobiol. Dis. 2021. 3. Gonzalez-Lizarraga. Sci. Rep. 2017.

Bexorg BrainEx™: Doxycycline Delivered to Human Brains Reduces α-Synuclein Aggregation to Non-Parkinsonian Levels

DISCOVERY





KEY POINT

Unexpected potency in human brains precisely confirms safe plasma and brain concentrations for correction of α-synuclein-driven pathology


Bruce D. Car, DVM,
PhD, DACVP
Chief Scientific Officer
biohaven
TRPM3 CNS Penetrant
biohaven

BHV-2120: CNS Penetrant Molecule for Multiple Indications

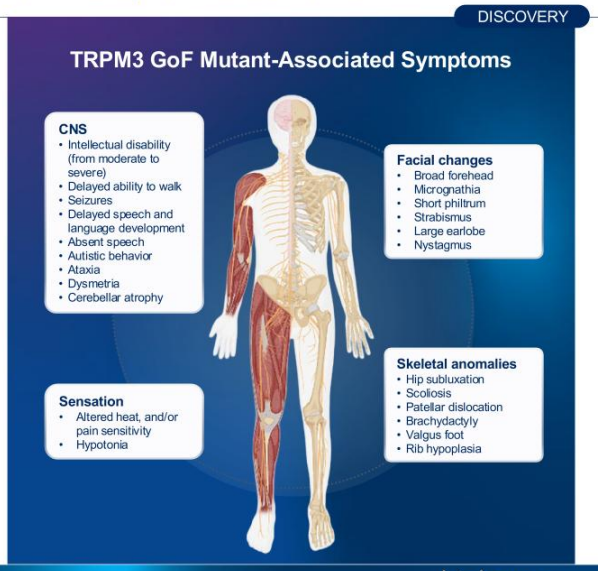
DISCOVERY

Central TRPM3

- Gain-of-function (GoF) variants in TRPM3 cause developmental and epileptic encephalopathies
- TRPM3 activation causes seizures in mice
- TRPM3 inhibition causes potent antiseizure efficacy in a preclinical model
- Brain-penetrant TRPM3 antagonists have the potential to treat a range of seizure, pain and neuropsychiatric disorders

BHV-2120

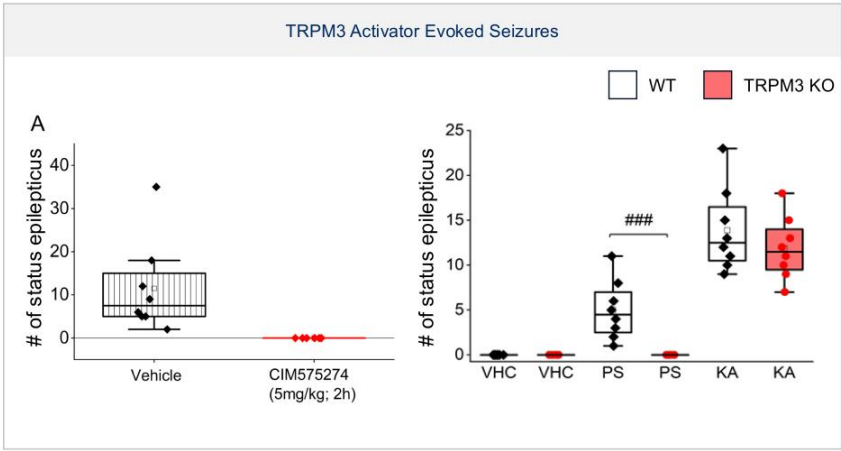
- BHV-2120 inhibition causes potent and long-lasting antiseizure efficacy rat maximal electroshock (MES)
- BHV-2120 is a development candidate demonstrating a wide therapeutic index preclinically
- Evaluating in additional seizure and neuropsychiatric models



Source: Roelens. Biochim Biophys Acta Mol Cell Res. 2024.

Central TRPM3 Inhibition Prevents Pregnenolone Sulfate-Evoked Status Epilepticus

DISCOVERY

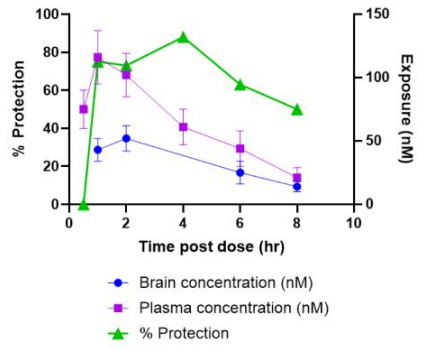


- Orally administered BHV-2120 completely blocks (PS)-evoked seizures
- PS evokes status epilepticus in wild-type (WT) mice but not TRPM3 knockout (KO) mice
- TRPM3 underlies PS ability to induce seizures

BHV-2120: Blocks Maximal Electroshock MES-Evoked Seizures

DISCOVERY

Time Course for Seizure Protection (0.1 mg/kg, oral dose)



- Rat MES is a highly translatable seizure model
- BHV-2120 is highly potent and effective at blocking MES-evoked seizures
- BHV-2120 effects are long-lasting with substantial efficacy remaining after brain concentration has diminished

Panel

MODERATOR

Brian Skorney
Equity Analyst

BAIRD

PANELISTS

Pierre Magistretti, MD, PhD
Ibn Sina Distinguished Professor
KAUST

Lawrence C. Newman, MD, FAHS, FAAN
Director, Brain Health
Atria Health and Research Institute

Bharat Awsare, MD
Executive Medical Director
Biohaven

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

BHVN
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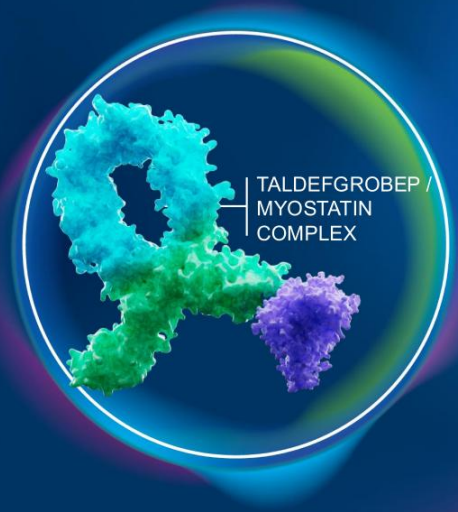
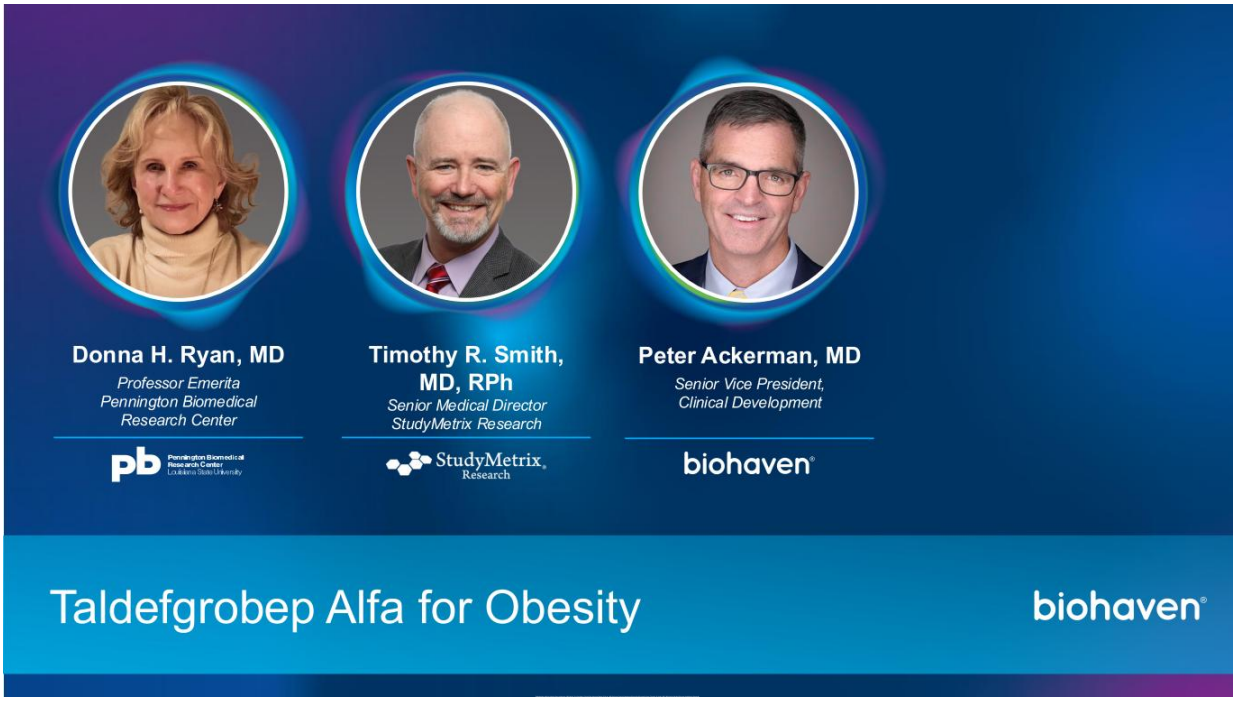
MYOSTATIN ACTIVIN INHIBITOR:
TALDEFGROBEP ALFA

Targeting High-Quality Weight Loss




Donna H. Ryan, MD
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Body Composition Concerns
With Weight Loss Medications
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Scientific advisor	AbbVie, Altimmune, Amgen, AstraZeneca, Boehringer Ingelheim, Biohaven, Calibrate, Carmot/Roche/Genentech, CinRx, Currax, eMed, Epitomee, Fractyl, i2o, ICON, Kailera, Lilly, Nestle, Novo Nordisk, Pfizer, Protagonist, Regeneron, Regor, Rhythm, Souffle Source Bio, Structure Therapeutics, Tenvie, Wondr Health, WW, Zealand
Speaker's bureau	Novo Nordisk, Lilly
Stock options	Epitomee, Calibrate, Roman
DSMB	IQVIA setmelanotide (2); Lilly (1); CinRx (1)

State-of-the-Art in Obesity Medicine

TALDEFGROBEP

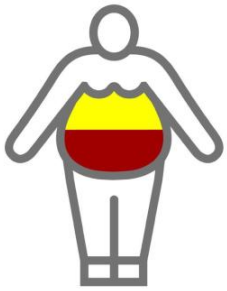
- Growing enthusiasm for robust weight loss achieved with GLP-1, GLP-1/GIP RA medications
  - More patients being treated and achieving **more weight loss, thus lean loss is a growing concern**
- Treatment includes broader patient profiles
  - More older individuals, more patients with chronic disease, many in lower BMI range = **more potential for excessive lean mass loss**
- Emerging new targets with new potential for disease modification (Glucagon, Amylin, Amylin/Calcitonin RAs)
  - Body composition effects are **always** a focus for new agents
- Growing guideline-driven movement for better diagnosis **beyond BMI**, and movement to **treat-to-target anthropometrics**

THE RESULT:
Growing concern for body composition optimization with pharmacotherapies

The Major Component of Lean Mass Loss Is Muscle

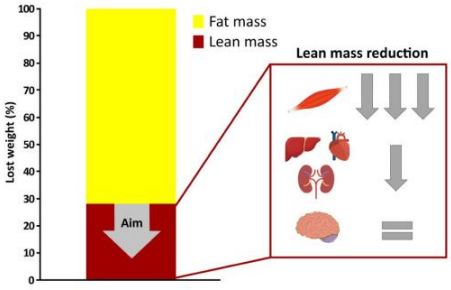
TALDEFGROBEP

Before Weight Loss[1]



Total body fat percentage can vary in adults with obesity (25-50+%). This percentage increases with age.

Composition of Weight Loss[1]



15-40% of weight loss due to sustained energy restriction comes from lean mass.

1. Christoffersen BØ. Obesity (Silver Spring). 2022. **2.** Mocciaro. BMJ Nutr Prev Health. 2025.

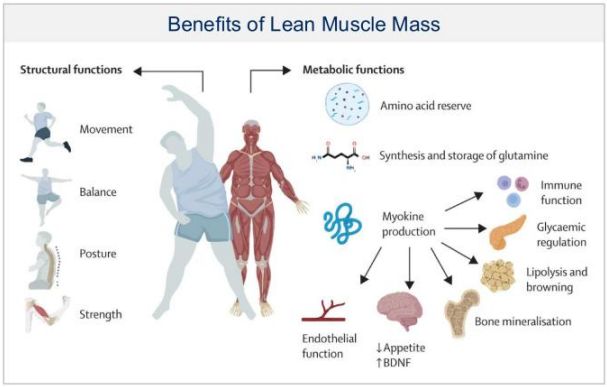
KEY POINT

Up to 40% of total body weight loss with GLP-1-based therapies is due to reductions in healthy lean mass[2]

Lean Muscle Mass Is Critical Determinant of Metabolic Health, Physical Function and Healthy Aging

TALDEFGROBEP

- Muscle mass is important to glucose tolerance, bone density and cognitive function[1-3]
- After 30, adults experience accelerating age-related decline in muscle mass and strength[4]
- Low muscle volume is associated with increased risk for morbidity and mortality, independent of body weight and physical function[5-8]



1. Merz. Compr Physiol. 2021. 2. Han. J Orthop Surg Res. 2023. 3. Tessier. JAMA Netw Open. 2022. 4. Wilkinson. Ageing Res Rev. 2018. 5. Linge. J Cachexia Sarcopenia Muscle. 2021. 6. Wang. PLoS One. 2023. 7. Valenzuela. BMC Musculoskelet Disord. 2020. 8. Medical Press. https://medicalxpress.com/news/2024-05-poor-muscle-health-common-people.html. Accessed 17-MAY-2026.

KEY POINT

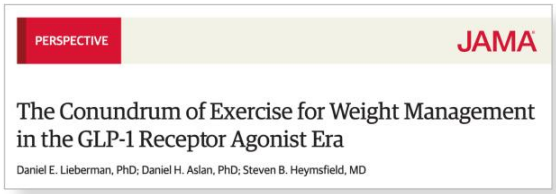
Excessive lean muscle loss can have significant long-term implications, especially in those at risk for sarcopenia

Lifestyle and Novel Pharmacotherapies for Weight Loss Have Not Been Effective in Preserving Muscle Mass

TALDEFGROBEP

LIFESTYLE

"The problem with exercise is effectiveness, not efficacy"[1]


PERSPECTIVE

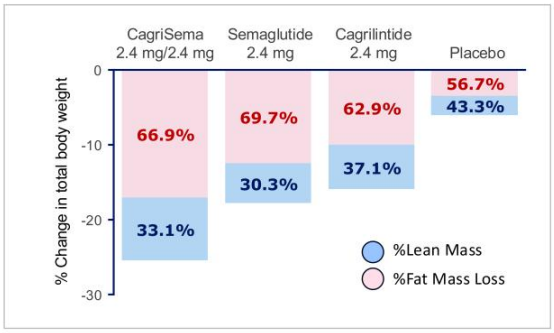
JAMA

The Conundrum of Exercise for Weight Management in the GLP-1 Receptor Agonist Era

Daniel E. Lieberman, PhD; Daniel H. Aslan, PhD; Steven B. Heymsfield, MD

NEW TARGETS

Amylin Calcitonin Dual Agonist Cagrilintide[2]



1. Lieberman. JAMA, May 2026. 2. Ravussin. 33rd European Congress on Obesity. 2026.

KEY POINT Amylin agonists like cagrilintide have not been effective in sparing lean muscle mass

Discontinuation of GLP-1 Agonists Is Associated With Rapid Weight Regain, Mostly in the Form of Visceral Fat

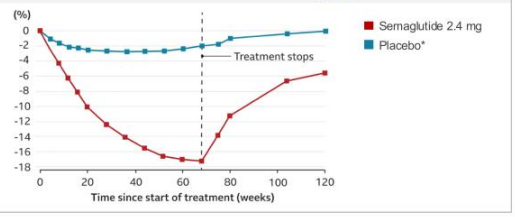
TALDEFGROBEP

- Approximately two-thirds of Americans stop GLP-1 therapy within one year of initiation[1]
  - GI-related side effects are the most common reasons for discontinuation[2]
- Approximately two-thirds of lost body weight returns within one year of stopping GLP-1 therapy[3]
  - **After stopping GLP-1 therapy, weight returns in the form of central obesity and visceral adiposity[1]**

Most Common GI-related Reasons for Discontinuation of GLP-1 Therapy[2]

Reason	Rate
Made me feel sick	64.4%
Made me throw up	45.4%
Caused diarrhea/gas/bloating	26.3%

Weight Rebound Following Discontinuation of Wegovy[3]



1. Young. Scientific American. 2024. 2. Sikirica. Diabetes Metab Syndr Obes. 2017.
3. Wilding. Diabetes Obes Metab. 2022. 4. Pownall. Obesity. 2015.

KEY POINT

Weight is regained primarily as fat
In Look AHEAD, a study of >5,000 persons with diabetes, weight regain was 100% fat[4]

State-of-the-Art, In-Clinic Assessment Tools: DEXA, BIA and 3-D DA To Be Validated by REAL Body Study

TALDEFGROBEP

	DEXA	BIA	3-D DA
PROS	Accurate bone mass, fat mass, lean mass and regional composition	Accurate extracellular water, intracellular water, total body water	Fat mass, fat free mass circumferences
CONS	Does not measure skeletal muscle, circumferences	Hydration affects accuracy; does not measure bone mineral content, circumferences	Does not measure skeletal muscle, bone mineral content

Fat mass

Lean soft tissue

Bone mineral content

Total body water

Fat free mass

Fat mass

Body cell mass

Skeletal muscle mass

Fat mass

Fat free mass

McMath. Obesity Reviews 2026

KEY POINT

Emerging body composition technologies are reshaping how obesity is diagnosed and how treatment success is defined

Inhibition of Myostatin + Activin Improves Body Composition Change

TALDEFGROBEP

EMBRAZE Study (Apitegromab + Tirzepatide) — Change in Baseline Body Composition at Week 24[1]

Body Compartment % (SE)	Apitegromab (10 mg/kg) + Tirzepatide n=43	Placebo + Tirzepatide n=44	Difference, Apitegromab vs. Placebo
%Change in TBW	-12.3	-13.4	-1.1
%TBW Loss due to LM	14.6 (3.19)	30.2 (2.89)	-15.6 (3.23)
%TBW Loss due to FM	85.3 (3.22)	69.5 (2.93)	15.8 (3.27)

COURAGE Study (Trevogrumab + Semaglutide +/- Garetosmab) — Change in Baseline Body Composition at Week 26[2]

Body Compartment % (SE)	Semaglutide n=151	Low-dose Combo n=149	Higher-dose Combo n=152	Triplet n=147
%Change in TBW	-10.6 (0.5)	-9.9 (0.5)	-11.1 (0.5)	-13.4*** (0.6)
%LM	-6.5 (0.5)	-3.3 (0.5)	-3.8 (0.5)	-2.0 (0.6)
%FM	-15.7	-17.3 (0.9)	-19.1 (0.9)	-27.1 (1.1)

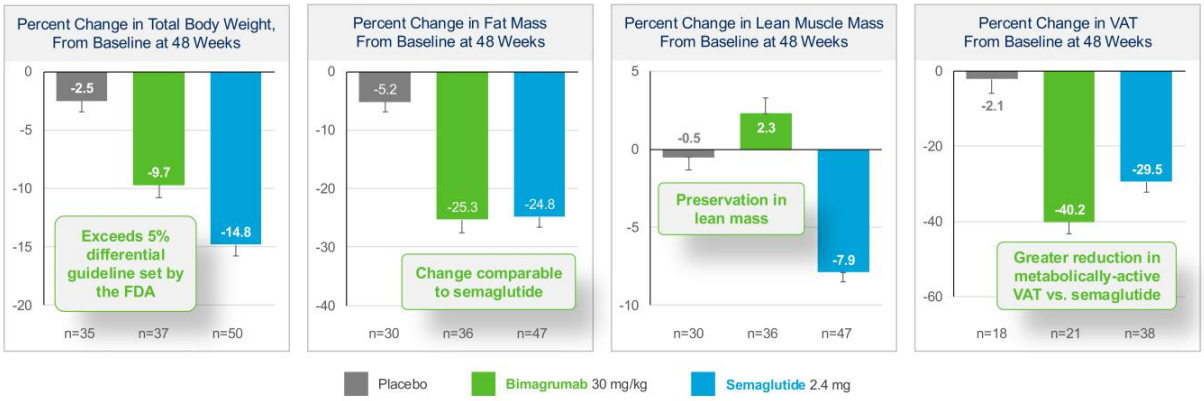
1. https://investors.scholarrock.com/news-releases/news-release-details/scholar-rock-reports-positive-phase-2-embraze-trial-results. **2.** https://investor.regeneron.com/news-releases/news-release-details/results-phase-2-courage-trial-demonstrating-potential-improve.
Low-dose combo – Trevogrumab 200 mg + semaglutide 2.4 mg; Higher-dose combo – Trevogrumab 400 mg + semaglutide 2.4 mg; Triplet – Trevogrumab 400 mg + garetosmab 10 mg/kg + semaglutide 2.4 mg.
***p<0.001; **SE**, standard error; **TBW**, total body weight; **LM**, lean mass; **FM**, fat mass

KEY POINT

Blocking myostatin alone yields negligible loss of fat mass and total body weight
Inhibition of myostatin plus activins drives favorable body composition change in obesity

Bimagrumab Provides Reason To "**Believe**" With Compelling Efficacy but Limited by Safety/Tolerability

TALDEFGROBEP



Heymsfield. Nature Medicine. 2026..

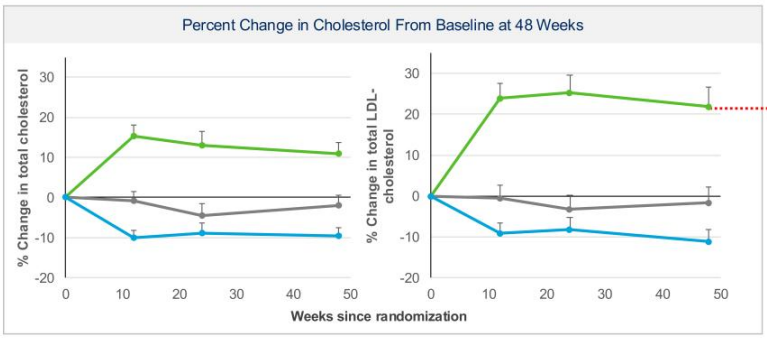
KEY POINT **Bimagrumab demonstrated the ability to achieve regulatory targets of TBW loss with comparable total fat loss to GLP-1**

Bimagrumab Provides Reason To "**Believe**" With Compelling Efficacy but Limited by Safety/Tolerability

TALDEFGROBEP

	Placebo	Bimagrumab (30 mg IV)	Semaglutide (2.4 mg SC)
Muscle Spasms	5.5%	73.7%	8.9%
Diarrhea	5.5%	49.1%	35.7%
Acne	3.6%	43.9%	8.9%

Poor tolerability due to irreversible ActRIIB binding



Elevation in lipids secondary to high peak exposures following IV administration

Heymsfield. Nature Medicine. 2026.

The Focus on Lean Loss With GLP-1 Therapies Is Not Going Away

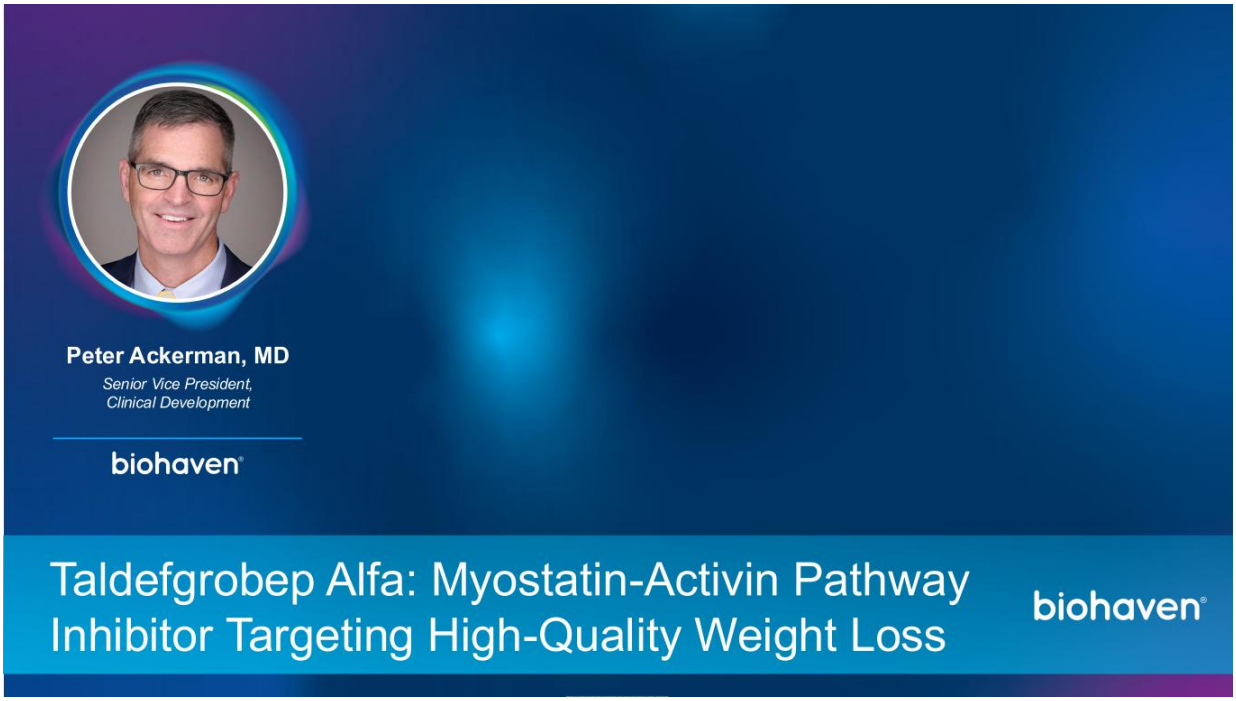
TALDEFGROBEP

Anthropometric targets (e.g., WHtR) are a guidelines-driven reality

GLP-1-associated frailty is a growing concern, especially in vulnerable populations

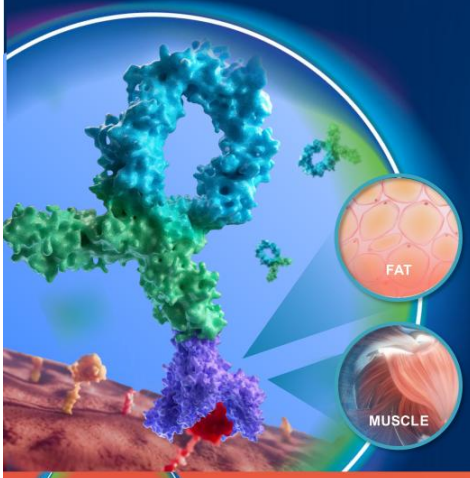
Preserving muscle mass is important for overall health, beyond physical function

Myostatin-activin pathway inhibitors have demonstrated early promise in people living with overweight and obesity


Peter Ackerman, MD
Senior Vice President,
Clinical Development
biohaven
Taldefgrobep Alfa: Myostatin-Activin Pathway Inhibitor Targeting High-Quality Weight Loss
biohaven

Targeting High-Quality Weight Loss With Myostatin-Activin Inhibition

TALDEFGROBEP



Taldefgrobep directly targets fat and muscle while avoiding intolerable adverse effects

Novel myostatin-activin MOA for healthy weight loss
Inhibits ActRII signaling in muscle and adipose tissue

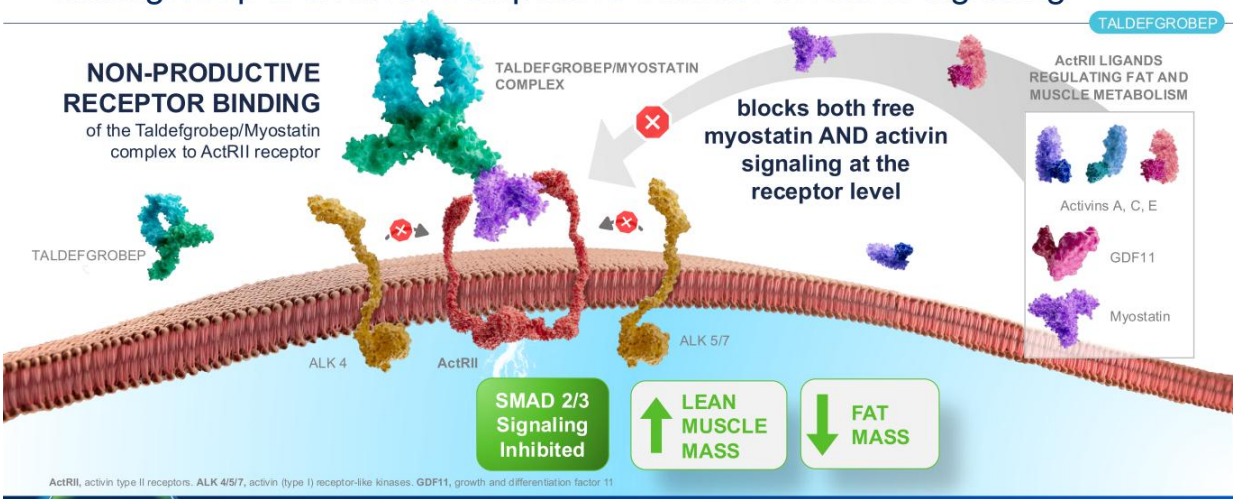
Favorable safety profile established in >700 treated to date
Low rates of muscle- and GI-related AEs

Convenient dosing
Administration by subcutaneous autoinjector

BREAKING NEWS

Phase 2 proof-of-concept study topline expected 2H 2026

Taldefgrobep Is a Novel Competitive Inhibitor of ActRII Signaling

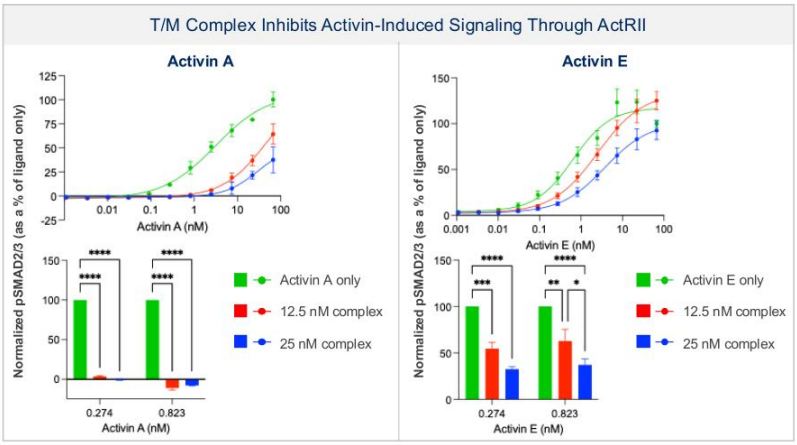


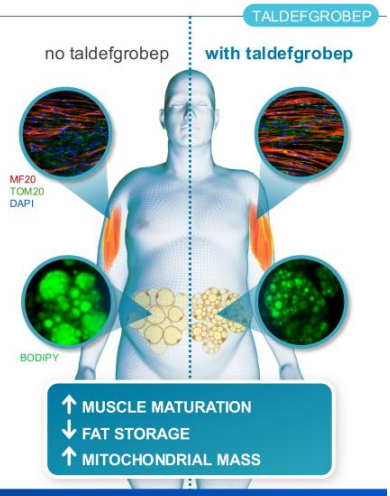
ActRII, activin type II receptors. **ALK 4/5/7**, activin (type I) receptor-like kinases. **GDF11**, growth and differentiation factor 11

KEY POINT

Taldefgrobep binds ligands and competitively inhibits receptor activation in tissues where myostatin and multiple activins (e.g., A, C, E) are active

Taldefgrobep/Myostatin Complex Competes With Activin Signaling To Improve Muscle Differentiation and Fat Storage





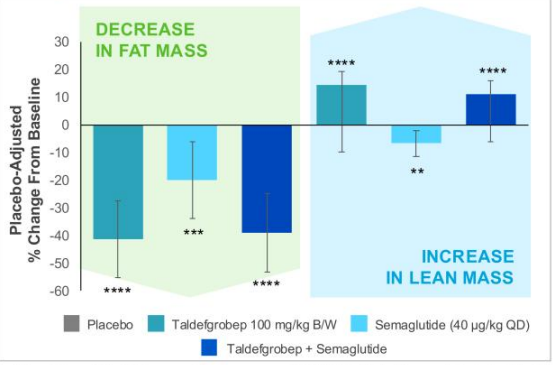
KEY POINT

The T/M complex, at clinically relevant exposures, inhibits activin A- and activin E-induced ActRII signaling

Taldefgrobep Improves Body Composition in Obese Mouse Model and Non-Obese Adults

TALDEFGROBEP

In Obese Mouse Model, **Taldefgrobep** Demonstrated Significant Reductions in Fat Mass While Increasing Lean Mass



In Healthy Adults, after One Month of Dosing[1], **Taldefgrobep** Demonstrated Meaningful Reductions in Fat Mass and Increases in Lean Mass

n=15 for vehicle; n=16 for all other groups. Error bars represent 95.00% CI of diff. Significance evaluated using Tukey's multiple comparisons test. **P < 0.01; ***P < 0.001; ****P < 0.0001; **QD,** once daily; taldefgrobep alfa. Bechtold. ObesityWeek 2024. Poster 350. **1.** CN001001 CSR, Day 57 data. **2.** Heymsfield. JAMA Network Open. 2021. **3.** Garito. Diabetes Obes Metab. 2018.

KEY POINT

In non-obese adults, taldefgrobep-induced changes in body composition are comparable to bimagrumab[2,3]

Taldefgrobep Has an Established, Favorable Safety Profile

TALDEFGROBEP

Safety database includes **more than 700** treated trial participants

Assessed across a **wide dose range** (4 mg to 180 mg SC QW) and **broad demography**

Data from repeat dosing up to **192 consecutive weeks**

- **LOW RATES** of SAEs and AEs leading to discontinuation
- **LOW RATES** of GI- and muscle-related AEs commonly reported with other myostatin-activin pathway inhibitors
- **No identified serious signature clinical safety events**

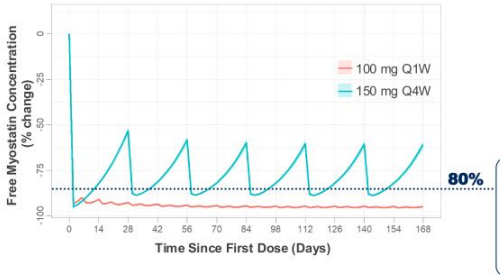
KEY POINT **Safety profile well-suited for indication in chronic weight management**

Taldefgrobep PK/PD Modeling Supports Convenient SQ Dosing in Adults With Obesity

TALDEFGROBEP

Pharmacodynamics of Taldefgrobep Weekly and Monthly Dosing

Free Myostatin Concentration Over Time



MODELING FOR DOSE SELECTION:

- Population PK/PD model using target-mediated drug disposition (TMDD) was developed to simulate taldefgrobep pharmacokinetics, free myostatin suppression and taldefgropeb/myostatin (T/M) complex concentrations in an obese population
- The model incorporated body weight effects on clearance, volume of distribution and relative bioavailability
- Using demographics from NHANES, simulations were conducted in 500 virtual adults with a BMI of 30-40 kg/m^2

MODELING PREDICTS:

- Taldefgrobep 100 mg Q1W and 150 mg Q4W should suppress free myostatin >80%
- T/M complex concentrations should exceed the established IC_{50} associated with ActRII signaling at both dose levels

KEY POINT

Taldefgrobep 100 mg Q1W and 150 mg Q4W are predicted to suppress free myostatin and yield T/M complex concentrations that competitively inhibit ActRII signaling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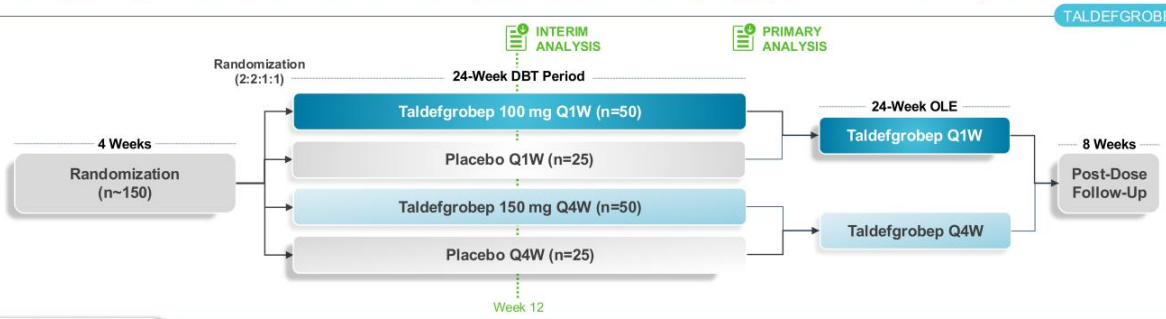
MD, RPh
Senior Medical Director
StudyMetrix Research
StudyMetrix Research
Ongoing Phase 2 Proof-of-Concept Study in Obesity
biohaven

Ongoing Phase 2 Monotherapy Dose-Ranging (Q1W + Q4W) Study

TALDEFGROBEP



KEY STUDY DETAILS

Study Design: Phase 2, randomized, double-blind, placebo-controlled dose-ranging study

Population: Male and female adults (18 to 65 years-old) with overweight or obesity

Blinded Interim Analysis (when 30% complete Week 12)**:** Taldefgrobep PK/PD (free myostatin and T/M complex concentrations) and plasma lipids by treatment assignment

Endpoints: % change in total body weight, fat mass and lean mass at Week 24. Whole-body MRI in subset

KEY POINT

PK/PD interim analysis completed
Topline primary analysis expected 2H 2026

Baseline Demography by Q1W vs. Q4W, Taldefgrobep + Placebo

TALDEFGROBEP

Parameter	Q1W (n=79)	Q4W (n=78)
Age, years, mean (SD)	46.6 (11.59)	48.1 (10.93)
Sex, female, n (%)	53 (67.1)	53 (67.9)
Race, n (%)		
White	59 (74.7)	57 (73.1)
Black	13 (16.5)	15 (19.2)
Asian	2 (2.5)	2 (2.6)
Other	5 (6.3)	4 (5.1)
Ethnicity, Hispanic/Latino, n (%)	24 (30.4)	25 (32.1)
TBW, kg, mean (SD)	99.2 (14.01)	101.1 (14.17)
WHtR, mean (SD)	0.7 (0.05)	0.7 (0.06)
BMI, kg/m², mean (SD)	35.3 (3.32)	35.5 (3.49)
BMI ≥35 kg/m², n (%)	40 (50.6)	41 (52.6)
HbA1c, %, mean (SD)	5.5 (0.34)	5.5 (0.32)

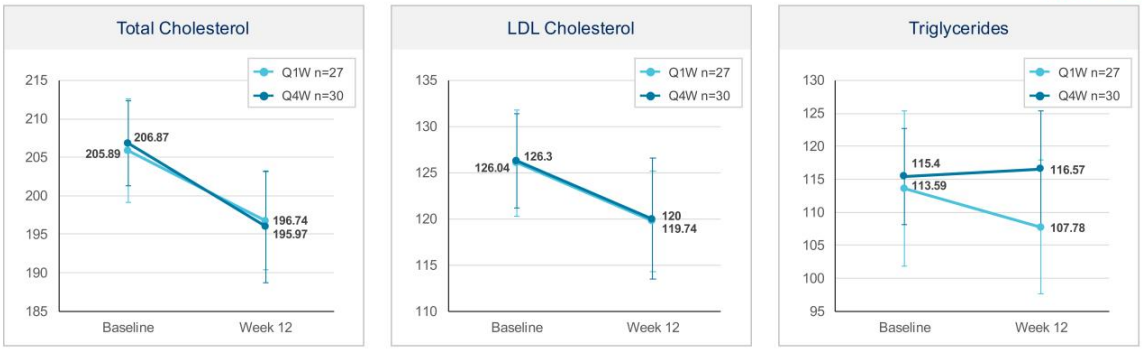
TBW, Total Body Weight; **Kg**, kilograms; **WHtR**, Waist-to-Height Ratio; **BMI**, Body Mass Index; **M²**, meters squared; **HbA1c**, Hemoglobin A1c; **SD**, Standard deviation

KEY POINT

Baseline characteristics evenly distributed across the treatment groups and consistent with standard obesity trial population

Blinded Interim Data by Q1W vs. Q4W, Taldefgrobep + Placebo
No Adverse Effects on LIPIDS at Week 12

TALDEFGROBEP



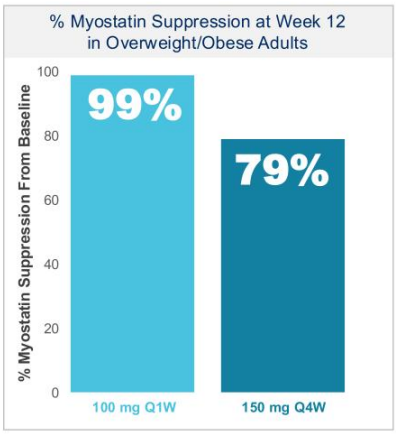
- No treatment-emergent G2-4 elevations in total cholesterol or triglyceride values
- 1 participant with emergent G3 LDL elevation; had G2 elevation at Baseline

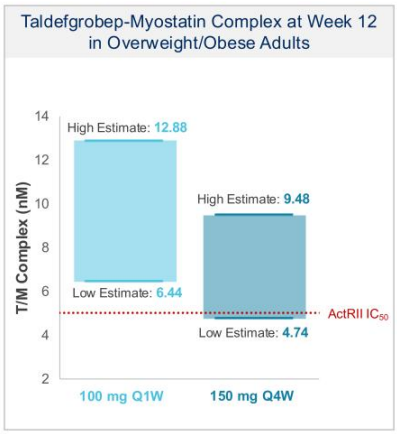
Error bars represent Standard Error

KEY POINT **No identified adverse trends in lipid parameters demonstrating differentiated safety from other myostatin-activin pathway inhibitors**

Interim Phase 2 PK/PD Data Supports Weekly and Monthly Dosing in Obesity

TALDEFGROBEP

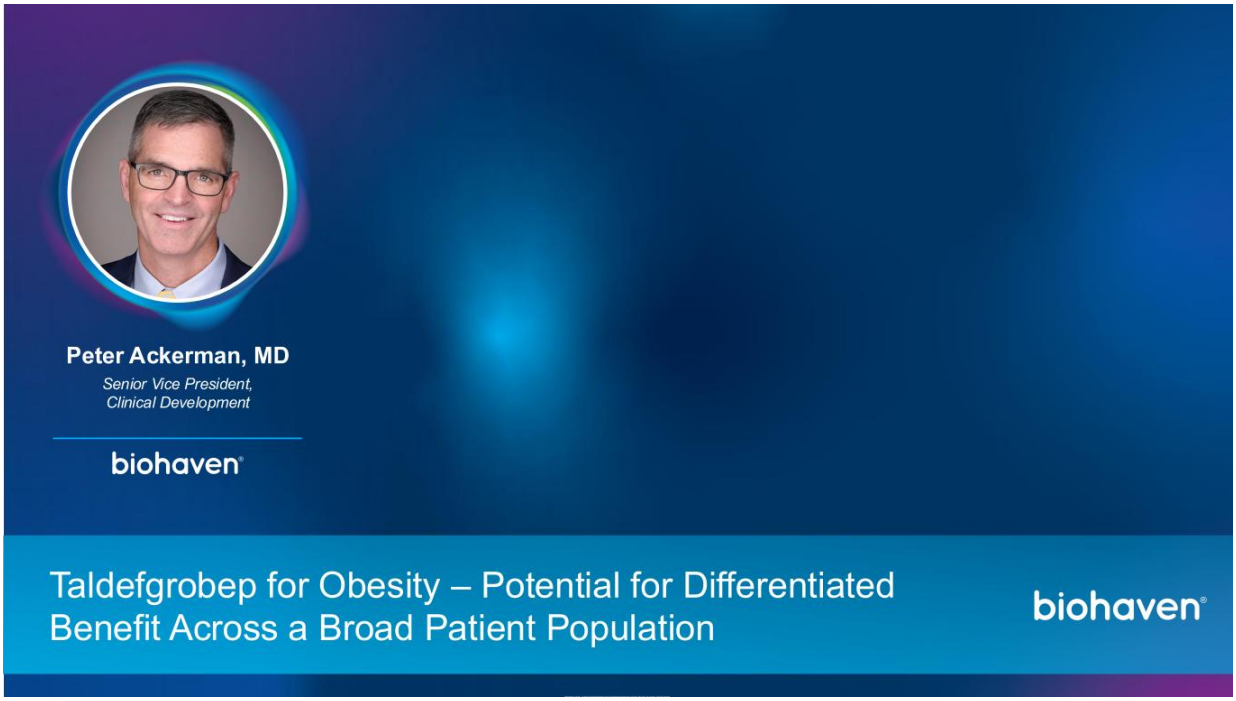




AT WEEK 12:

- Observed mean taldefgrobep concentrations are consistent with model-predicted
- Robust suppression of free myostatin throughout Q1W and Q4W dosing intervals
- T/M complex concentrations comparable between dosing regimens and at/above target ActRII IC_{50}

KEY POINT **Interim data suggest monthly dosing can achieve robust myostatin suppression and formation of T/M complex levels at/above targeted ActRII IC_{50} levels**


Peter Ackerman, MD
Senior Vice President,
Clinical Development
biohaven
Taldefgrobep for Obesity – Potential for Differentiated Benefit Across a Broad Patient Population
biohaven

Taldefgrobep Offers a Novel Approach To Address the Needs for People Living With Obesity

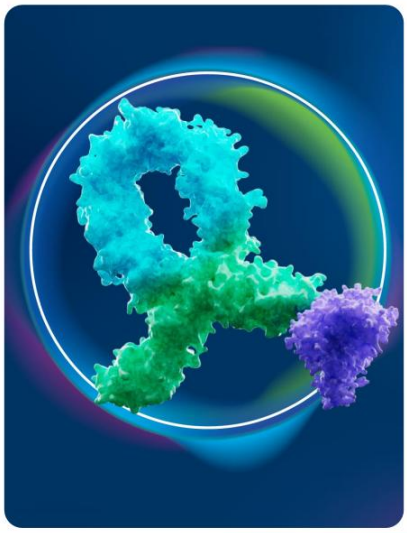
TALDEFGROBEP

Total body weight loss meeting current regulatory standards

Benefit as monotherapy and in combination with GLP-1 therapies

Convenient subcutaneous autoinjector with potential for monthly dosing

Favorable safety and tolerability



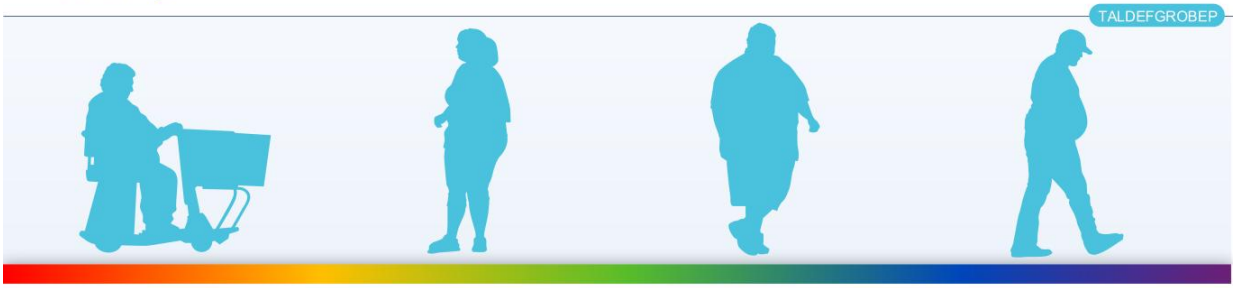
Fat mass loss comparable to GLP-1 therapies

Visceral adipose tissue loss favorable to GLP-1 therapies

Increase in lean muscle mass highly differentiated from GLP-1 therapies

Increase in bone density favorable to GLP-1 therapy

Taldefgrobep Can Benefit a Broad Spectrum of People Living With Obesity



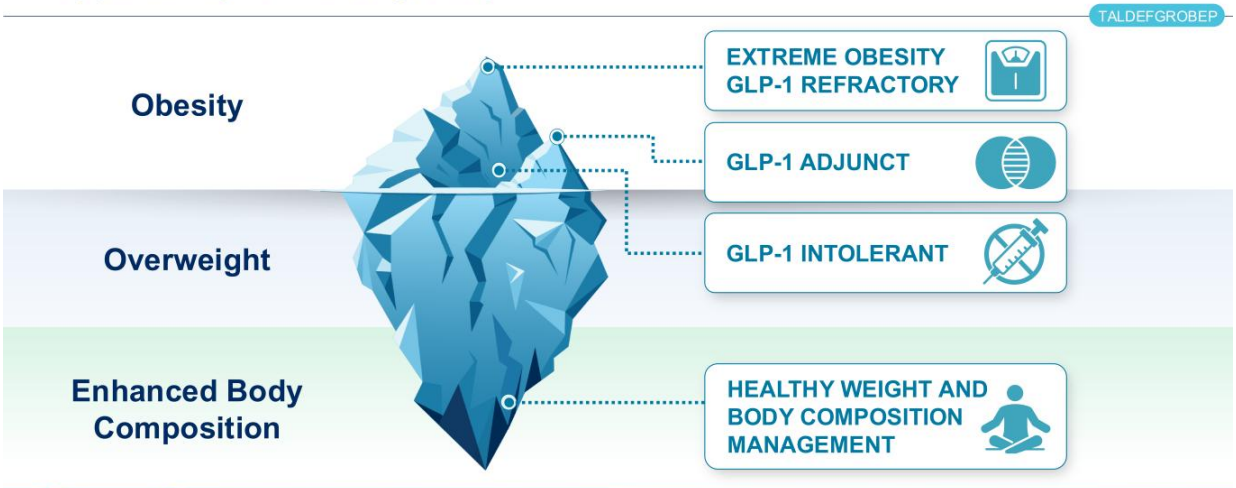
6.6M-10M	5-8M	5-7M	5-10M
Older patients at risk of sarcopenia	People intolerant or refractory to GLP-1	People living with BMI ≥40	People unable to tolerate high dose GLP-1
MONOTHERAPY		GLP-1 ADJUNCT	

Source: BHVN Market Research and Analytics Data on file

KEY POINT Meaningful reductions in fat mass, preservation of lean muscle mass, once-monthly dosing and high tolerability drive market potential

A Shift Toward Body Composition Targets Expands the Market Opportunity for Taldefgrobep

TALDEFGROBEP



KEY POINT

Obesity may be the category's tip of the iceberg

Panel

MODERATOR

Amy Li
Equity Analyst
Jefferies

PANELISTS

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Senior Vice President, Clinical Development
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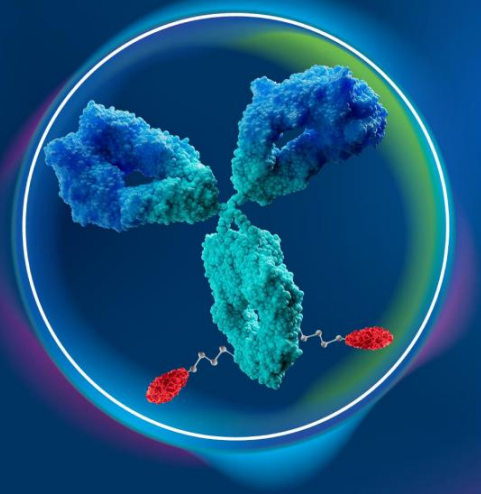
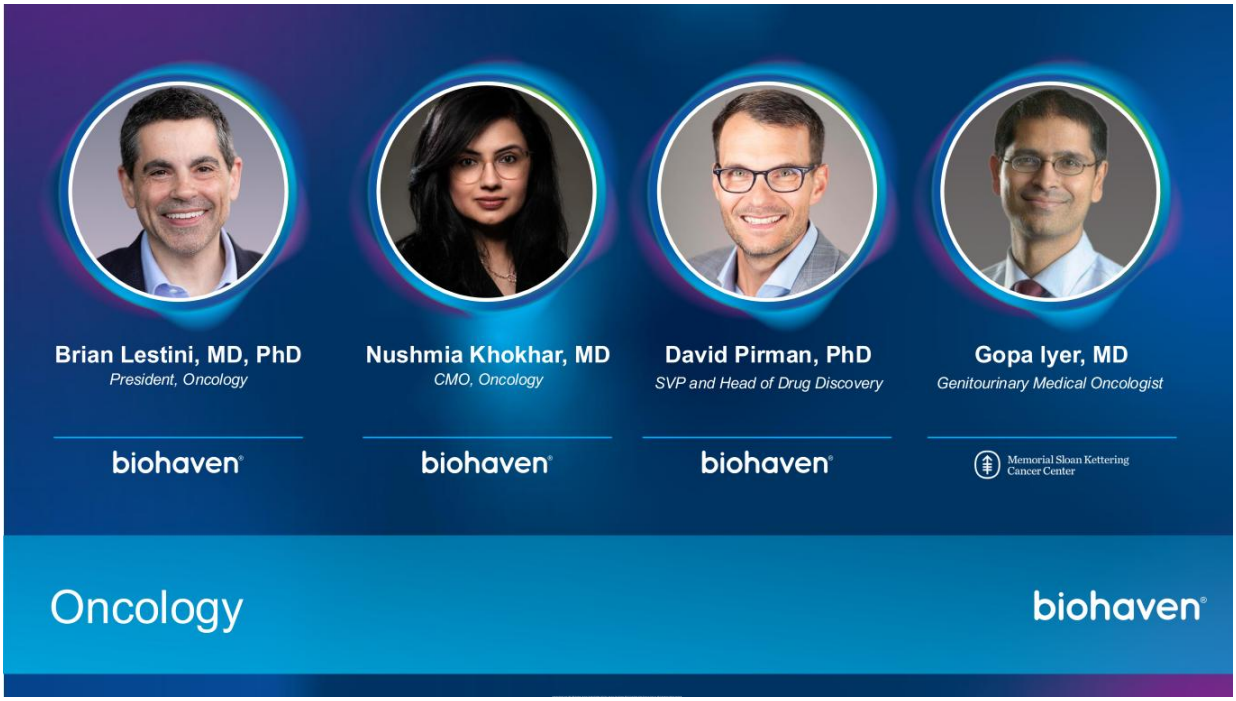
ONCOLOGY

Modular Next-Generation ADC Technologies: Optimizing for Clinical Performance

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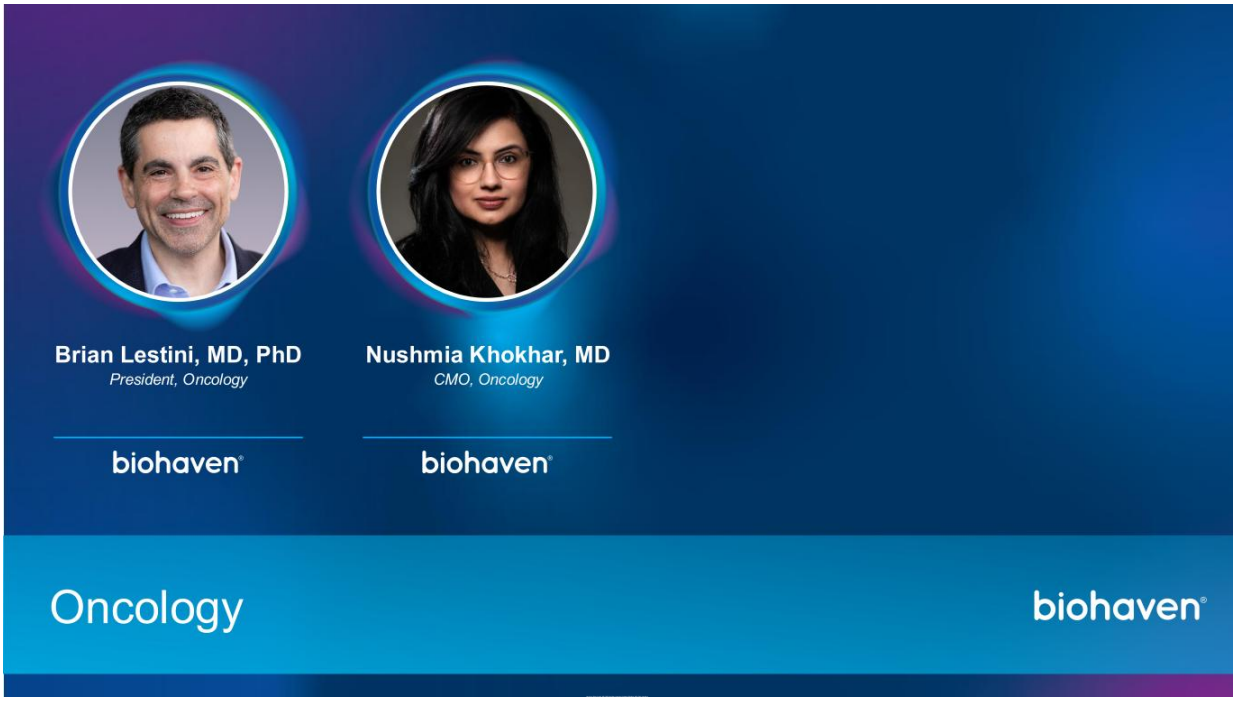
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Oncology
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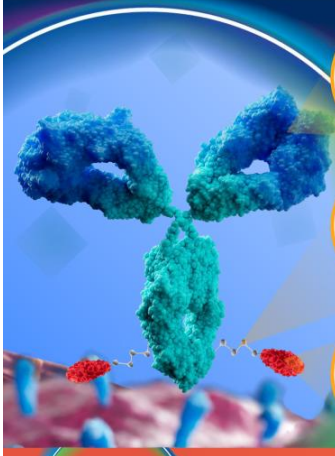
Innovative Biohaven Technologies Enabling Differentiated Next-Generation ADCs

ONCOLOGY



OPTIMIZED MONO AND BISPECIFIC MABS

NEXT-GEN MODULAR ADC CONJUGATION TECHNOLOGIES

PROPRIETARY TOPOIX AND MULTI-CLASS PAYLOADS

Clinical Proof-of-Principle Establishing the Power and Flexibility of the Platform to Optimize Across Broad Range of ADC Designs and Combination Strategies Including CPI

First clinical demonstration (BHV-1510 Trop2)
Highly stable, differentiated PK and safety, compelling activity with CPI combination

First-in-class potential FGFR3 ADC (BHV-1530)
Novel mAb, potential to address both FGFR3 alterations and overexpression

Platform tech enables multi-class payload loading
Clinically differentiated TopoIx payload, foundational for CPI and other potentially synergistic MOA combinations

BREAKING NEWS

- **BHV-1510:** Robust enrollment in endometrial + cemiplimab combination expansion cohort
- **BHV-1530:** First activity observed, including pretreated FGFR3-altered urothelial cancer patient
- **Discovery:** Preclinical data supporting next-wave bispecific mAb, multi-payload formats

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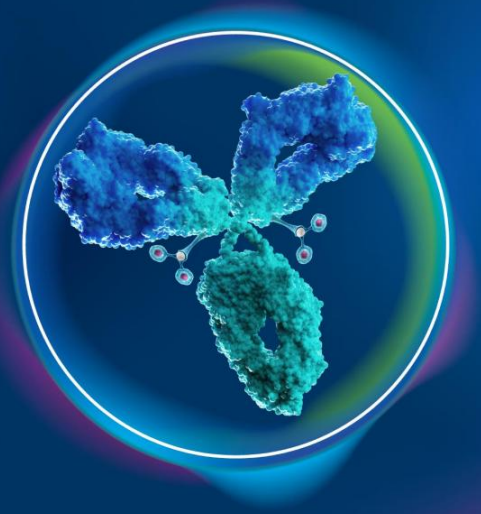
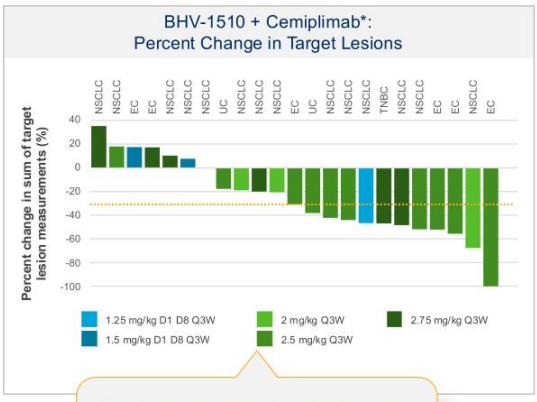
BHV-1510

Trop2 ADC

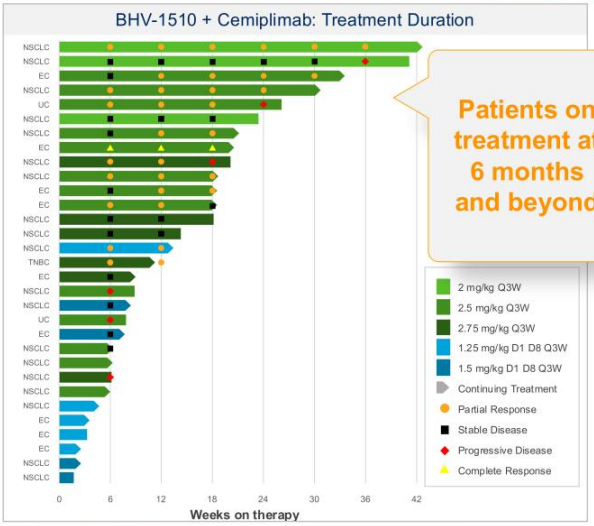


BHV-1510 + Cemiplimab Leads to Rapid, Deep and Durable Responses in Heavily Pretreated Patients, Majority With Prior Anti-PD(L)1

ONCOLOGY



Majority (87.1%) had prior anti-PD(L)1 exposure



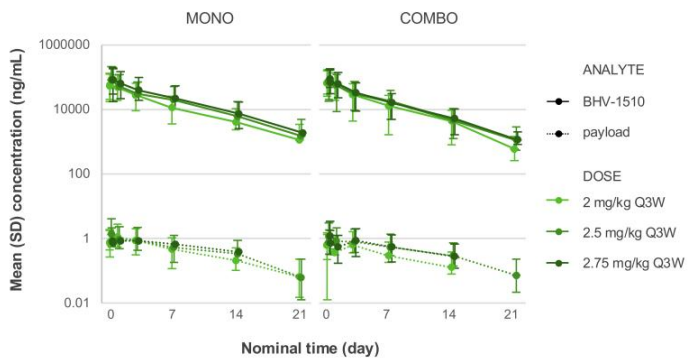
Patients on treatment at 6 months and beyond

*Cemiplimab (anti-PD1) provided through a supply agreement with Regeneron; dose of cemiplimab 350 mg Q3W
Source: Micaily. ESMO Immuno-Oncology Congress 2025. Poster 252P.

BHV-1510 Demonstrates a Favorable PK Profile With Highly Stable ADC

ONCOLOGY

BHV-1510 (ADC) and Payload Concentration-Time Plots for Cycle 1 (with or without Cemiplimab)



Source: Micaily. ESMO Immuno-Oncology Congress 2025. Poster 252P.

KEY POINT

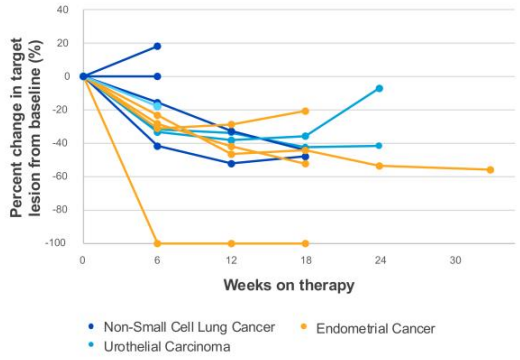
The unconjugated payload concentration was low with a payload-to-ADC molar ratio <1%, indicating that ADC was highly stable in the circulation

Encouraging Early Clinical Activity and High Response Rates of BHV-1510 + Cemiplimab Enable First Tumor-Specific Expansions

ONCOLOGY

- **Dose escalation complete:** Compelling efficacy in difficult-to-treat patients
  - Responses in heavily pretreated patients, including with brain metastases; majority with prior anti-PD(L)1 exposure
- **Rapid onset of benefit:** Tumor shrinkage / PRs at 1st scan
- **Differentiated safety profile:** Low rates of hematological toxicities and diarrhea; no ILD observed*
- **Favorable PK profile:** Highly Stable ADC

BHV-1510 2.5 mg/kg + Cemiplimab Q3W:
Target Lesion Change From Baseline



* By independent adjudication
Source: Micaily. ESMO Immuno-Oncology Congress 2025. Poster 252P.

KEY POINTS

- **Early data suggests synergy with anti-PD-1 and potential to move into earlier lines**
- **Endometrial cancer expansion cohort with combination enrolling robustly - data to inform pivotal path**

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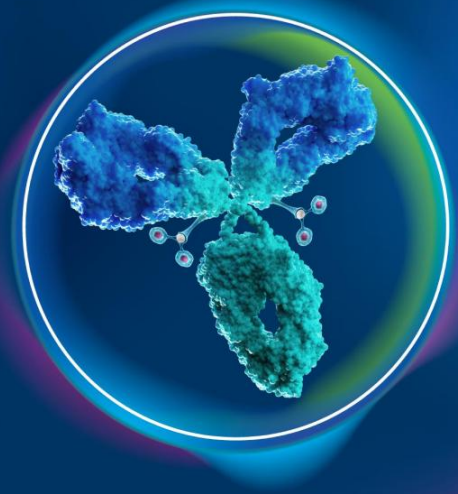
BHV-1530

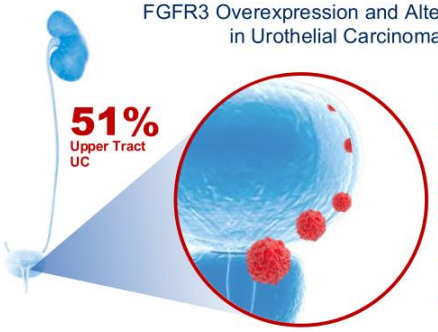
FGFR3 ADC



BHV-1530: Favorable Early Clinical Profile
No FGFR-Class Toxicities and Early Signs of Antitumor Activity

ONCOLOGY

FGFR3 Overexpression and Alteration (%) in Urothelial Carcinoma



FGFR3 ~50% of HNSCC | ~40% of NSCLC | 4% to ~8% alterations in other cancers

As of April 2026. Data from ongoing study

Compelling preclinical efficacy across FGFR3-altered and FGFR3-overexpressing tumor models: Demonstrated as monotherapy and in combination with CPI

Clinical progress: First patient dosed April 2025: initial cohorts successfully completed:

- No dose limiting toxicities
- No treatment related SAEs
- TRAEs predominantly mild (Grade 1–2)
- No hyperphosphatemia, nail disorders, central serous retinopathy

Early signs of activity: Early tumor reduction in patients with FGFR3 alterations and wild-type overexpression, as dosing in the predicted efficacious range

KEY POINT

Early tumor reductions in FGFR3-altered and WT overexpressing patients, including urothelial cancer
Dose escalation continuing with no DLTs to date

BHV-1530: Phase 1 Study in Advanced Tumors

ONCOLOGY

KEY STUDY DETAILS

Study Design: Open label, dose escalation (Ph1)
Population: Advanced UC, HNSCC, NSCLC having failed SOC therapy
Treatment Duration: Until disease progression or toxicity
Endpoints: Safety and tolerability, ORR, PFS, PK and ADA

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

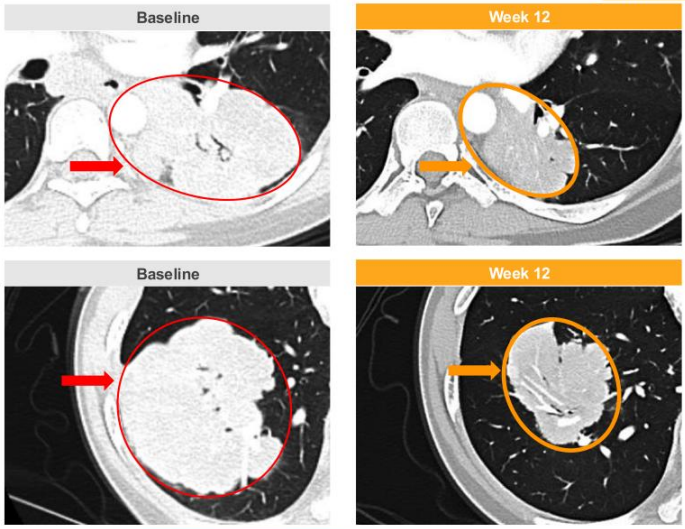
KEY POINT

Early tumor reduction in patients as dosing in the predicted efficacious range

Case Narrative: Metastatic Urothelial Cancer

ONCOLOGY

- 28 y/o female with urothelial cancer with a FGFR3::TACC3 fusion, with metastasis to lungs and thoracic lymph node
- 4 prior lines of therapy including
  - Padcev and Keytruda and 2 FGFR targeting small molecules-Balversa and LOXO-435
- Tolerating treatment with mild nausea and no FGFR related toxicity



BHV-1530: Potential First FGFR3 ADC — Broader Reach, No Class Toxicities, Clear Development Path

BHV-1530 ADC vs. Small-Molecule FGFR3 Inhibitor

	Small Molecule Inhibitor	BHV-1530
Target Population	FGFR3-altered only ~limited addressable population	**Altered AND overexpressing — full FGFR3+ population**
Class Toxicities	Hyperphosphatemia nail disorders, retinopathy	**None observed — no FGFR inhibitor-class toxicities**
Mechanism	Kinase inhibition resistance develops readily	**ADC: targeted delivery of cytotoxic payload**
CPI Combination	Limited — overlapping toxicity concerns	**Engineered for CPI synergy Topoix → ICD →**

DEVELOPMENT ROADMAP

PH1 DOSE ESCALATION
NOW • ACTIVE
- No DLTs; no FGFR-class toxicities
- Early tumor reduction in altered + WT overexpressing

DOSE OPTIMIZATION+POC
- Identify recommended Ph2 dose
- UC expansion POC
- Confirm activity across FGFR3 subtypes

COMBO EXPANSION
- Expansion cohort in UC with CPI combo
- Pivotal design conversations begin

1L mUC - PIVOTAL PATH
- 1L mUC combination with CPI
- Monotherapy in 2L+-selected pts

Summary: BHV-1510 and BHV-1530 Program Milestones and Next Steps

ONCOLOGY

BHV-1510

Trop2 ADC | Solid Tumors (NSCLC • Endometrial Ca • Urothelial Ca)

PRECLINICAL
COMPLETE

Superior cytotoxicity and immunogenic cell death vs. benchmark Topo-I ADCs; strong *in vivo* anti-PD-1 synergy; favorable PK, stability and safety profile

PHASE 1 DOSE ESCALATION
COMPLETE

Mono and PD-1 combo activity across solid tumors; differentiated safety — no ILD, low hematologic toxicity and diarrhea; <1% free payload in circulation

INITIAL PROOF-OF-CONCEPT CLINICAL DATA (ESMO IO 2025)
COMPLETE

BHV-1510 + Cemiplimab: rapid, deep, durable responses in heavily pretreated patients; most had prior anti-PD(L)1 exposure

PHASE 2 EXPANSION — ENDOMETRIAL CANCER
ACTIVE

Expansion cohort with anti-PD-1 combination enrolling; early efficacy readouts to inform pivotal path in endometrial cancer

BHV-1530

FGFR3 ADC – Potential First Urothelial Carcinoma ADC targeting • FGFR3-Driven Tumors

PRECLINICAL
COMPLETE

Robust antitumor activity in FGFR3-altered and overexpressing models - expanding addressable biology vs. small molecules; CPI combination synergy; superior efficacy vs. erdafitinib and EV

PHASE 1 DOSE ESCALATION — UC AND FGFR3-DRIVEN TUMORS
ACTIVE

Ongoing — no DLTs observed; no FGFR inhibitor-class toxicities; high systemic stability; early clinical activity as dosing in predicted efficacious range

NEAR-TERM: POC AND EXPANSION DATA
UPCOMING

Multiple near-term value drivers from dose-escalation readouts; proof-of-concept data expected to trigger expansion cohorts in UC and beyond

STRATEGIC PATH: 1L mUC + BROAD EXPANSION
UPCOMING

Clear path into 1L metastatic UC and earlier disease settings; mono and combination potential; expansion to NSCLC, HNSCC and other FGFR3-high tumors

Source: Biohaven data on file; Micaily. ESMO Immuno-Oncology Congress 2025. Poster 252P. **ADC**, antibody–drug conjugate; **ICD**, immunogenic cell death; **EV**, enfortumab vedotin; **mUC**, metastatic urothelial carcinoma.

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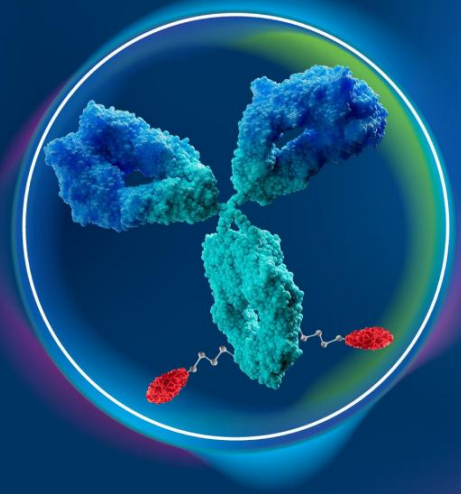
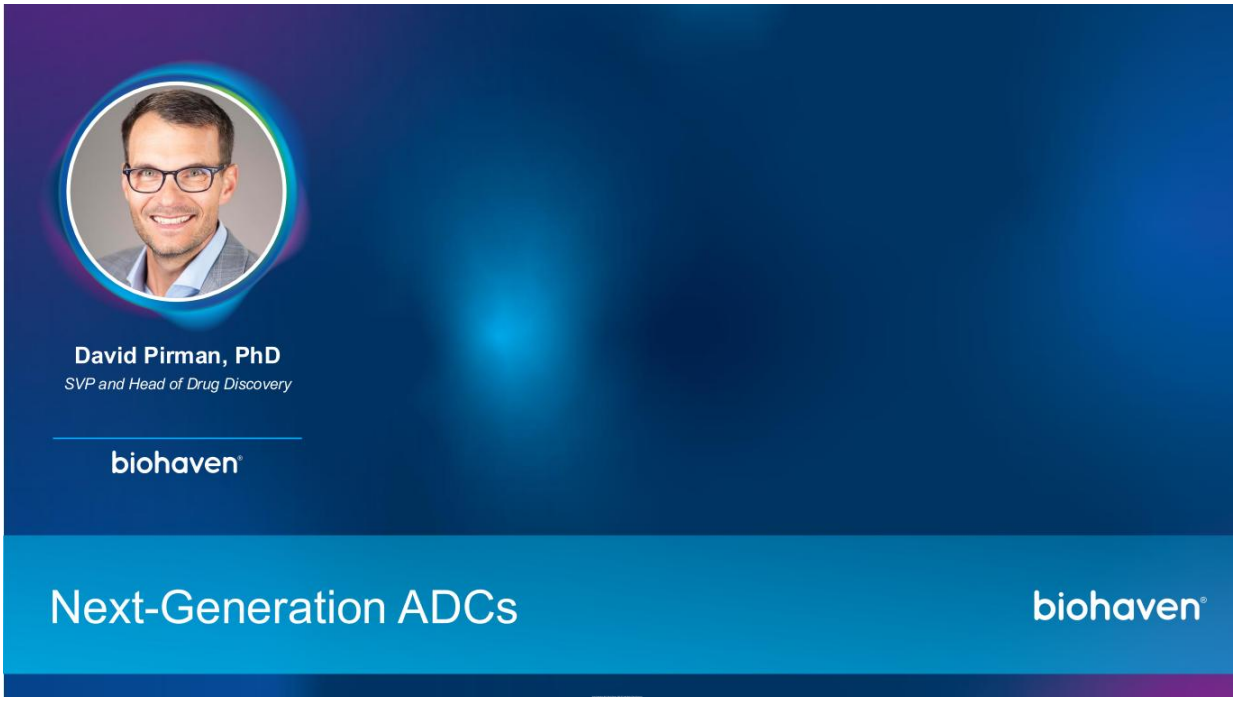
ADC DISCOVERY PLATFORM

Biohaven Technologies Enabling Next Wave of Differentiated ADCs



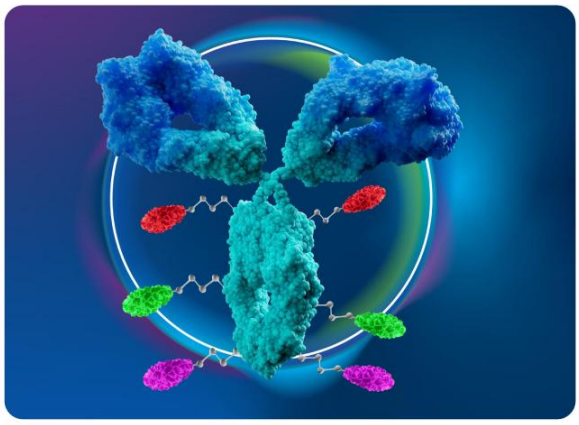

David Pirman, PhD
SVP and Head of Drug Discovery
biohaven
Next-Generation ADCs
biohaven

Leveraging Unique Modular Technologies To Overcome Key Clinical Limitations of Current-Generation ADCs

ONCOLOGY

Novel **mono- and bi-specific mAbs** against validated and emerging targets

Affinity tuned mAbs to improve tumor penetrance and limit off-target toxicities



Synergistic **multi-payload** optionality with **diverse MOA** to overcome resistance from conventional ADC

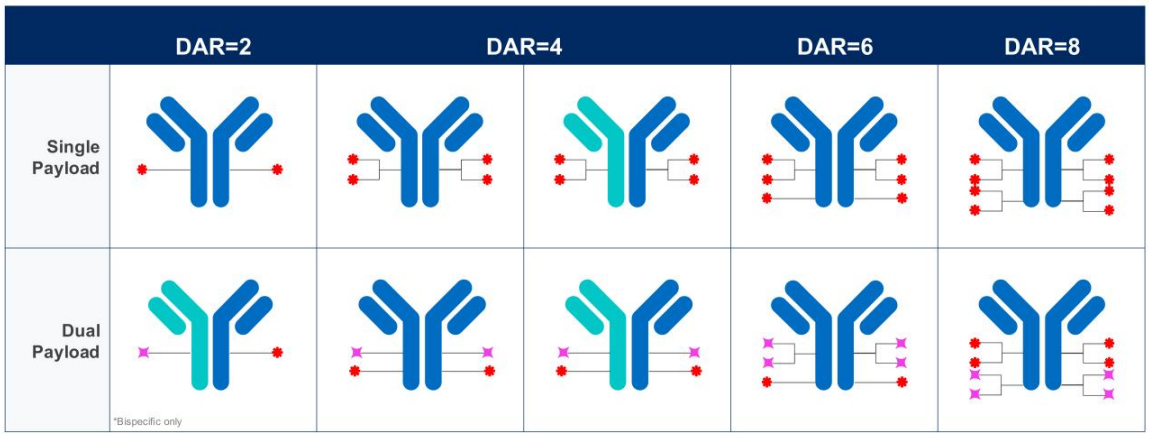
Multiple **site-specific stable conjugation** technologies to optimize precise linker-payload stoichiometries

OBJECTIVES

Enhance efficacy and therapeutic index through rational combinations that address tumor heterogeneity, improved immune activation and mechanisms of payload resistance

Complimentary Conjugation Technologies Enable ADCs With Precise DAR Ratios of Multiple Payloads Across Most Antibody Designs

ONCOLOGY

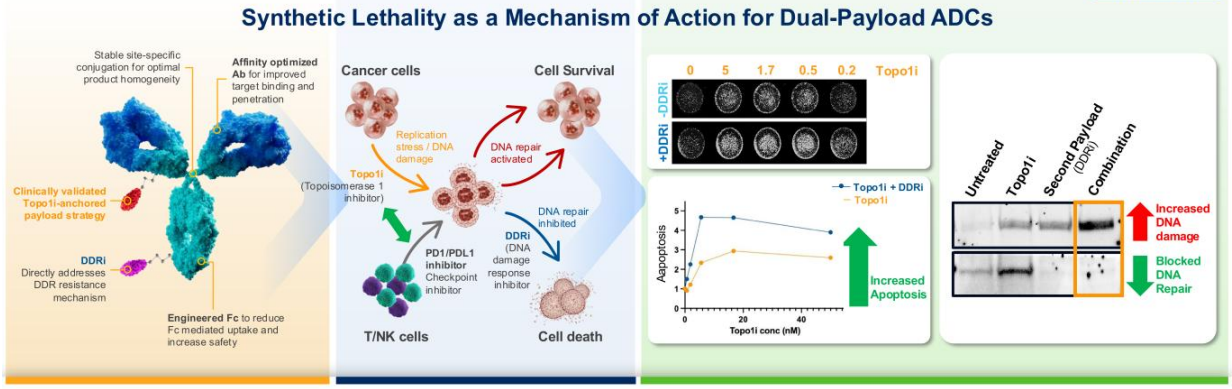


KEY POINTS

- Leverage serial conjugations to generate a diversity of stable, site-specific multi-payload combinations
- Applicable to mono- and bispecific mAbs and other Fc-fused antigen targeting modalities

Multi-Payload Combinations Provide Potential To Synergize Through Overlapping Mechanisms of Cell Killing and Enhancing Antitumor Immunity

ONCOLOGY



Dual-Payload ADC Architecture | Mechanism of Synergy | Payload Synergy Observed at the Molecular Level

Synergistic ADC Design

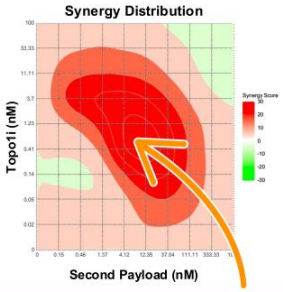
Topo1 inhibition and synergistic payloads profoundly inhibit DDR signaling, driving an accumulation of DNA damage that dramatically increases cell killing in rapidly proliferating cancer cells **as well as stimulating an enhanced antitumor immune response**

Robust Screening Efforts Identify Payloads That Synergize With Topo1i for Next-Generation Biohaven Dual-Payload ADCs

ONCOLOGY

In vitro cell-based synergy screen identifies compounds that synergize with Topo1i and are suitable for ADC conjugation

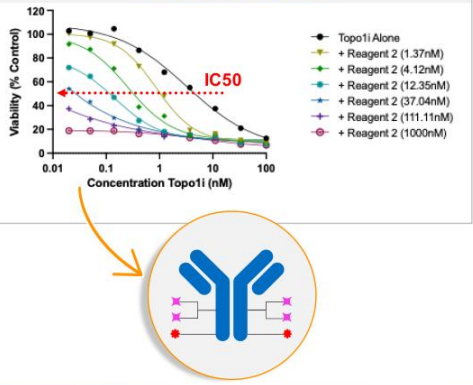
Topo1i + Second Payload Demonstrates Synergistic Interaction



Target synergy partner and concentration range for optimal tumor cell killing
Synergy score to define optimal DAR

Top synergy hits from combination screen demonstrate increased efficacy and DAR4+2 may be optimal

Potency Shift of Topo1i in Combination With Second Payload



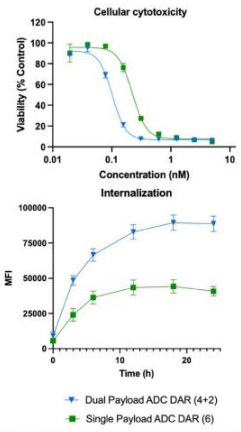
Biohaven Platform Enables the Development of Next-Generation ADCs With Improved Activity and Potential Transformational Functional Properties

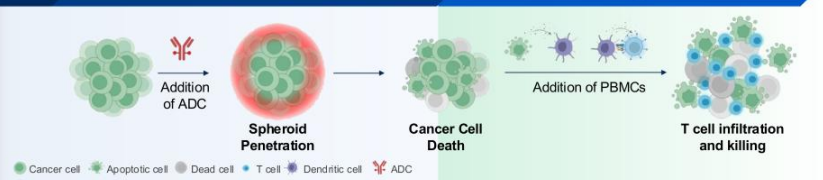
ONCOLOGY

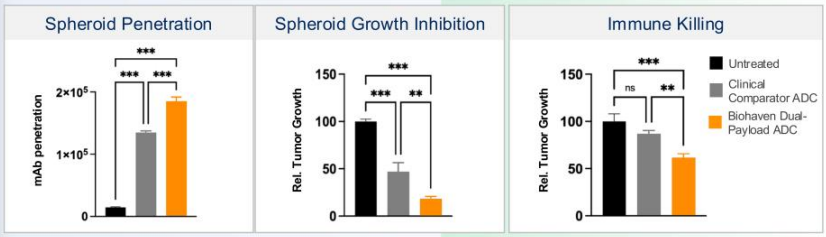
Dual-payload ADC approach demonstrates superiority vs. clinical competitors *in vitro*

Improved 2D Cytotoxicity and Internalization | **Enhanced 3D Spheroid Penetration** | **Increased Immunogenic Cell Death**

Biohaven's Dual-Payload ADC



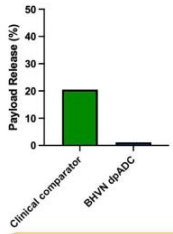




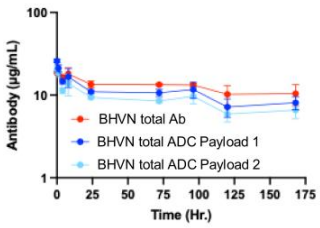
Superior Dual-Payload Path to the Clinic Targeting CRC

ONCOLOGY

Neutrophil Elastase Mediates Payload Release

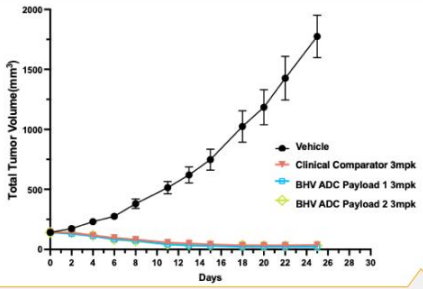


Mouse PK: IV Administration 3mg/kg BHVN dpADC DAR (4+2)



Biohaven Dual-Payload Shows Superior Stability and Half-Life >8 Hours in Mice

Total Tumor Volume



Biohaven Dual-Payload Shows Strong (>98%) Tumor Growth Inhibition

KEY POINTS

- Serial site-specific conjugations produce highly effective dual-payload ADCs
- Stable conjugations expected to improve dose-limiting toxicities driven by premature payload release

Panel

MODERATOR

Tyler Van Buren
Equity Analyst
TD Cowen

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SVP and Head of Drug Discovery
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Genitourinary Medical Oncologist
Memorial Sloan Kettering Cancer Center

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David Pirman, PhD
SVP and Head of Drug Discovery
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Malini Gupta, MD, ECNU, FACE, FITS
Director of G2Endo, Endocrinology and Metabolism 2025 AACE Chair
G2ENDO
Professor Jonathan Barratt, PhD, FRCP
The Mayer Professor of Renal Medicine, Department of Cardiovascular Sciences
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Tova Gardin, MD, MPP
Chief Translational Officer
biohaven
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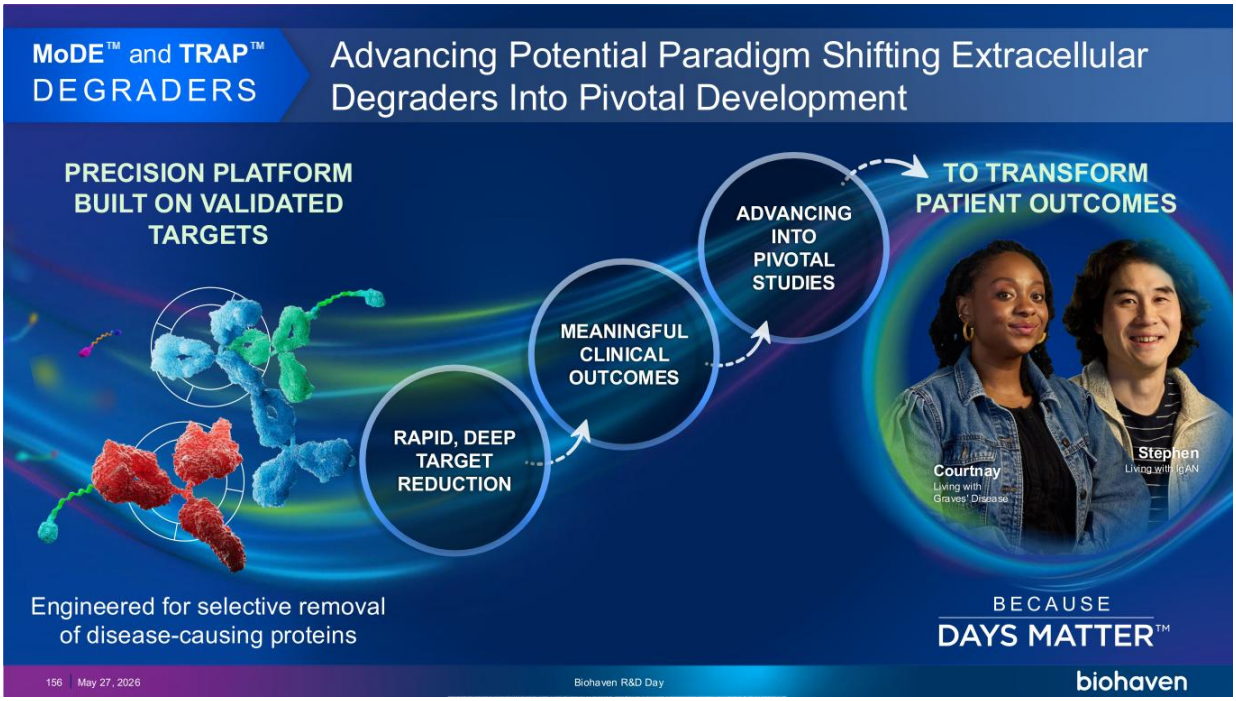
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Advancing Potential Paradigm Shifting Extracellular Degraders Into Pivotal Development
PRECISION PLATFORM BUILT ON VALIDATED TARGETS
RAPID, DEEP TARGET REDUCTION
MEANINGFUL CLINICAL OUTCOMES
ADVANCING INTO PIVOTAL STUDIES
TO TRANSFORM PATIENT OUTCOMES
Courtnay
Living with Graves' Disease
Stephen
Living with IgAN
Engineered for selective removal of disease-causing proteins
BECAUSE
DAYS MATTER™
156 | May 27, 2026
Biohaven R&D Day
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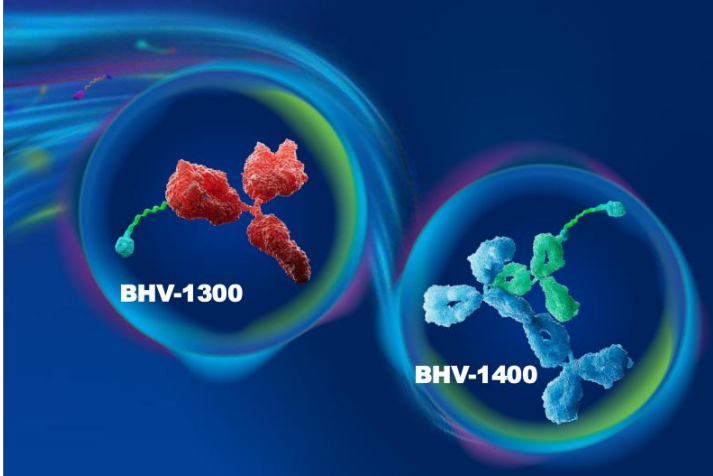
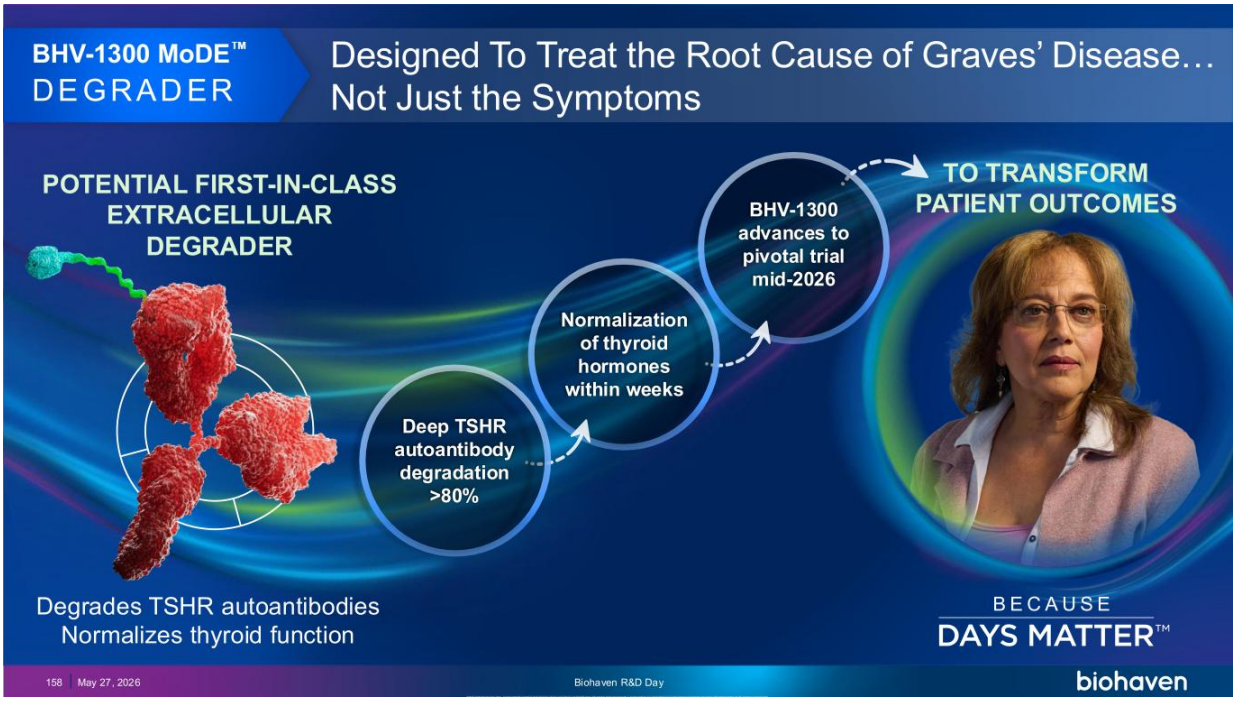
MoDE™ and TRAP™
DEGRADERS

First Extracellular Protein Degraders in the Clinic Demonstrate Rapid and Robust Pharmacodynamic Effects and Compelling Safety in Nearly 200 Individuals Dosed



- Safe
- Well-tolerated
- Highly selective
- Deep and rapid lowering
- Patient outcomes
- Pivotal trials mid-2026


BHV-1300 MoDE™
DEGRADER
Designed To Treat the Root Cause of Graves' Disease…
Not Just the Symptoms
POTENTIAL FIRST-IN-CLASS
EXTRACELLULAR
DEGRADER
Deep TSHR autoantibody degradation >80%
Normalization of thyroid hormones within weeks
BHV-1300 advances to pivotal trial mid-2026
TO TRANSFORM
PATIENT OUTCOMES
Degrades TSHR autoantibodies
Normalizes thyroid function
BECAUSE
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Living with Graves' Disease
Graves' disease affects nearly 1 in 100 Americans.[1]
About 4 out of 5 cases of hyperthyroidism in the United States are caused by Graves' disease.[1]
KIM
COURTNAY
CAMERON
MICHELE
PAIGE
EMMA
1. Akram S, Elfenbein DM, Chen H, Schneider DF, Sippel RS. Assessing American Thyroid Association guidelines for total thyroidectomy in Graves' disease. Journal of Surgical Research. 2020;245:64–71.
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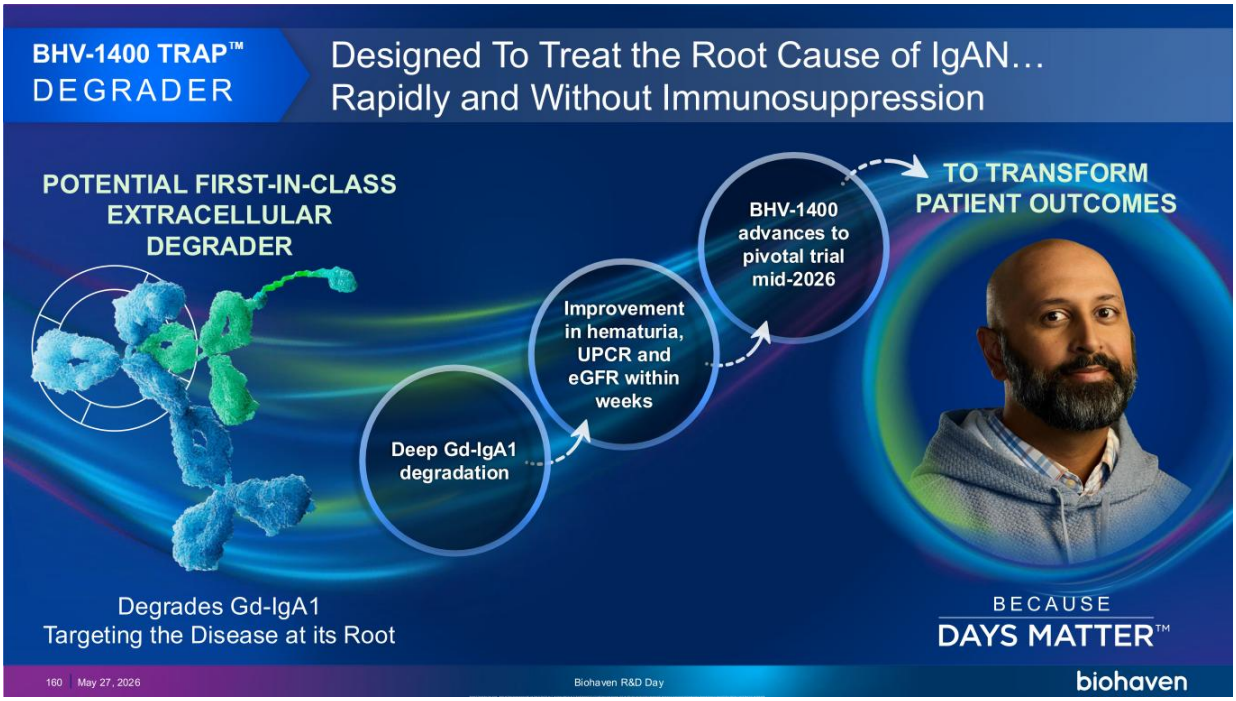
BHV-1400 TRAP™
DEGRADER
Designed To Treat the Root Cause of IgAN…
Rapidly and Without Immunosuppression
POTENTIAL FIRST-IN-CLASS
EXTRACELLULAR
DEGRADER
Degrades Gd-IgA1
Targeting the Disease at its Root
Deep Gd-IgA1 degradation
Improvement in hematuria, UPCR and eGFR within weeks
BHV-1400 advances to pivotal trial mid-2026
TO TRANSFORM
PATIENT OUTCOMES
BECAUSE
DAYS MATTER™
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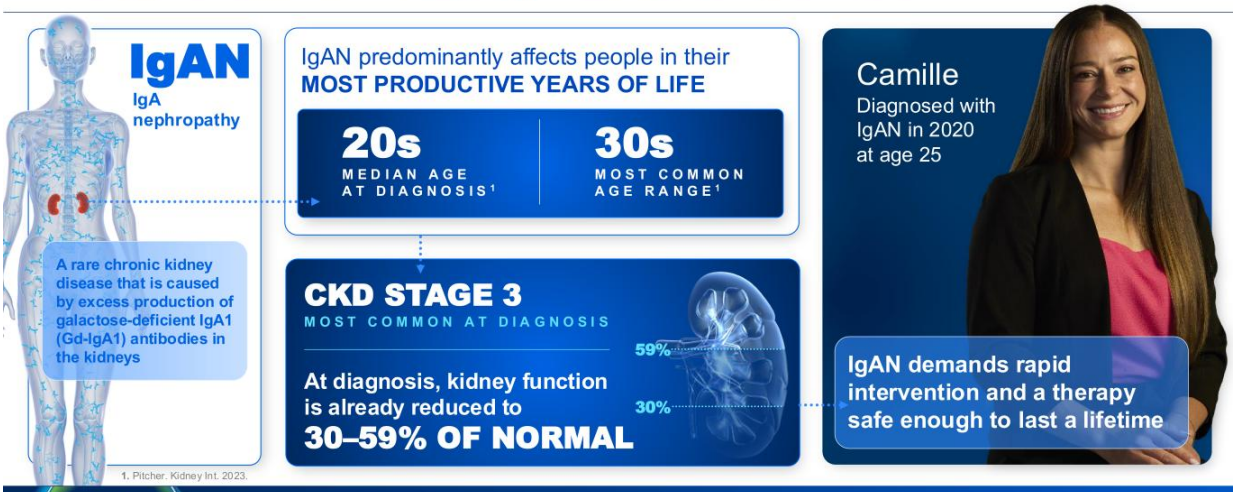
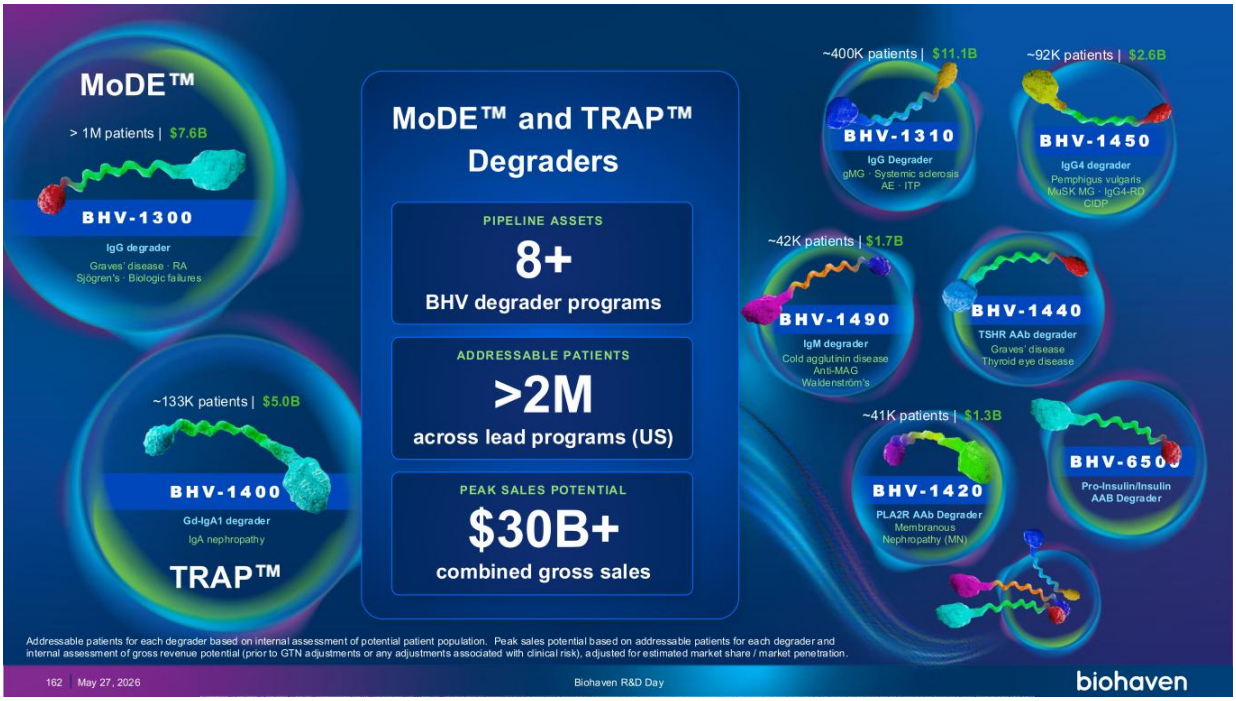
By the Time IgAN Is Diagnosed, Kidney Function Is Already Significantly Compromised



1. Pitcher. Kidney Int. 2023.

TREATMENT GOAL Every month matters. Rapid intervention to preserve kidney function and limited remaining nephrons


MoDE™
> 1M patients | $7.6B
BHV-1300
IgG degrader
Graves' disease · RA
Sjögren's · Biologic failures
~133K patients | $5.0B
BHV-1400
Gd-IgA1 degrader
IgA nephropathy
TRAP™
MoDE™ and TRAP™ Degraders
PIPELINE ASSETS
8+
BHV degrader programs
ADDRESSABLE PATIENTS
>2M
across lead programs (US)
PEAK SALES POTENTIAL
$30B+
combined gross sales
~400K patients | $11.1B
BHV-1310
IgG Degrader
gMG · Systemic sclerosis
AE · ITP
~92K patients | $2.6B
BHV-1450
IgG4 degrader
Pemphigus vulgaris
MuSK MG · IgG4-RD
CIDP
~42K patients | $1.7B
BHV-1490
IgM degrader
Cold agglutinin disease
Anti-MAG
Waldenström's
BHV-1440
TSHR AAb degrader
Graves' disease
Thyroid eye disease
~41K patients | $1.3B
BHV-1420
PLA2R AAb Degrader
Membranous
Nephropathy (MN)
BHV-650
Pro-Insulin/Insulin
AAB Degrader
Addressable patients for each degrader based on internal assessment of potential patient population. Peak sales potential based on addressable patients for each degrader and internal assessment of gross revenue potential (prior to GTN adjustments or any adjustments associated with clinical risk), adjusted for estimated market share / market penetration.
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MoDE™ and TRAP™ Degraders
Precision technology to
TRANSFORM LIVES
BECAUSE
DAYS MATTER™
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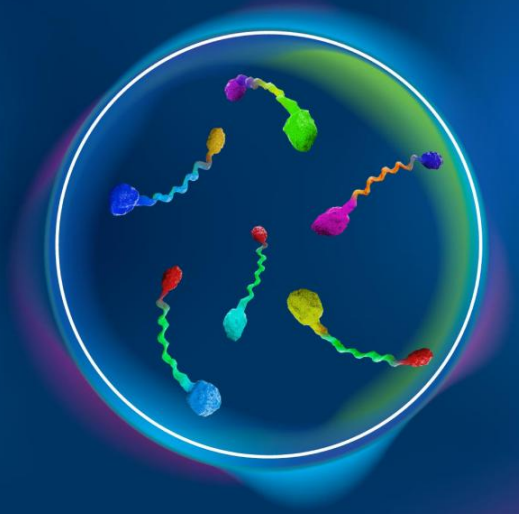
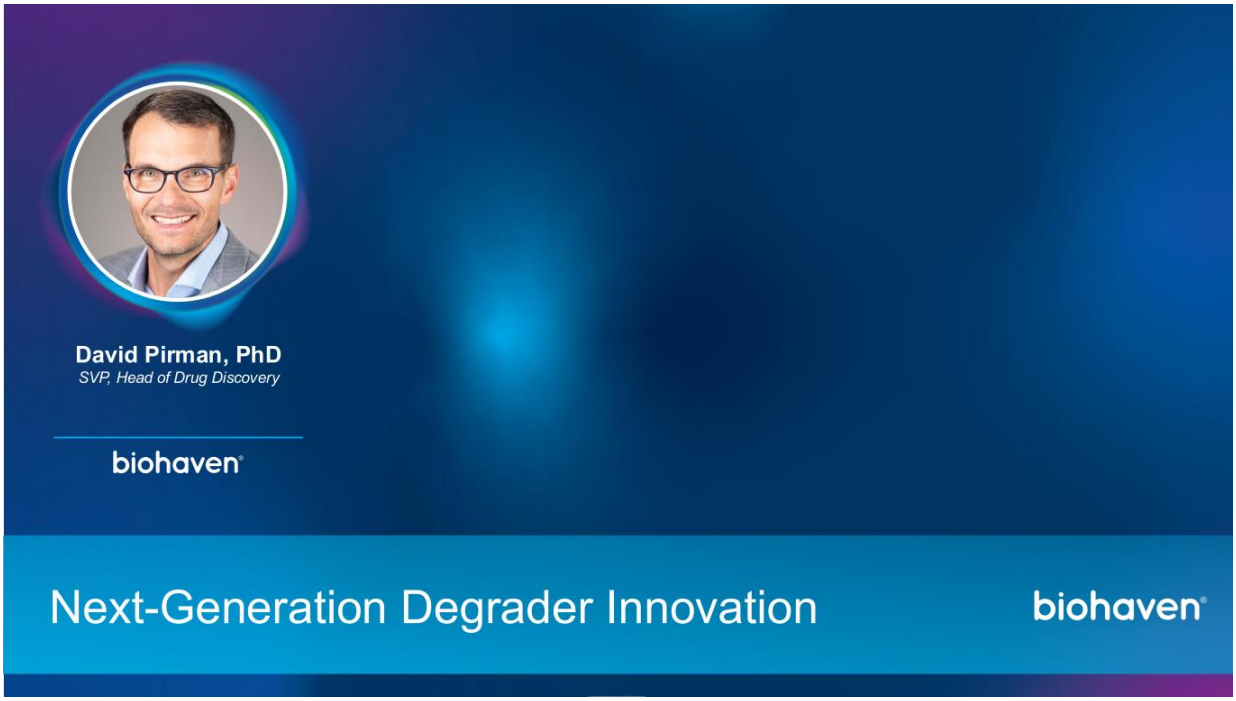
biohaven®

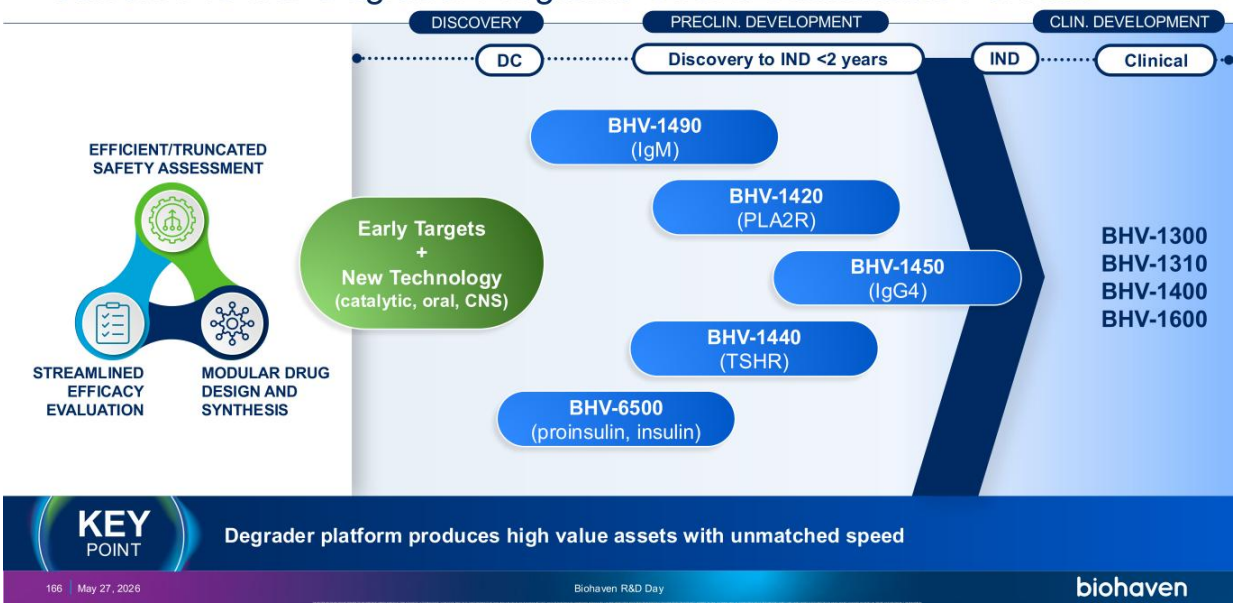
NEXT-WAVE DEGRADERS

Novel Assets and Next-Generation Technology




David Pirman, PhD
SVP, Head of Drug Discovery
biohaven
Next-Generation Degrader Innovation
biohaven

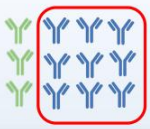
Current Pre-IND Degrader Programs Offer a Sustainable Portfolio



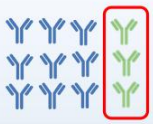
KEY POINT Degrader platform produces high value assets with unmatched speed

Building an Extensive Asset Platform With MoDEs™ and TRAPs™

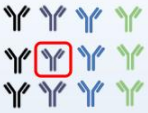
DISCOVERY



MoDE™
e.g., IgG, IgM



MoDE IgG4 Subclass
e.g., MuSK myasthenia gravis, pemphigus vulgaris



TRAP™ Targeting AAb, Antigen or Protein
e.g., IgAN, Graves', idiopathic membranous nephropathy

Aligning disease indications with appropriate degrader technology

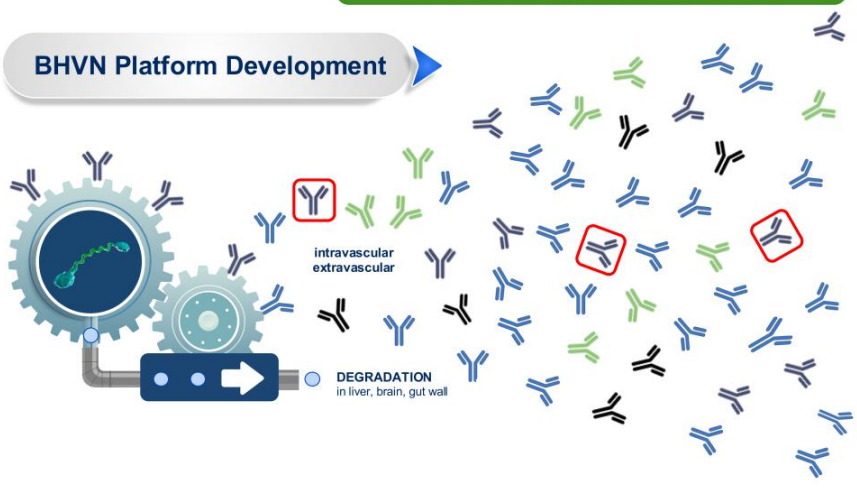
Novel degrader approaches and technologies created to address novel targets and unmet need

*Indications are exemplary, many of which are early programs

Beyond MoDEs™ and TRAPs™: Novel Technologic Solutions Drive Improved Efficacy and Target Profiles

DISCOVERY

MULTIPLE TECHNOLOGY SOLUTIONS

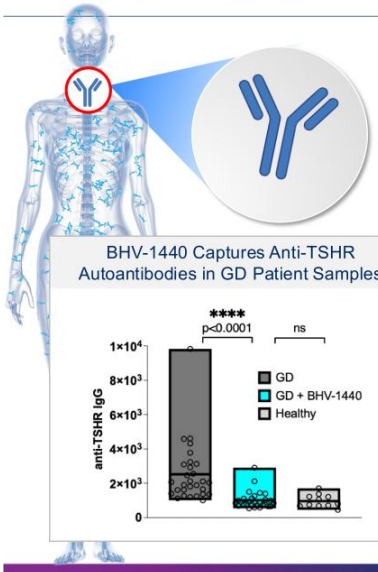


- Novel ASGPR ligands
- Oral degraders
- Novel, tissue-specific degradation pathways
- Specific B-cell targeting, tolerizing
- Catalytic degraders

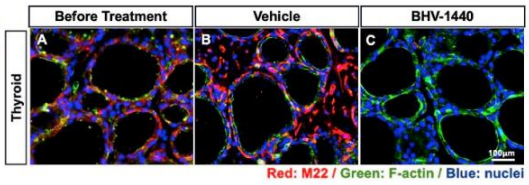

biohaven®
BHV-1440
TSHR TRAP™ Targeting Autoantibodies Driving Graves' Disease
DAYS MATTER™

BHV-1440 Anti-TSHR Auto-Ab TRAP™ Degrader for the Treatment of Graves' Disease

DISCOVERY



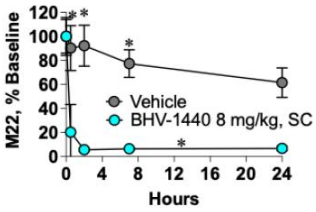
Specific removal of anti-TSHR autoantibody from tissue and circulation



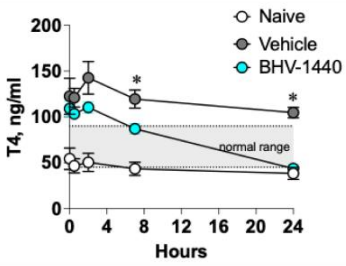
Red: M22 / Green: F-actin / Blue: nuclei

BHV-1440 Captures Anti-TSHR Autoantibodies in GD Patient Samples

BHV-1440 Rapidly Depletes Patient-Derived Anti-TSHR IgG (M22) From Circulation and Normalizes T4 Levels



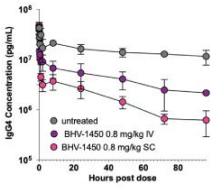
BHV-1440 Rapidly Normalizes T4 Levels

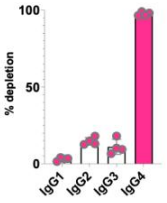



biohaven®
BHV-1450
IgG4 MoDE™ Degrader
for the Treatment of
Pemphigus Vulgaris
DAYS
MATTER™

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

DISCOVERY





Pemphigus vulgaris

LGI-1 encephalitis

Thrombotic thrombo-cytopenic purpura

MuSK myasthenia gravis

Antidrug antibodies

TARGETING IgG4 ONLY

- Deeper depletion (>80%) of anti-Dsg1/3 than FcRN inhibition with its limited reduction of 50–70%
- Tissue removal facilitates faster symptomatic reversal

Mori. *Am J Pathol.* 2012. Koneczny. *Autoimmun Rev.* 2020. van Sonderen. *Nat Rev Neurol.* 2017.

KEY POINT

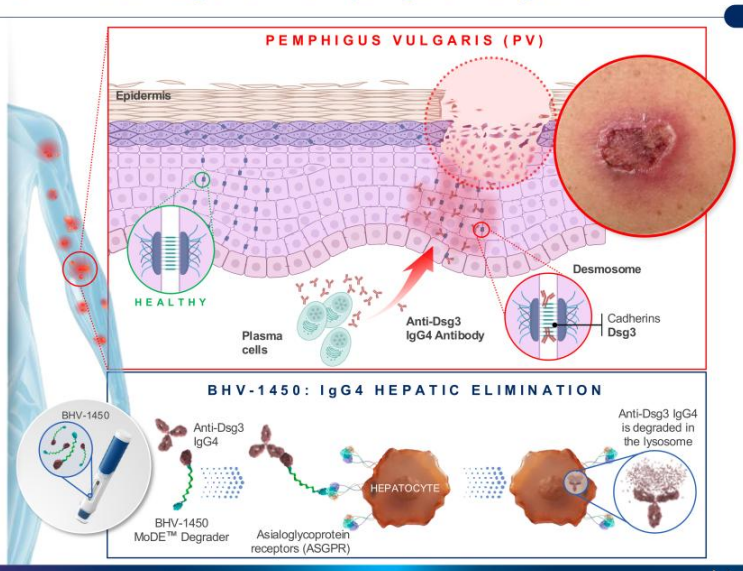
BHV-1450 specifically degrades the IgG4 subclass: IgG1, IgG2 and IgG3 remain
BHV-1450 on track for IND in Q1 2027

BHV-1450, an IgG4 Selective Degrader, Reverses the Anti-Dsg3-Mediated Skin Damage of Pemphigus Vulgaris

DISCOVERY

PEMPHIGUS VULGARIS (PV)

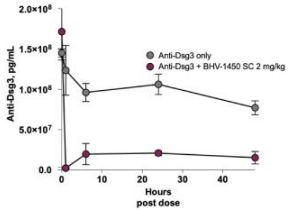
- Impacting 30–50K patients in the US
- PV is a painful, blistering, autoimmune disease with skin and mucous membrane erosions
- IgG4 autoantibodies target desmoglein 3 (Dsg3), essential for keratinocyte cell-cell adhesion



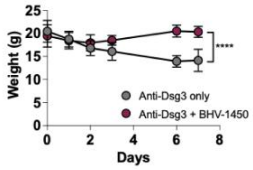
BHV-1450 Rapidly Removes Anti-Desmogleins Which Drive Disease From Circulation and From Tissue

DISCOVERY

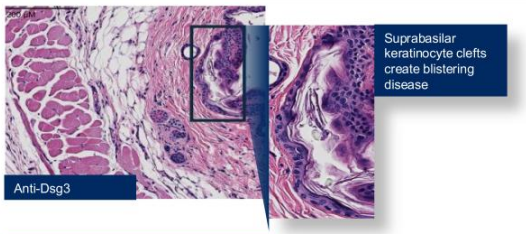
BHV-1450 Removes Anti-Dsg3 Ab From Circulation

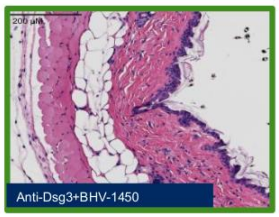


BHV-1450 Rescues Body Weight Loss in PV-like model



BHV-1450 Rescues Blistering Disease Phenotype in a PV-Like Model

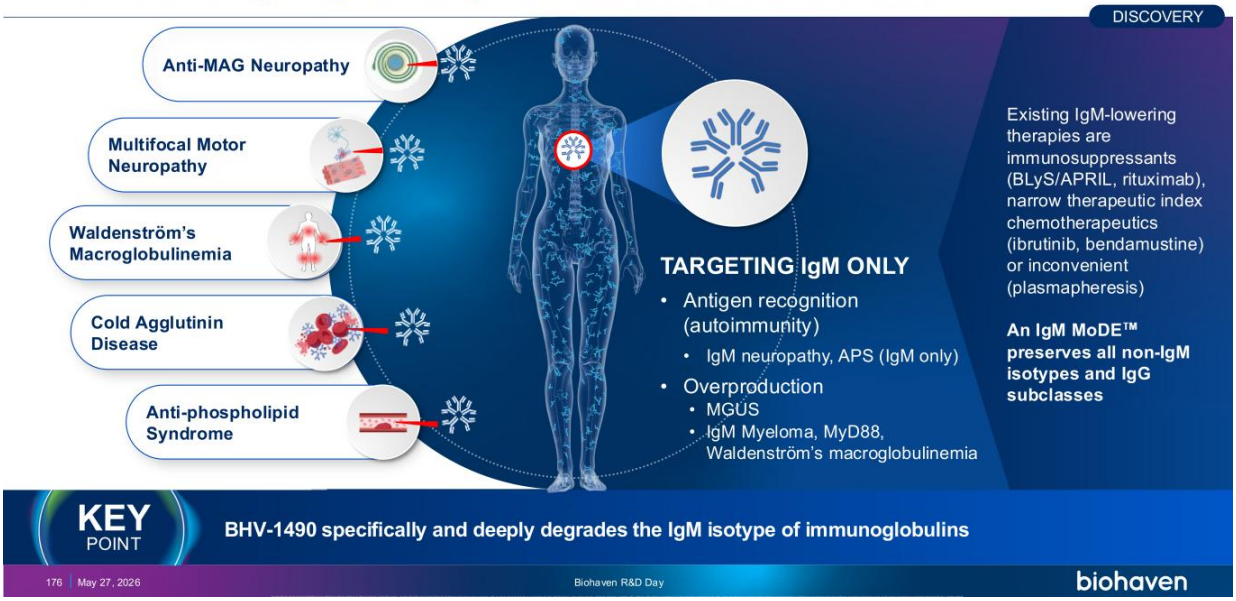




No observation of any suprabasilar keratinocyte clefts create blistering disease


biohaven®
BHV-1490
IgM MoDE™ Degrader Treatment of IgM-Driven Disease
DAYS MATTER™

Removal of IgM Specifically Addresses Several Diseases



KEY POINT **BHV-1490 specifically and deeply degrades the IgM isotype of immunoglobulins**

IgM-Mediated Diseases Have Significant Unmet Need and Are Suitable for MoDE™ Degraders

DISCOVERY

IgM-mediated diseases caused by pathogenic autoreactive IgM

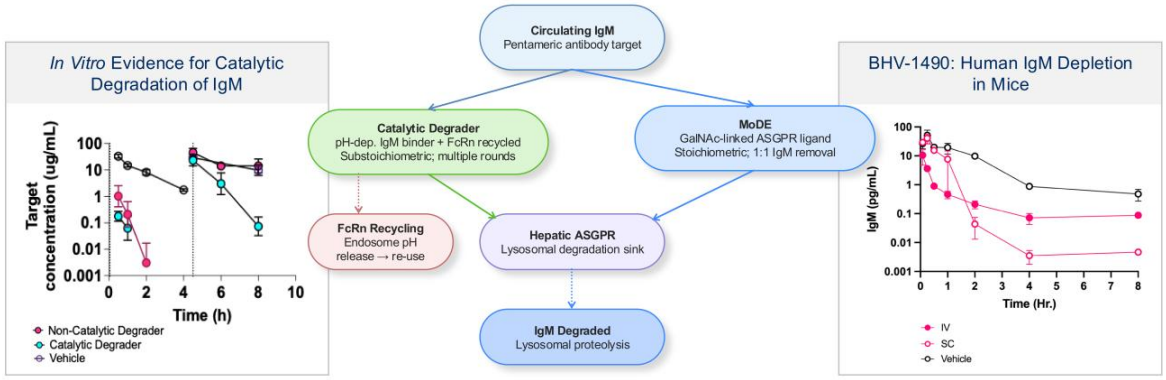
Significant market opportunity in IgM-mediated diseases with unmet clinical need with streamlined clinical path towards POC

Indication	US Patients	IgM Burden	Competition	Rationale and endpoint	Pricing Structure
Anti-MAG neuropathy	5–10K	Low	None approved; rituximab off-label ~$15K	• Anti-MAG titer is low — attractive for SC autoinjector dosing • IgM titer and nerve conduction velocity	Orphan; first-in-class
Multifocal motor neuropathy	3–5K	Low	IVIG ~$136–500K/yr (infusion)	• Anti-GM1 IgM is low-titer monoclonal. Stoichiometric SC weekly dose tractable. • IgM titer and grip strength	SC vs. IVIG cost-effectiveness
APS-IgM only	3–7K	Low	Warfarin <$1K/yr; rivaroxaban ~$5K/yr	• IgM aCL/aβ2GPI titers are low in isolated phenotype — no class-switch • IgM titer-stroke recurrence	First IgM-specific label; stroke value ~$250K
Schnitzler syndrome	200	Very Low	Anakinra off-label ~$80K/yr	• Lowest IgM titer of all indications. MGUS-level monoclonal IgM • IgM titer UAS7, C-reactive protein	Ultra-rare orphan; no approved IgM-directed Rx
Cold agglutinin disease	5K	Medium	Sutimlimab (Enjaymo) $440K/yr WAC	• Monoclonal IgM is high but levels could be assessed and lowered over time • Hemoglobin	Below sutimlimab; SC vs. IV

IgM Degraders: Catalytic and MoDE™ Degraders Provide Optionality Across Indications

DISCOVERY

Biohaven IgM-MoDE Platform
Dual Molecular Architecture



KEY POINT

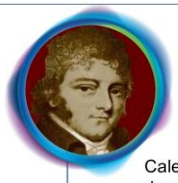
- **BHV-1490 leverages a novel ASGPR ligand to rapidly remove IgM from circulation**
- **BHV-1490 on track to initiate preclinical development in 2027**


Malini Gupta, MD,
ECNU, FACE, FITS
Director of G2Endo, Endocrinology
and Metabolism 2025 AACE Chair
G2ENDO
Graves' Disease:
Old Disease, New Therapeutic Landscape
biohaven

History of Graves' Disease

DEGRADERS

Persian physician Abicenna documented patients with goiter and increased appetite



Caleb Hillier Parry described hyperthyroidism and goiter in Europe

Karl Adolph van Basedow, described a constellation of symptoms, independently in Germany

1000 AD | 1100 AD | 1786 | 1835 | 1840

Sayyid Zayn al-Din Isma'il al-Husayni al-Jurjani (Ismail Gorgani) described this in a medical encyclopedia

Irish surgeon Robert James Graves linked many symptoms with thyroid enlargement in multiple patients in Dublin

Dr. Robert Graves

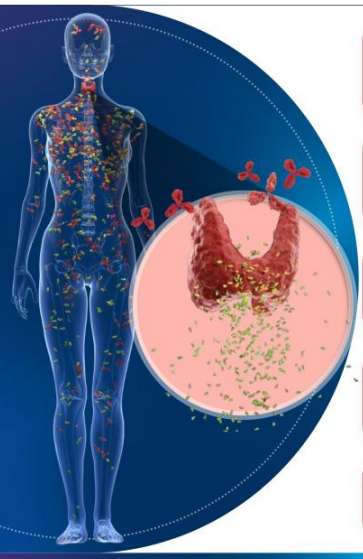
His fame rests chiefly on his Clinical Lectures, which were a model for the day and recommended by Armand Trousseau in France (1801–1867), who suggested the term Graves' disease.

Trousseau was the first in France to perform a tracheotomy, and he wrote a monograph on this as well as intubation in 1851.

What is Graves' Disease?

DEGRADERS

Graves' disease is an immune system disorder that affects the thyroid gland. It causes the body to make too much thyroid hormone.

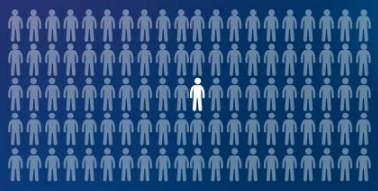


- Nervousness, irritability insomnia, depression
- Broken hair, hair loss
- Weight loss, strong feeling of hunger, diarrhea
- Enlarged thyroid gland
- Fragile fingernails, shaking hands
- Increased heart rate, arrhythmia, high blood pressure
- Warm, moist skin, increased body temperature
- Muscle cramps, muscle weakness
- Miscellaneous cycle disorders

Demographics: Graves' Disease Impacts 1% of the Global Population

DEGRADERS

Graves' disease affects nearly 1 in 100 Americans.[1]

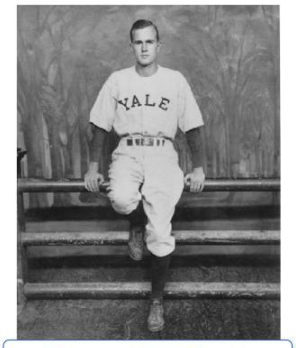


About 4 out of 5 cases of hyperthyroidism in the United States are caused by Graves' disease.[1]

Worldwide incidence of Graves' disease[2]

1. Akram. Journal of Surgical Research. 2020. 2. McLeod. Endocrine. 2012.

Notable Persons With Graves' Disease



George H.W. Bush

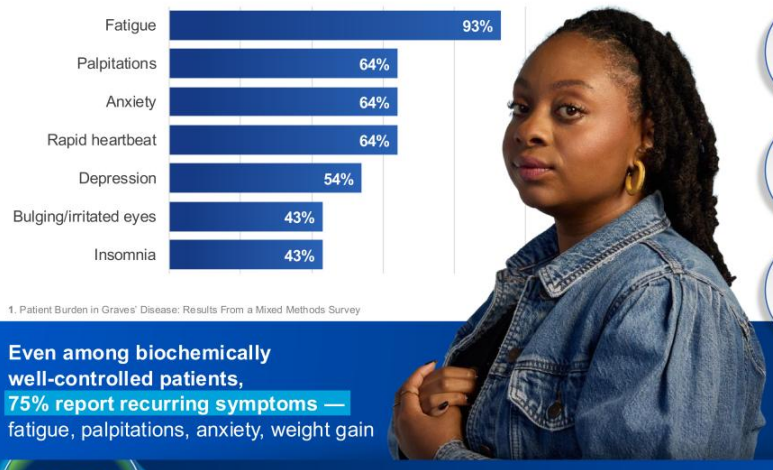
Barbara Bush

DEGRADERS

- Actor Marty Feldman
- Actor Rodney Dangerfield
- Sprinter Gail Devers
- Singer Missy Elliott
- Artist Yayoi Kusama
- Actress Dame Maggie Smith

The Under-Recognized Burden of Graves' Disease[1]

DEGRADERS



1. Patient Burden in Graves' Disease: Results From a Mixed Methods Survey

93% report multiple symptoms (≥2)

79% experience 4+ symptoms

72% experience 5+ symptoms

Even among biochemically well-controlled patients, 75% report recurring symptoms — fatigue, palpitations, anxiety, weight gain

Courtnay
Living with Graves' disease

KEY POINT

Current treatments achieve biochemical control but do not address the underlying antibody-driven disease, antibodies continue to circulate, targeting the thyroid, orbit, brain, and crossing the placenta

Living With Graves' Disease — The Human Toll[1]

DEGRADERS

EMOTIONAL TOLL

100% Emotional

57% Physical

50% Social

FUNCTIONAL IMPACT

36% Daily activities

36% Family planning

29% Work/financial

> ***The anxiety makes it really hard to do normal people stuff sometimes.*** *I'll drive to the grocery store and then not go inside because I have anxiety for no reason.*
>
> — Patient A

> ***I had to leave my job.*** *I don't get to see my friends as much anymore.*
>
> — Patient B

> *I'm 90% a no on having children… knowing that that's an option* ***being taken away without my choice*** *affects it.*
>
> — Patient C

Emma
Living with Graves' disease

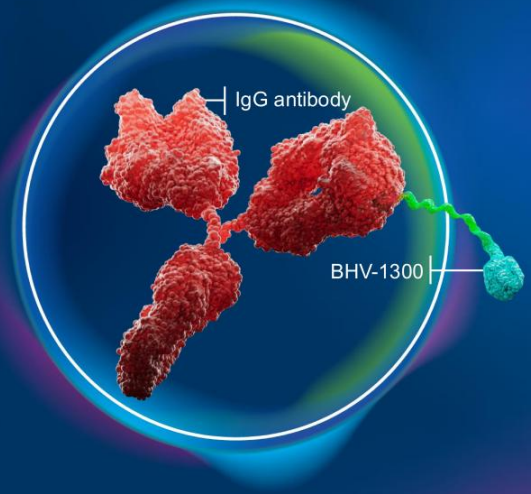
1. Patient Burden in Graves' Disease: Results From a Mixed Methods Survey

KEY POINT

Patients on antithyroid drugs continue to suffer. Symptoms are pervasive and multi-system.

biohaven®

The Science of Graves' Disease

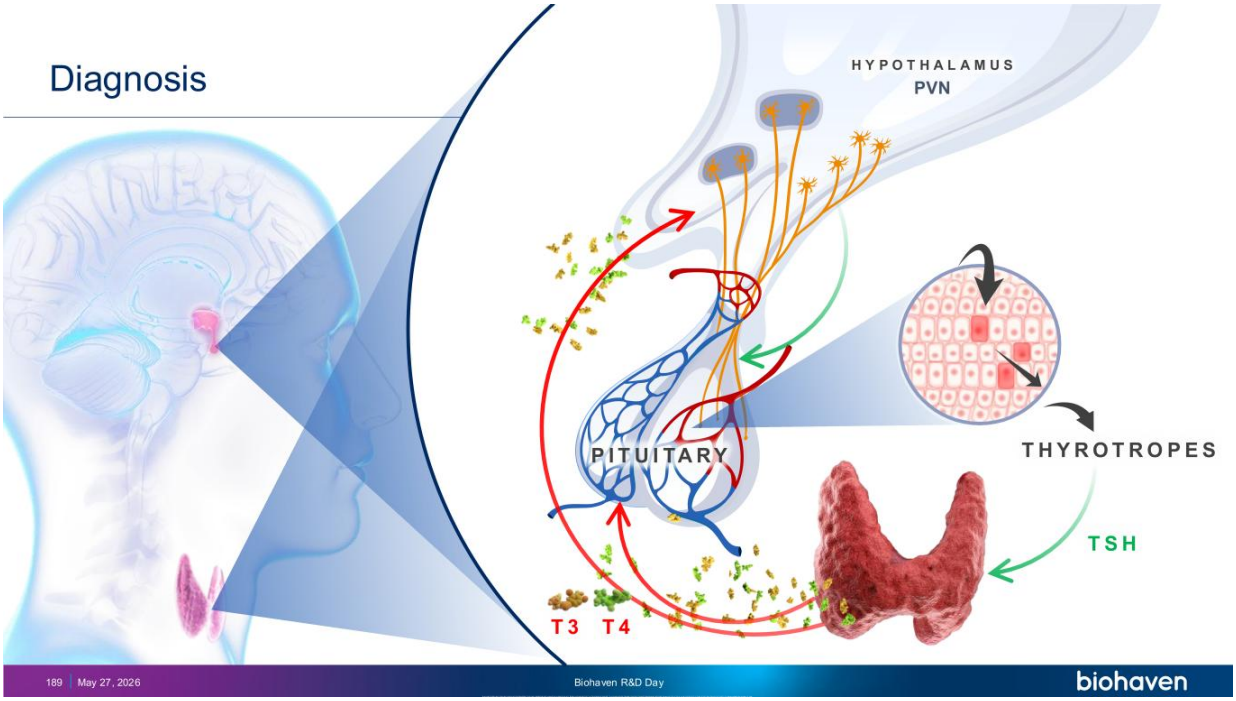


How Is Graves' Disease Diagnosed?

DEGRADERS




History	Physical Exam	Lab Testing	Imaging
• History of symptoms and review of symptoms • Family history of autoimmune disease, thyroid disease • Social history	Including eye and hearing	TSH, free T4, free T3, TRAb, TSI, TPO Ab	Ultrasound, CT, I-123 thyroid uptake and scan


Diagnosis
HYPOTHALAMUS
PVN
PITUITARY
THYROTROPES
TSH
T3 T4
189 | May 27, 2026
Biohaven R&D Day
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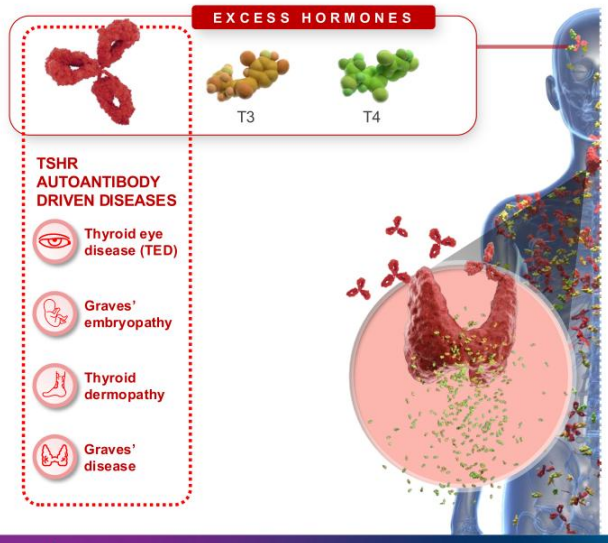
Root Cause of Graves' Disease and Extrathyroidal Manifestations



The TSHR autoantibody causes more than hyperthyroidism

TSHR autoantibodies don't just attack the thyroid, they target TSHR-expressing cells across multiple organs

TSHR Autoantibodies (TSHR-IgG1) Cause Hyperthyroidism

DEGRADERS

	Hyperthyroidism (from a toxic nodule)	Graves' disease hyperthyroidism	Autoimmune hypothyroidism (Hashimoto's)
Thyroid stimulating hormone (TSH)	↓	↓	↑
Thyroxine (T4)	↑	↑	↓
Thyronine (T3)	↑	↑	↓
Thyroid receptor antibody (TRAb)	−	+	−
Thyroid stimulating immunoglobulin (TSI)	−	+	−
Thyroid peroxidase antibody (TPO Ab)	−	+	+

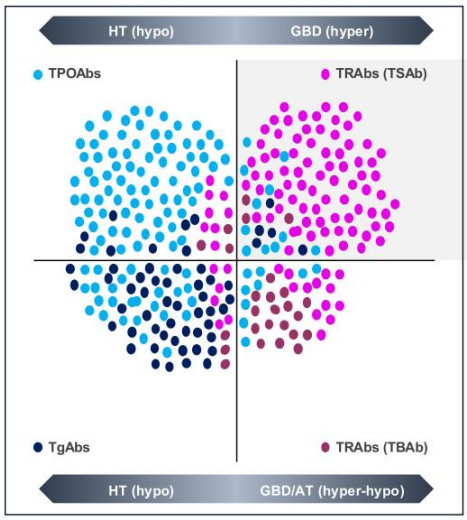
KEY POINT

TSHR-IgG1 causes Graves' Hyperthyroidism, the diagnosis of which is made when a patient has elevated thyroid hormones and TSHR autoantibodies present

The Antibody Landscape in Autoimmune Thyroid Disease

Most Hashimoto's patients have TPO antibodies, these attack the thyroid and cause it to underproduce hormones (**hypo**thyroidism)

Some Hashimoto's patients also have thyroglobulin antibodies, a second marker, but less common



Graves' patients have stimulating TRAb

These force the thyroid to overproduce hormones (hyperthyroidism)

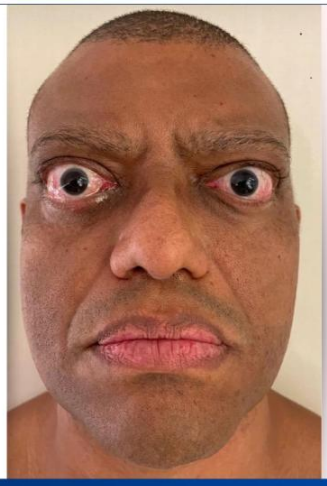
A small group also have blocking TRAb, these shut the thyroid down, causing a rare shift from hyper- to hypothyroidism

Adapted from: Vargas-Uricoechea H, Nogueira JP, Pinzón-Fernández MV, Schwarzstein D. The Usefulness of Thyroid Antibodies in the Diagnostic Approach to Autoimmune Thyroid Disease. *Antibodies*. 2023; 12(3):48. https://doi.org/10.3390/antib12030048

Thyroid Eye Disease (TED)

DEGRADERS

TRAb autoantibodies cross-react with IGF-1R on orbital fibroblasts which leads to inflammation and tissue remodeling



CLINICAL CONSEQUENCES

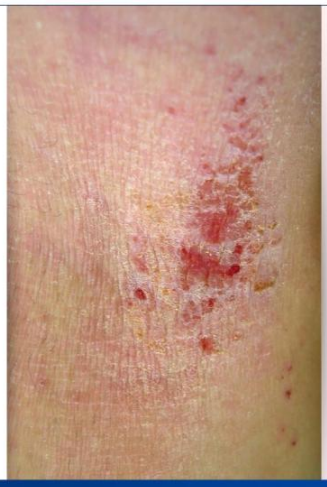
- Proptosis (exophthalmos) — orbital fat expansion pushes the globe forward
- Lid retraction and stare
- Diplopia (double vision)
- Pain and pressure sensation
- Periorbital edema
- Vision loss (severe cases)

KEY POINT 50% of Graves' patients develop TED — it can occur even with normal thyroid function

Pretibial Myxedema, a Form of Graves' Dermopathy

DEGRADERS

TRAb autoantibodies bind TSHR on dermal fibroblasts which leads to glycosaminoglycan deposition and dermal thickening.



CLINICAL CONSEQUENCES

- Non-pitting, waxy skin plaques
- Hyperkeratosis and skin thickening
- Cosmetic disfigurement
- Discomfort and reduced mobility (severe)
- Elephantiasic form (rare, most severe)
- **Can extend to feet, ankles, arms and other sites**

KEY POINT

Like TED, pretibial myxedema is driven by TRAb autoantibodies activating fibroblasts, a shared autoimmune mechanism, different tissue target

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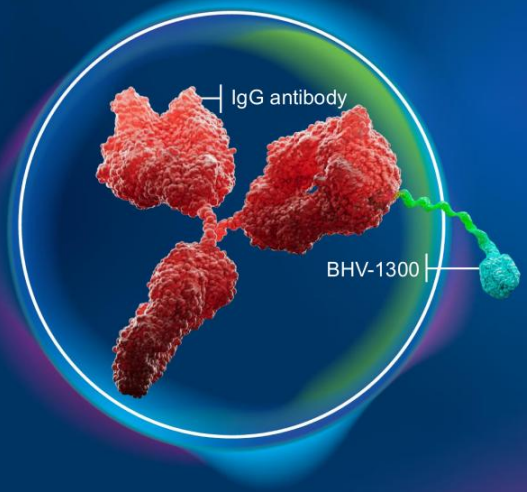
NEW TREATMENTS IN GRAVES' DISEASE

The Evolving Therapeutic Landscape



Current Treatments for Graves' Disease

CONSERVATIVE

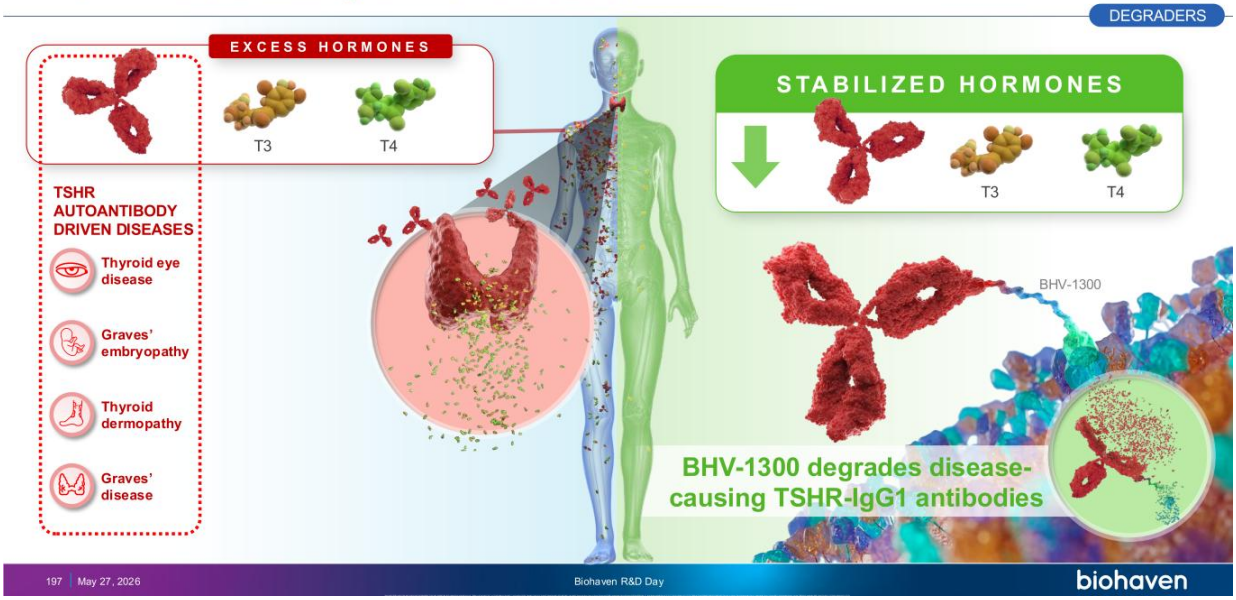
1. **Use of thionamides**
   (ATDs, like methimazole, carbimazole, and propylthiouracil (PTU)
   Aplastic anemia, granulocytosis, peripheral neuritis, liver issues, secreted in breastmilk
2. **Use of steroids**

ABLATIVE

3. **Surgical removal of the thyroid**
   Lifelong T4 replacement, surgical complications
4. **Use of I-131 radiation treatment**
   Cannot use in pregnancy, TED worsens

BHV-1300 MoDE™ Targets the Root Cause of Graves' Disease and TSHR Autoantibody-Driven Diseases

DEGRADERS



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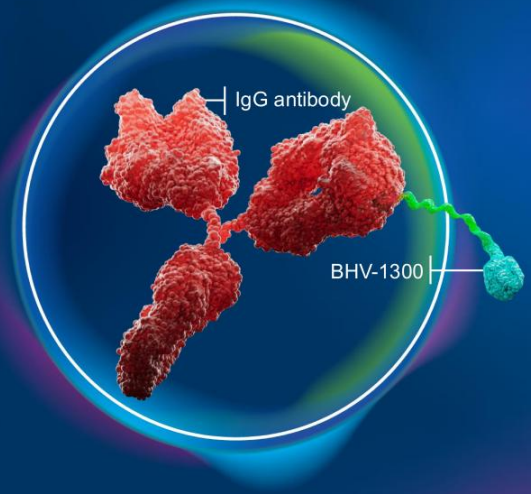
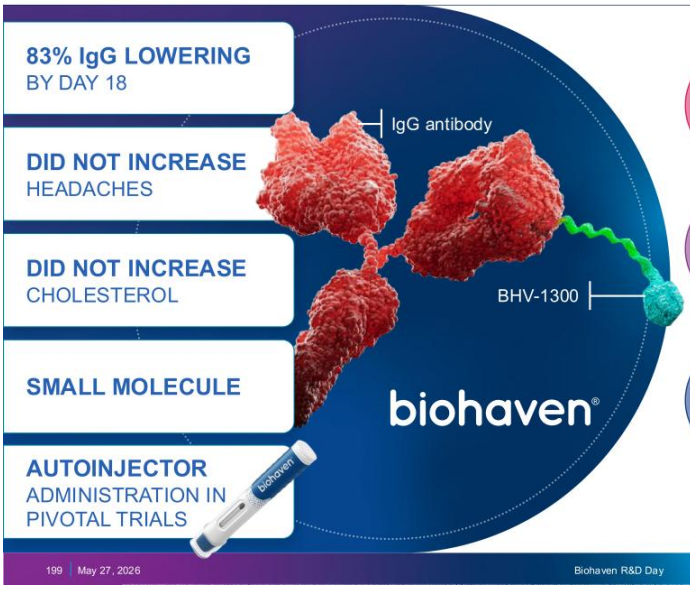
BHV-1300 in Graves' Disease



Not FcRn Inhibitor: Biohaven IgG MoDE™ Degrader Differentiates as a Novel MOA, Potential Paradigm Shifting Therapy



DEGRADERS

IMAAVY™ J&J

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

Vyvgart® argenx

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

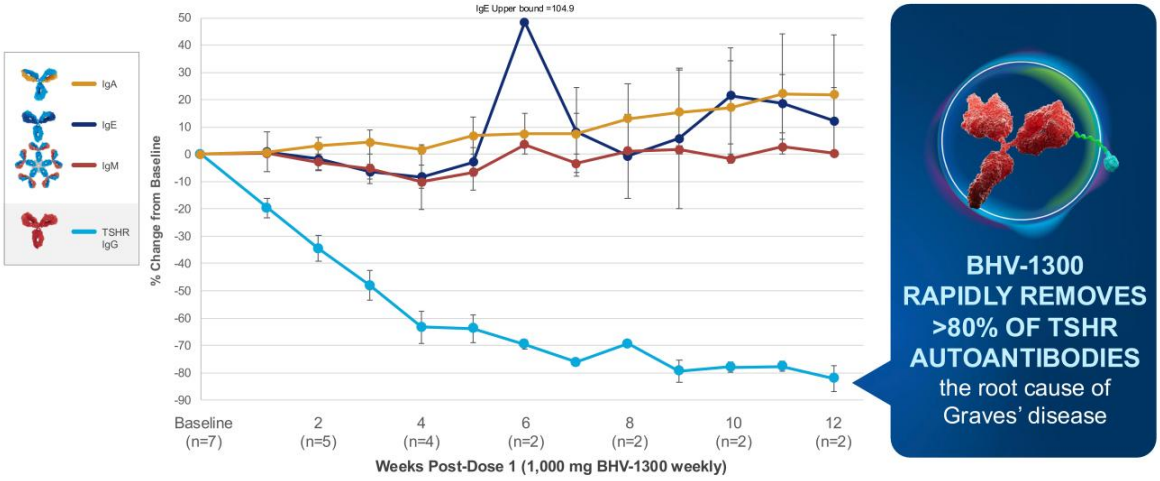
Rystiggo® UCB

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

1. Median of the maximal total IgG % change from baseline 2. 84% IgG lowering (twice the labeled frequency) in Phase 1 Ling. Clin Pharmacol Ther. 2019. 3. Howard, Jr. ADAPT (SC) Data – 2024; 4. Ulrichts. J. Clin. Invest. 2018. 5. MAD data unavailable. MG Data from Bril, Lancet Neurology. 2023 – MyCarinG study.

BHV-1300 Rapidly Degrades Disease-Causing Autoantibodies That Target the Thyroid-Stimulating Hormone Receptors (TSHR) in Patients with Graves' Disease

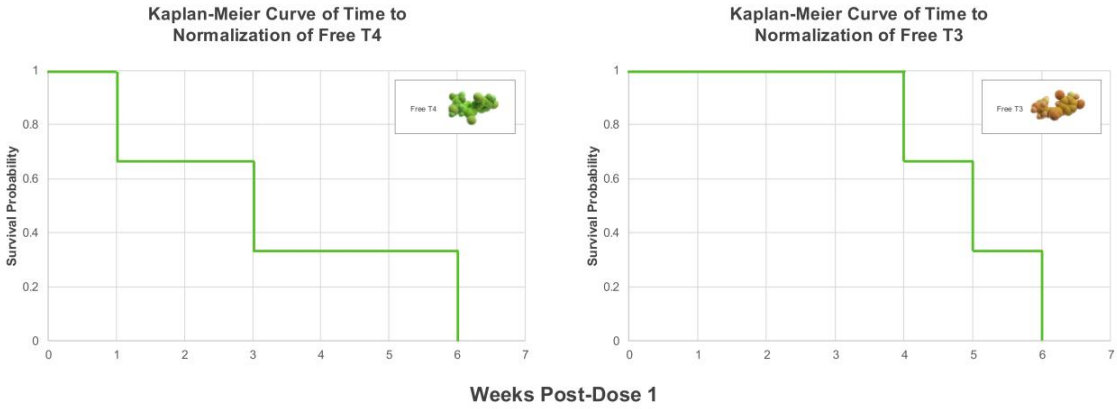
DEGRADERS



Preliminary data from ongoing study, analysis conducted May 20, 2026. *Graph represents mean in participants administered BHV-1300 1,000 mg SC weekly. Values below the lower limit of quantification were set to a value of LOQ/2.

BHV-1300 Rapidly Normalizes Thyroid Hormones in Patients With Graves' Hyperthyroidism

DEGRADERS



Preliminary data from ongoing study, analysis conducted April 8, 2026. Graphs represent time to normalization of Free T3 and Free T4 in participants (n=3) with Graves' disease and overt hyperthyroidism at baseline administered BHV-1300 1,000 mg SC weekly for 12 weeks (n=2) or BHV-1300 1000 mg SC weekly for 4 weeks followed by 500 mg SC weekly for 8 weeks (n=1).

KEY POINT

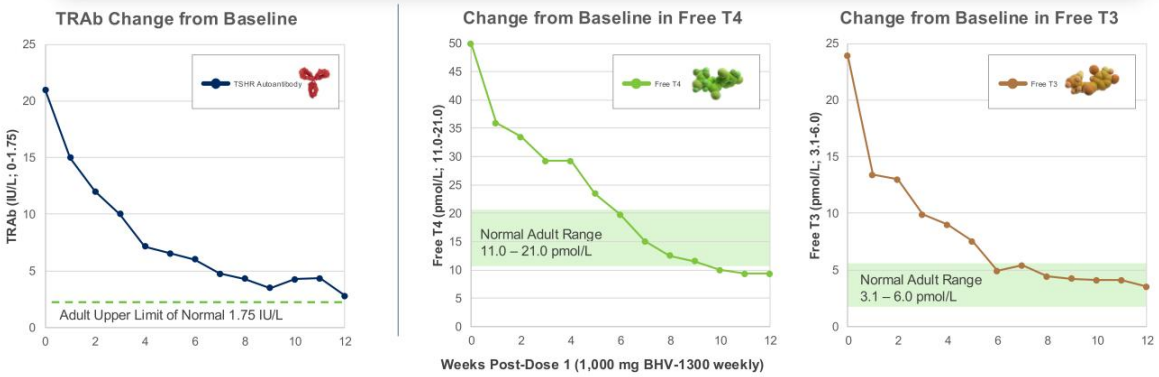
In hyperthyroid patients receiving BHV-1300 1,000 mg SC weekly, Free T4 normalized within an average of 3 weeks and Free T3 normalized within an average of 5 weeks

Early Graves' Patient Experience: Most Severely Hyperthyroid Patient BHV-1300 Rapidly Normalizes Thyroid Hormones

DEGRADERS

CASE DETAILS

- Male patient in his late 50s
- Severely elevated thyroid hormone levels at baseline
- Patient reported **improvement in sweating, palpitations, diarrhea, fatigue and motivation** at 30 days compared to baseline
- TSH normalized within 12 weeks of BHV-1300 initiation



Preliminary data from ongoing study, analysis conducted April 8, 2026.

Early Graves' Patient Experience: Severely Hyperthyroid Patient BHV-1300 Rapidly Normalizes TSH and Hyperthyroid Symptoms

DEGRADERS

CASE DETAILS

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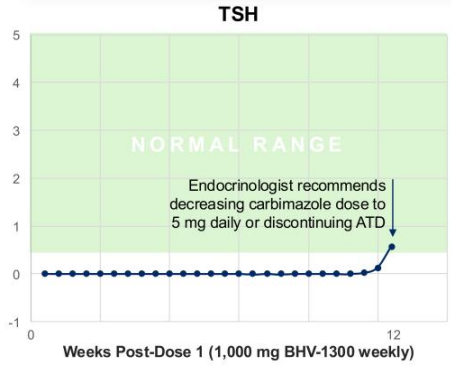


Baseline	Thypro-39 symptoms	End of dosing
	Trembling hands	Resolved
	Sweating	Resolved
	Palpitations	Resolved

Preliminary data from ongoing study, analysis conducted April 8, 2026.

Lead MoDE™ Degrader, BHV-1300, Enters Phase 3

DEGRADERS

KEY STUDY DETAILS

Study Design: Randomized, double-blind, placebo-controlled trial
Population: Male and female adults with Graves' disease
Endpoints: Normal T3, T4 and TSH off ATD at week 26

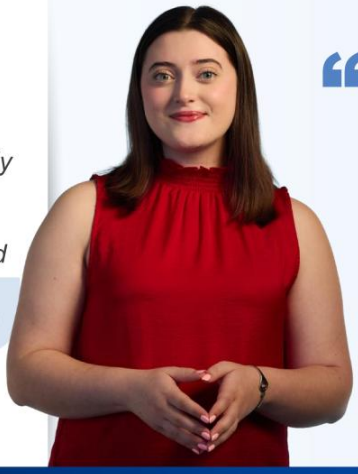
ATD, antithyroid drugs

KEY POINT BHV-1300 pivotal trial in Graves' disease to commence in the coming weeks

Patients Want To Target the Root Cause[1]

DEGRADERS

> *That's the most attractive thing, **removing the root cause rather than putting a Band-Aid on it**. It's essentially like **repairing the thyroid** or putting it **back into its original coding**, that it should work the way that it was originally designed to do.*

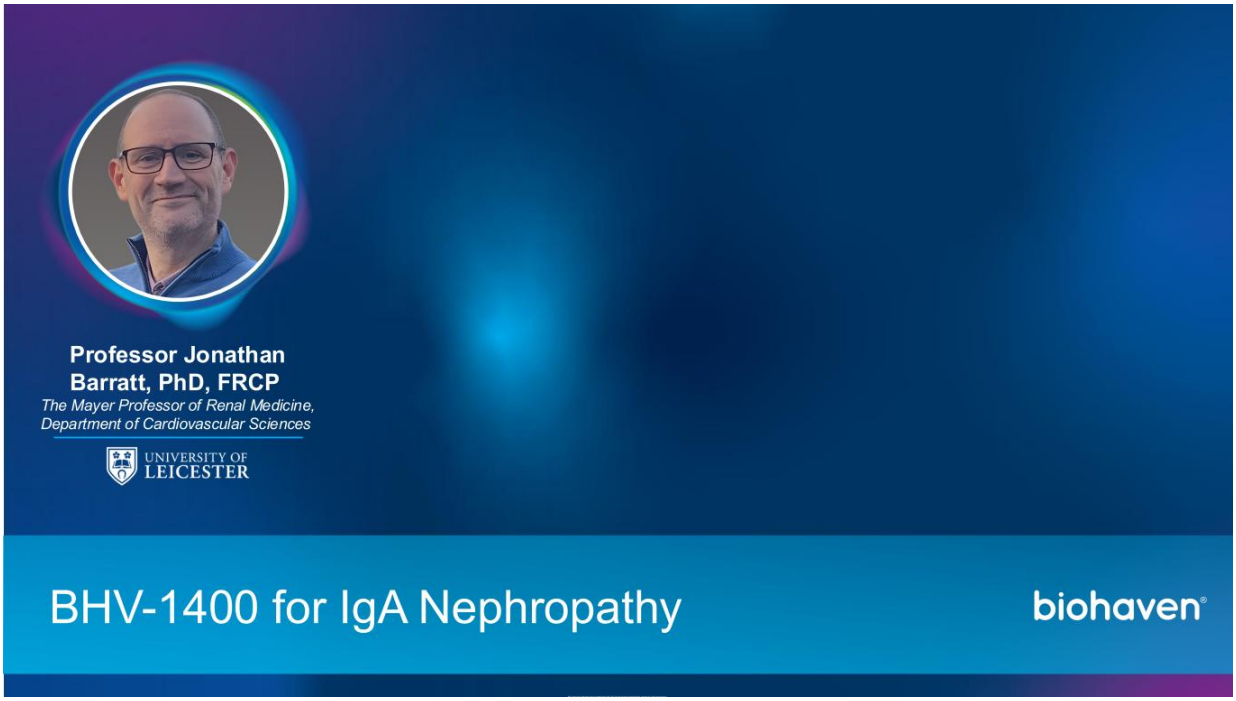


> *Going back to root cause is a pretty big deal. A lot of times, treatments just cover the symptoms. **You're putting a Band-Aid over what is a much larger wound**.*

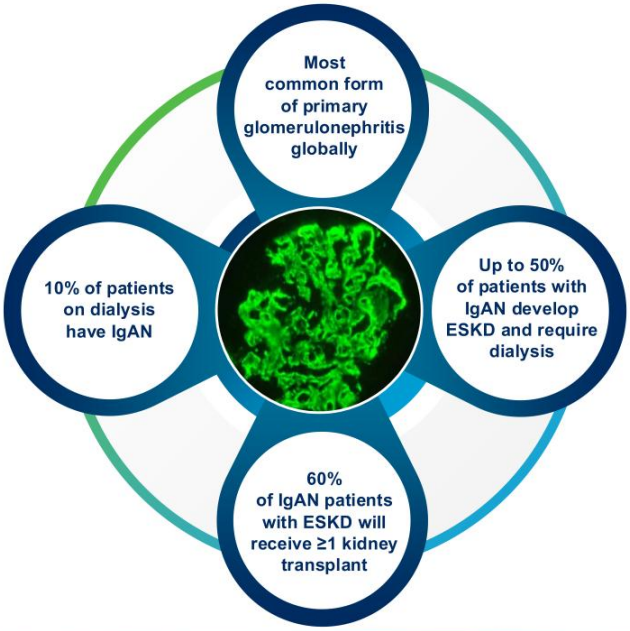
Paige
Living with Graves' disease

1. Patient Burden in Graves' Disease: Results From a Mixed Methods Survey

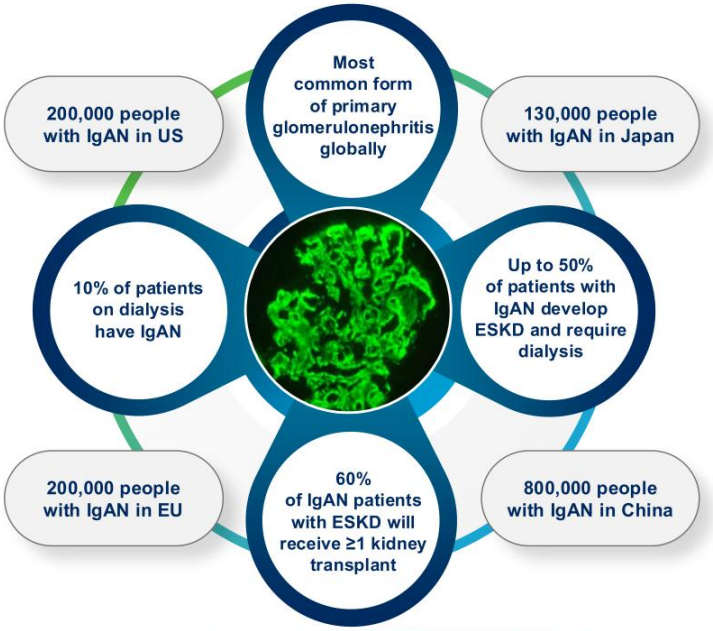
KEY POINT **BHV-1300 is a precision degrader designed to target the autoantibody — addressing the root cause of Graves' disease**


Professor Jonathan Barratt, PhD, FRCP
The Mayer Professor of Renal Medicine, Department of Cardiovascular Sciences
UNIVERSITY OF LEICESTER
BHV-1400 for IgA Nephropathy
biohaven

Jonathan Barratt	
Consulting and speaker fees	Alnylam, Argenx, Astellas, BioCryst, Calliditas, Chinook, Dimerix, Galapagos, Novartis, Omeros, Travere Therapeutics, Vera Therapeutics, Visterra
Grant support	Argenx, Calliditas, Chinook, Galapagos, GlaxoSmithKline, Novartis, Omeros, Travere Therapeutics, Visterra
Clinical trials	ADU-CL-19 and ALIGN (Chinook), APPLAUSE (Novartis), ARTEMIS-IGAN (Omeros), ENVISION (Visterra), NeflgARD (Calliditas), ORIGIN (Vera Therapeutics)
Research projects	Argenx, Calliditas, Chinook, Galapagos, GlaxoSmithKline, Novartis, Omeros, Travere Therapeutics, Visterra

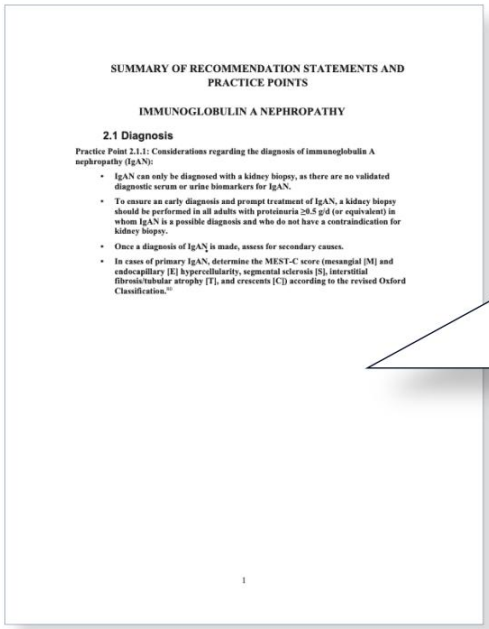


Barrett. 2026.



Barrett. 2026.

KDIGO



SUMMARY OF RECOMMENDATION STATEMENTS AND PRACTICE POINTS

IMMUNOGLOBULIN A NEPHROPATHY

2.1 Diagnosis

Practice Point 2.1.1: Considerations regarding the diagnosis of immunoglobulin A nephropathy (IgAN):

- IgAN can only be diagnosed with a kidney biopsy, as there are no validated diagnostic serum or urine biomarkers for IgAN.
- To ensure an early diagnosis and prompt treatment of IgAN, a kidney biopsy should be performed in all adults with proteinuria ≥0.5 g/d (or equivalent) in whom IgAN is a possible diagnosis and who do not have a contraindication for kidney biopsy.
- Once a diagnosis of IgAN is made, assess for secondary causes.
- In cases of primary IgAN, determine the MEST-C score (mesangial [M] and endocapillary [E] hypercellularity, segmental sclerosis [S], interstitial fibrosis/tubular atrophy [T], and crescents [C]) according to the revised Oxford Classification.[80]

1

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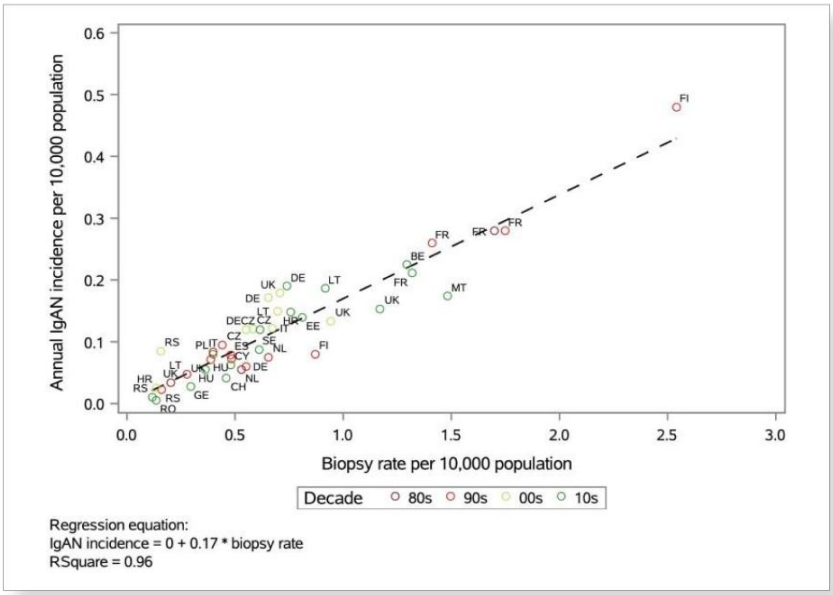
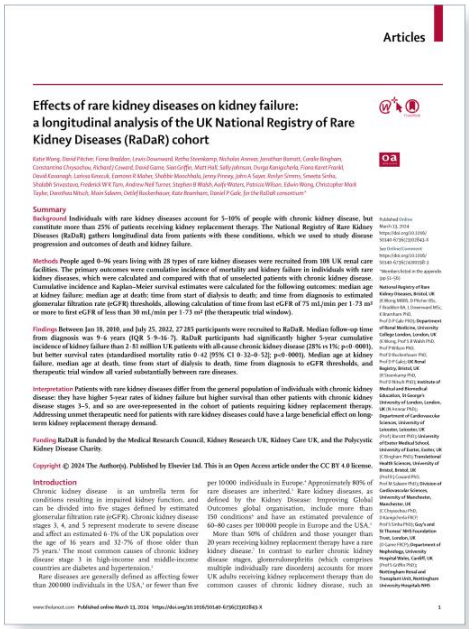


Buisker. Clin Kidney J. 2025.

RaDaR

National Registry of Rare Kidney Diseases



Articles

Effects of rare kidney diseases on kidney failure: a longitudinal analysis of the UK National Registry of Rare Kidney Diseases (RaDaR) cohort

Katie Wong, David Pitcher, Fiona Bradlow, Lewis Dosanwand, Retha Steenkamp, Nicholas Aresese, Jonathan Barratt, Carole Bingham, Constantina Chrysochou, Richard J Coward, David Game, Sian Griffin, Matt Hall, Sally Johnson, Durga Kanigicherla, Fiona Karet Frankl, David Kavanagh, Larissa Kenezuk, Eamonn R Maher, Shabbir Moochhala, Jenny Prinsey, John A Sayer, Kevlyn Simms, Smeeta Sinha, Shalabh Srivastava, Frederick WK Tam, Andrew Neil Turner, Stephen B Walsh, Aarfy Waters, Patricia Wilson, Edwin Wong, Christopher Mark Taylor, Dorothea Nitsch, Mark Sabeen, Detlef Bockenhauer, Kate Bramham, Daniel P Gale, for the RaDaR consortium*

Summary

Background Individuals with rare kidney diseases account for 5–10% of people with chronic kidney disease, but constitute more than 25% of patients receiving kidney replacement therapy. The National Registry of Rare Kidney Diseases (RaDaR) gathers longitudinal data from patients with these conditions, which we used to study disease progression and outcomes of death and kidney failure.

Methods People aged 0–96 years living with 28 types of rare kidney diseases were recruited from 108 UK renal care facilities. The primary outcomes were cumulative incidence of mortality and kidney failure in individuals with rare kidney diseases, which were calculated and compared with that of unselected patients with chronic kidney disease. Cumulative incidence and Kaplan–Meier survival estimates were calculated for the following outcomes: median age at kidney failure; median age at death; time from start of dialysis to death; and time from diagnosis to estimated glomerular filtration rate (eGFR) thresholds, allowing calculation of time from last eGFR of 75 mL/min per 1·73 m² or more to first eGFR of less than 30 mL/min per 1·73 m² (the therapeutic trial window).

Findings Between Jan 18, 2010, and July 25, 2022, 27 285 participants were recruited to RaDaR. Median follow-up time from diagnosis was 9·6 years (IQR 5·9–16·7). RaDaR participants had significantly higher 5-year cumulative incidence of kidney failure than 2·81 million UK patients with all-cause chronic kidney disease (28% vs 1%; p<0·0001), but better survival rates (standardised mortality ratio 0·42 [95% CI 0·32–0·52]; p<0·0001). Median age at kidney failure, median age at death, time from start of dialysis to death, time from diagnosis to eGFR thresholds, and therapeutic trial window all varied substantially between rare diseases.

Interpretation Patients with rare kidney diseases differ from the general population of individuals with chronic kidney disease: they have higher 5-year rates of kidney failure but higher survival than other patients with chronic kidney disease stages 3–5, and so are over-represented in the cohort of patients requiring kidney replacement therapy. Addressing unmet therapeutic need for patients with rare kidney diseases could have a large beneficial effect on long-term kidney replacement therapy demand.

Funding RaDaR is funded by the Medical Research Council, Kidney Research UK, Kidney Care UK, and the Polycystic Kidney Disease Charity.

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See Online/Comment https://doi.org/10.1016/S0140-6736(24)00538-2

*Members listed in the appendix (pp 15–16)

National Registry of Rare Kidney Diseases, Bristol, UK (K Wong MBBS, D Pitcher BSc, F Bradlow BA, L Dosanwand MSc, K Bramham PhD, Prof D P Gale FRCP); Department of Renal Medicine, University College London, London, UK (K Wong, Prof S B Walsh PhD, Prof P Wilson PhD, Prof D Bockenhauer PhD, Prof D P Gale); UK Renal Registry, Bristol, UK (R Steenkamp PhD, Prof D Nitsch PhD); Institute of Medical and Biomedical Education, St George's University of London, London, UK (N Aresese PhD); Department of Cardiovascular Sciences, University of Leicester, Leicester, UK (Prof J Barratt PhD); University Hospitals of Leicester NHS Trust, Leicester, UK (C Bingham PhD); Translational Health Sciences, University of Bristol, Bristol, UK (Prof R J Coward PhD); Prof M Sabeen PhD); Division of Cardiovascular Sciences, University of Manchester, Manchester, UK (C Chrysochou PhD, D Kanigicherla FRCP, Prof S Sinha PhD); Guy's and St Thomas' NHS Foundation Trust, London, UK (D Game FRCP); Department of Nephrology, University Hospital Wales, Cardiff, UK (Prof S Griffin PhD); Nottingham Renal and Transplant Unit, Nottingham University Hospitals NHS

RaDaR
National Registry of Rare Kidney Diseases

In a study of 27,285 patients from the U.K. National Registry of Rare Kidney Diseases

5%
Rare kidney diseases made up at least 5% of total CKD cases

10%
Up to 10% of total CKD cases were forms of rare kidney diseases

25%
Patients with rare kidney diseases make more than 25% of patients receiving kidney replacement therapy

Lancet Pub

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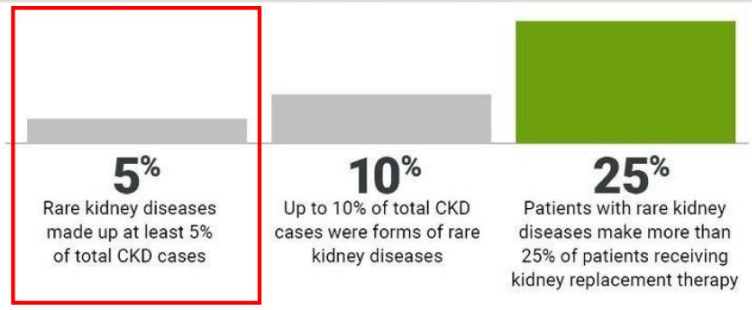

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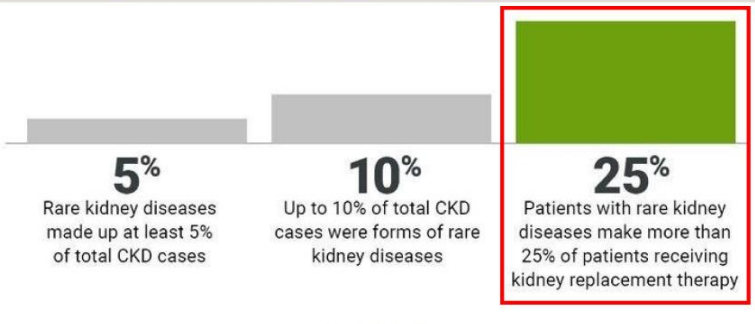

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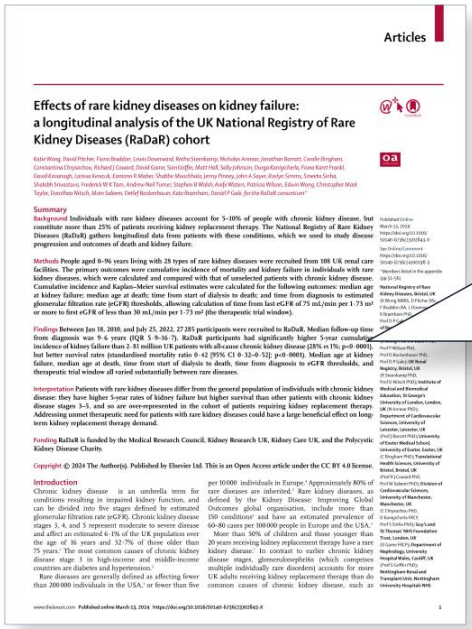

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Funding RaDaR is funded by the Medical Research Council, Kidney Research UK, Kidney Care UK, and the Polycystic Kidney Disease Charity.

Introduction

Chronic kidney disease is an umbrella term for conditions resulting in impaired kidney function, and can be divided into five stages defined by estimated glomerular filtration rate (eGFR). Chronic kidney disease stages 3, 4, and 5 represent moderate to severe disease and affect an estimated 6·1% of the UK population over the age of 16 years and 32·7% of those older than 75 years.[1] The most common causes of chronic kidney disease stage 3 in high-income and middle-income countries are diabetes and hypertension.[2]

Rare diseases are generally defined as affecting fewer than 200 000 individuals in the USA,[3] or fewer than five per 10 000 individuals in Europe.[4] Approximately 80% of rare diseases are inherited.[5] Rare kidney diseases, as defined by the Kidney Disease: Improving Global Outcomes global organisation, include more than 150 conditions[6] and have an estimated prevalence of 60–80 cases per 100 000 people in Europe and the USA.[7]

More than 50% of children and those younger than 20 years receiving kidney replacement therapy have a rare kidney disease.[7] In contrast to earlier chronic kidney disease stages, glomerulonephritis (which comprises multiple individually rare disorders) accounts for more UK adults receiving kidney replacement therapy than do common causes of chronic kidney disease, such as

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Patients with rare kidney diseases differ from the general population of individuals with chronic kidney disease: they have **higher 5-year rates of kidney failure** but **higher survival** than other patients with chronic kidney disease stages 3–5, and so are **over-represented in the cohort of patients requiring kidney replacement therapy.**

Addressing unmet therapeutic need for patients with rare kidney diseases could have a large beneficial effect on long-term kidney replacement therapy demand.

Articles

Effects of rare kidney diseases on kidney failure: a longitudinal analysis of the UK National Registry of Rare Kidney Diseases (RaDaR) cohort

Katie Wong, David Pitcher, Fiona Braddon, Lewis Downward, Retha Steenkamp, Nicholas Annear, Jonathan Barratt, Coralie Bingham, Constantina Chrysochou, Richard J Coward, David Game, Sian Griffin, Matt Hall, Sally Johnson, Durga Kanigicherla, Fiona Karet Frankl, David Kavanagh, Larissa Kerecuk, Eamonn R Maher, Shabbir Moochhala, Jenny Pinney, John A Sayer, Roslyn Simms, Smeeta Sinha, Shalabh Srivastava, Frederick W K Tam, Andrew Neil Turner, Stephen B Walsh, Aoife Waters, Patricia Wilson, Edwin Wong, Christopher Mark Taylor, Dorothea Nitsch, Moin Saleem, Detlef Bockenhauer, Kate Bramham, Daniel P Gale, for the RaDaR consortium*

Summary

Background Individuals with rare kidney diseases account for 5–10% of people with chronic kidney disease, but constitute more than 25% of patients receiving kidney replacement therapy. The National Registry of Rare Kidney Diseases (RaDaR) gathers longitudinal data from patients with these conditions, which we used to study disease progression and outcomes of death and kidney failure.

Methods People aged 0–96 years living with 28 types of rare kidney diseases were recruited from 108 UK renal care facilities. The primary outcomes were cumulative incidence of mortality and kidney failure in individuals with rare kidney diseases, which were calculated and compared with that of unselected patients with chronic kidney disease. Cumulative incidence and Kaplan–Meier survival estimates were calculated for the following outcomes: median age at kidney failure; median age at death; time from start of dialysis to death; and time from diagnosis to estimated glomerular filtration rate (eGFR) thresholds, allowing calculation of time from last eGFR of 75 mL/min per 1·73 m² or more to first eGFR of less than 30 mL/min per 1·73 m² (the therapeutic trial window).

Findings Between Jan 18, 2010, and July 25, 2022, 27 285 participants were recruited to RaDaR. Median follow-up time from diagnosis was 9·6 years (IQR 5·9–16·7). RaDaR participants had significantly higher 5-year cumulative incidence of kidney failure than 2·81 million UK patients with all-cause chronic kidney disease (28% vs 1%; $p<0·0001$), but better survival rates (standardised mortality ratio 0·42 [95% CI 0·32–0·52]; $p<0·0001$). Median age at kidney failure, median age at death, time from start of dialysis to death, time from diagnosis to eGFR thresholds, and therapeutic trial window all varied substantially between rare diseases.

Interpretation Patients with rare kidney diseases differ from the general population of individuals with chronic kidney disease: they have higher 5-year rates of kidney failure but higher survival than other patients with chronic kidney disease stages 3–5, and so are over-represented in the cohort of patients requiring kidney replacement therapy. Addressing unmet therapeutic need for patients with rare kidney diseases could have a large beneficial effect on long-term kidney replacement therapy demand.

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Introduction

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*Members listed in the appendix (pp 53–59)

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Original Article

OPEN

Long-Term Outcomes in IgA Nephropathy

David Pitcher,[1,2] Fiona Braddon,[1] Bruce Hendry,[3] Alex Mercer,[4] Kate Osmaston,[1] Moin A. Saleem,[5] Retha Steenkamp,[1] Katie Wong,[1,2] A. Neil Turner,[6] Kaijun Wang,[1] Daniel P. Gale,[2] and Jonathan Barratt[7]

Abstract

Background IgA nephropathy can progress to kidney failure, and risk assessment soon after diagnosis has advantages both for clinical management and the development of new therapeutics. We present relationships among proteinuria, eGFR slope, and lifetime risks for kidney failure.

Methods The IgA nephropathy cohort (2299 adults and 140 children) of the UK National Registry of Rare Kidney Diseases (RaDaR) was analyzed. Patients enrolled had a biopsy-proven diagnosis of IgA nephropathy plus proteinuria >0.5 g/d or eGFR <60 ml/min per 1.73 m². Incident and prevalent populations and a population representative of a typical phase 3 clinical trial cohort were studied. Analyses of kidney survival were conducted using Kaplan–Meier and Cox regression. eGFR slope was estimated using linear mixed models with random intercept and slope.

Results The median (Q1, Q3) follow-up was 5.9 (3.0, 10.5) years; 50% of patients reached kidney failure or died in the study period. The median (95% confidence interval [CI]) kidney survival was 11.4 (10.5 to 12.5) years; the mean age at kidney failure/death was 48 years, and most patients progressed to kidney failure within 10–15 years. On the basis of eGFR and age at diagnosis, almost all patients were at risk of progression to kidney failure within their expected lifetime unless a rate of eGFR loss ≤1 ml/min per 1.73 m² per year was maintained. Time-averaged proteinuria was significantly associated with worse kidney survival and more rapid eGFR loss in incident, prevalent, and clinical trial populations. Thirty percent of patients with time-averaged proteinuria of 0.44 to <0.88 g/g and approximately 20% of patients with time-averaged proteinuria <0.44 g/g developed kidney failure within 10 years. In the clinical trial population, each 10% decrease in time-averaged proteinuria from baseline was associated with a hazard ratio (95% CI) for kidney failure/death of 0.89 (0.87 to 0.92).

Conclusions Outcomes in this large IgA nephropathy cohort are generally poor with few patients expected to avoid kidney failure in their lifetime. Significantly, patients traditionally regarded as being low risk, with proteinuria <0.88 g/g (<100 mg/mmol), had high rates of kidney failure within 10 years.

CJASN 18: 727–738, 2023. doi: https://doi.org/10.2215/CJN.0000000000000135

Introduction

IgA nephropathy is the most common form of primary glomerulonephritis and a major cause of CKD and kidney failure worldwide.[1,2] Most patients are diagnosed before age 40 years.[3–5] Life expectancy in countries where IgA nephropathy is commonly encountered varies from 70 to 85 years.[6] Current perceptions of risk of progression are based on outcome data typically spanning 10 or 15 years,[5,7] a relatively short period that represents less than half the remaining lifespan of the typical patient with IgA nephropathy.

To facilitate investment in new therapies, a focus of recent research has been to identify surrogate end points that predict long-term clinical outcomes.[8,9] Reduction in proteinuria has recently been accepted by regulatory authorities as a reasonably likely surrogate end point for IgA nephropathy.[10] The design of ongoing phase 2 and 3 randomized controlled trials (RCTs) focuses on generating data over a 1- to 2-year period for proteinuria and rate of eGFR loss. After the inception of this approach, more than 15 phase 2 or 3 RCTs for new therapeutic approaches for IgA nephropathy are in progress in 2022.

Outstanding questions are first, the extent to which such short-term proteinuria and eGFR data predict the long-term rate of eGFR loss and risk of kidney failure in IgA nephropathy, and second, the degree of proteinuria reduction that would be associated with slowing eGFR decline so that kidney failure is not reached during a patient's lifetime. According to the Kidney Disease Improving Global Outcomes (KDIGO) 2021 Clinical Practice Guideline for the Management of Glomerular Diseases,[11] a reduction of proteinuria to <1 g/d is considered as a reasonable treatment target in patients with IgA nephropathy. However, long-term outcomes for patients with proteinuria <1 g/d need to be better understood.

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[5]University of Bristol & Bristol Royal Hospital for Children, Bristol, United Kingdom
[6]University of Edinburgh, Edinburgh, United Kingdom
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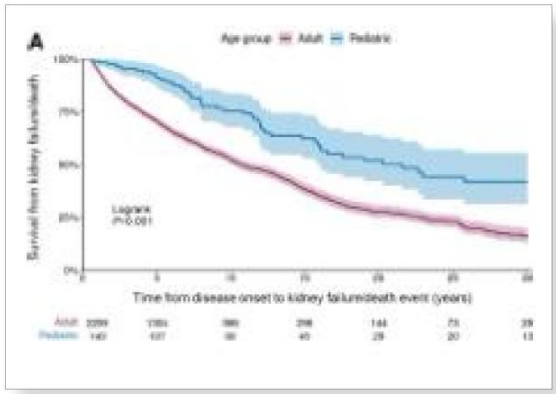
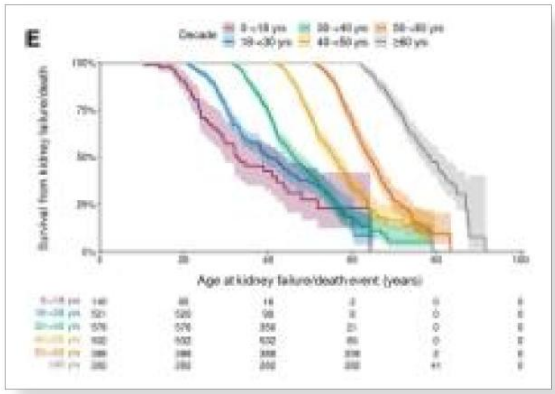

A
Age group
Adult
Pediatric
Survival from kidney failure/death
Log-rank
P<0.001
Time from disease onset to kidney failure/death event (years)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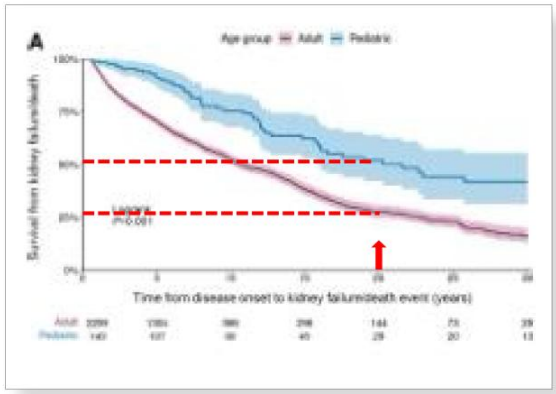
Survival from kidney failure/death
Age at kidney failure/death event (years)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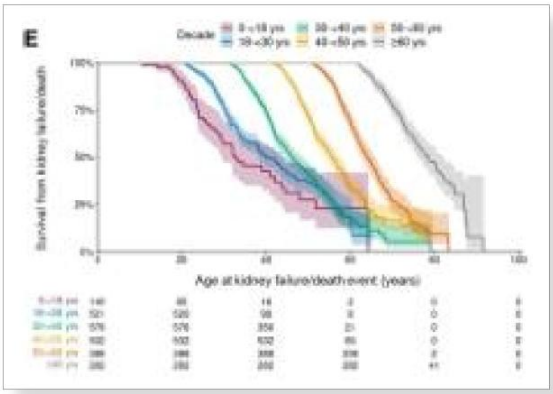
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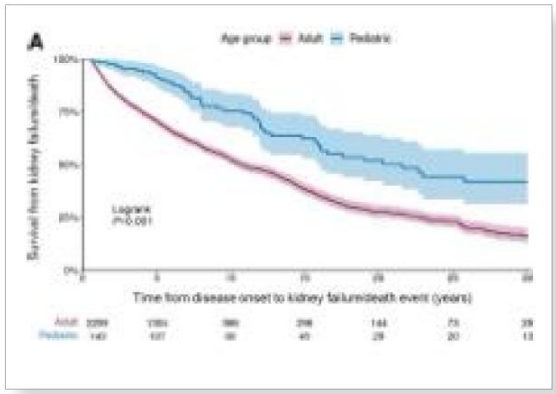
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Age group
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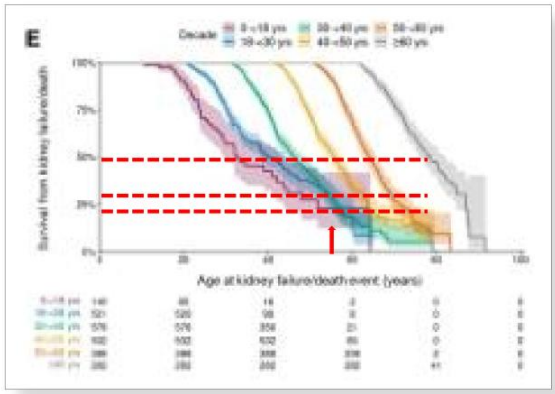

E
Decade
Survival from kidney failure/death
Age at kidney failure/death event (years)

Extent of proteinuria predicts how quickly you develop kidney failure

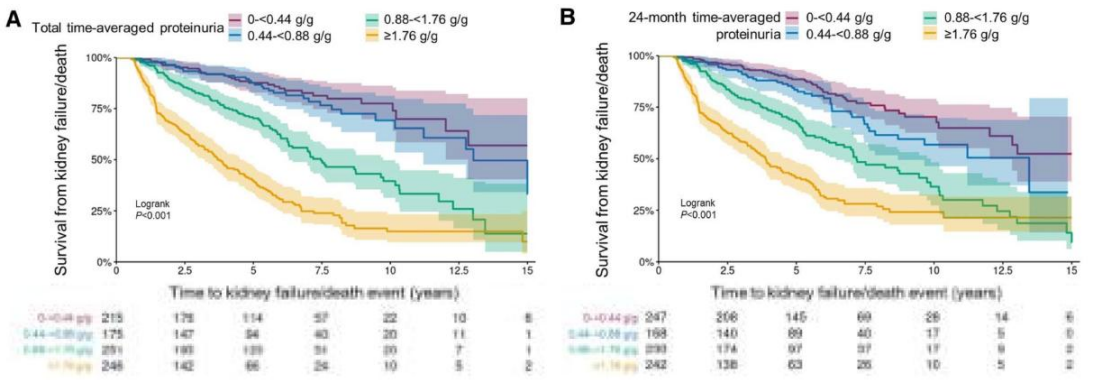
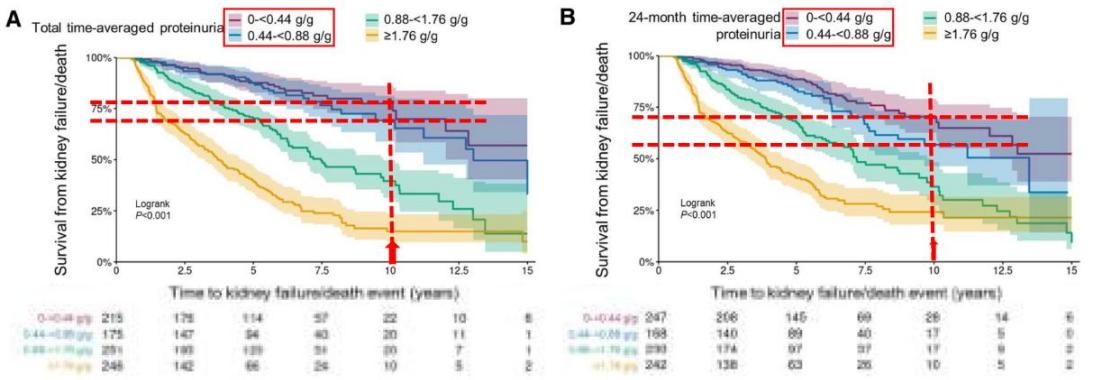


Figure 2. Kaplan–Meier survival curves of time to kidney failure/death event in population 1. (A) Using total follow-up time-averaged proteinuria. (B) Using 24-month time-averaged proteinuria. 0.44 g/g=50 mg/mmol; 0.88 g/g=100 mg/mmol; 1.76 g/g=200 mg/mmol.

Extent of proteinuria predicts how quickly you develop kidney failure



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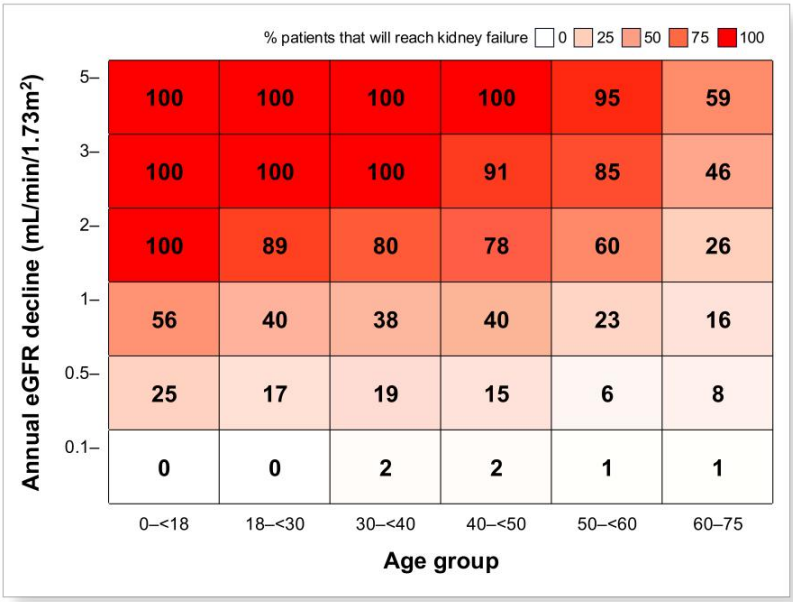
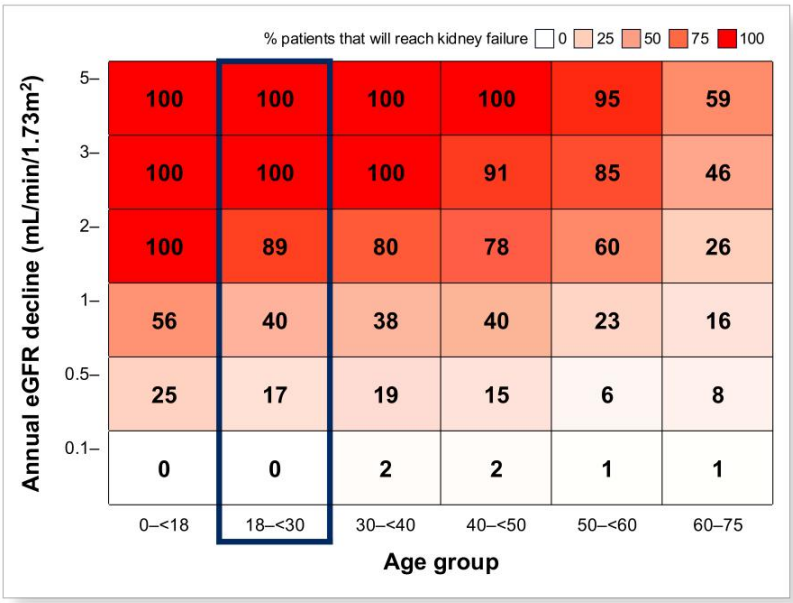
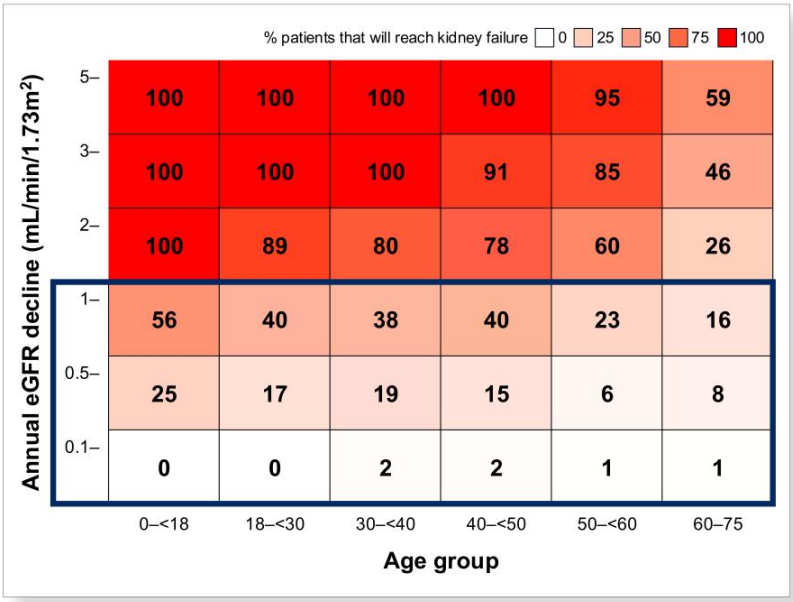
RaDaR
National Registry of Rare Kidney Diseases




% patients that will reach kidney failure 0 25 50 75 100
Annual eGFR decline (mL/min/1.73m²)
5– 100 100 100 100 95 59
3– 100 100 100 91 85 46
2– 100 89 80 78 60 26
1– 56 40 38 40 23 16
0.5– 25 17 19 15 6 8
0.1– 0 0 2 2 1 1
0–<18 18–<30 30–<40 40–<50 50–<60 60–75
Age group

RaDaR
National Registry of Rare Kidney Diseases



Original Article

Long-Term Outcomes in IgA Nephropathy

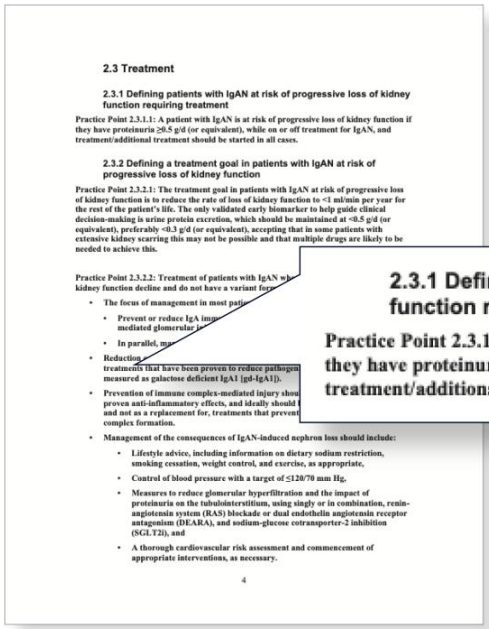
KI REPORTS

Three-Year Clinical Outcomes of the First South Asian Prospective Longitudinal Observational IgA Nephropathy Cohort

Long-term outcomes of IgA nephropathy in China

CKD progression, kidney failure, and mortality among US patients with IgA nephropathy

KDIGO



2.3 Treatment

2.3.1 Defining patients with IgAN at risk of progressive loss of kidney function requiring treatment

Practice Point 2.3.1.1: A patient with IgAN is at risk of progressive loss of kidney function if they have proteinuria ≥0.5 g/d (or equivalent), while on or off treatment for IgAN, and treatment/additional treatment should be started in all cases.

2.3.2 Defining a treatment goal in patients with IgAN at risk of progressive loss of kidney function

Practice Point 2.3.2.1: The treatment goal in patients with IgAN at risk of progressive loss of kidney function is to reduce the rate of loss of kidney function to <1 ml/min per year for the rest of the patient's life. The only validated early biomarker to help guide clinical decision-making is urine protein excretion, which should be maintained at <0.5 g/d (or equivalent), preferably <0.3 g/d (or equivalent), accepting that in some patients with extensive kidney scarring this may not be possible and that multiple drugs are likely to be needed to achieve this.

Practice Point 2.3.2.2: Treatment of patients with IgAN wh
kidney function decline and do not have a variant form

- The focus of management in most pati
  - Prevent or reduce IgA imm
  mediated glomerular i
  - In parallel, ma
- Reduction
treatments that have been proven to reduce pathogen
measured as galactose deficient IgA1 [gd-IgA1]).
- Prevention of immune complex-mediated injury shou
proven anti-inflammatory effects, and ideally should
and not as a replacement for, treatments that prevent
complex formation.
- Management of the consequences of IgAN-induced nephron loss should include:
  - Lifestyle advice, including information on dietary sodium restriction, smoking cessation, weight control, and exercise, as appropriate,
  - Control of blood pressure with a target of ≤120/70 mm Hg,
  - Measures to reduce glomerular hyperfiltration and the impact of proteinuria on the tubulointerstitium, using singly or in combination, renin-angiotensin system (RAS) blockade or dual endothelin angiotensin receptor antagonism (DEARA), and sodium-glucose cotransporter-2 inhibition (SGLT2i), and
  - A thorough cardiovascular risk assessment and commencement of appropriate interventions, as necessary.

4

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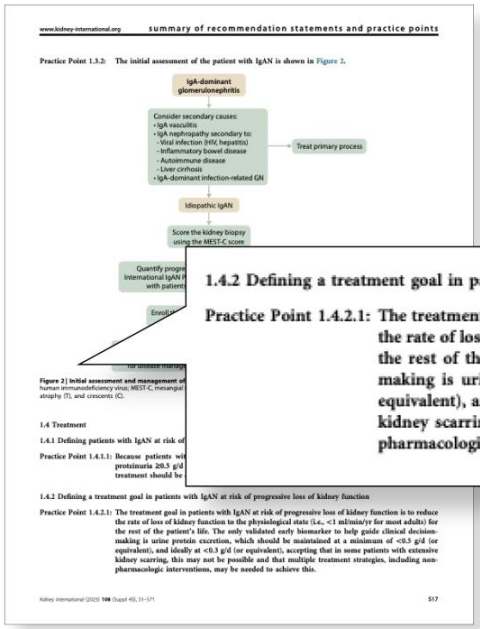
KDIGO



www.kidney-international.org summary of recommendation statements and practice points

Practice Point 1.3.2: The initial assessment of the patient with IgAN is shown in Figure 2.

Figure 2| Initial assessment and management of human immunodeficiency virus; MEST-C, mesangial atrophy (T), and crescents (C).

1.4 Treatment

1.4.1 Defining patients with IgAN at risk of

Practice Point 1.4.1.1: Because patients wit proteinuria 20.3 g/d treatment should be

1.4.2 Defining a treatment goal in patients with IgAN at risk of progressive loss of kidney function

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Kidney International (2021) 100 (Suppl 4S), S1–S171 S17

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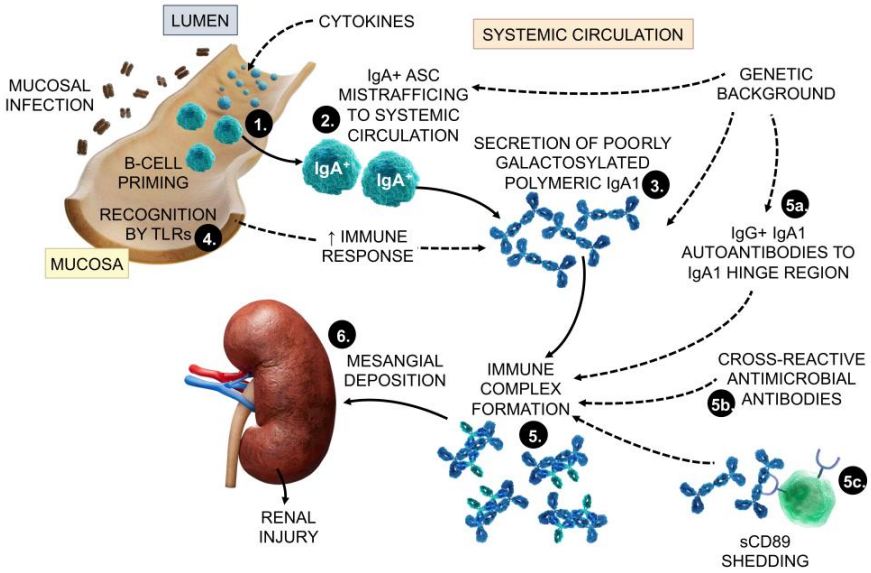
LUMEN
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1.
B-CELL PRIMING
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IgG+ IgA1 AUTOANTIBODIES TO IgA1 HINGE REGION
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CROSS-REACTIVE ANTIMICROBIAL ANTIBODIES 5b.
5c.
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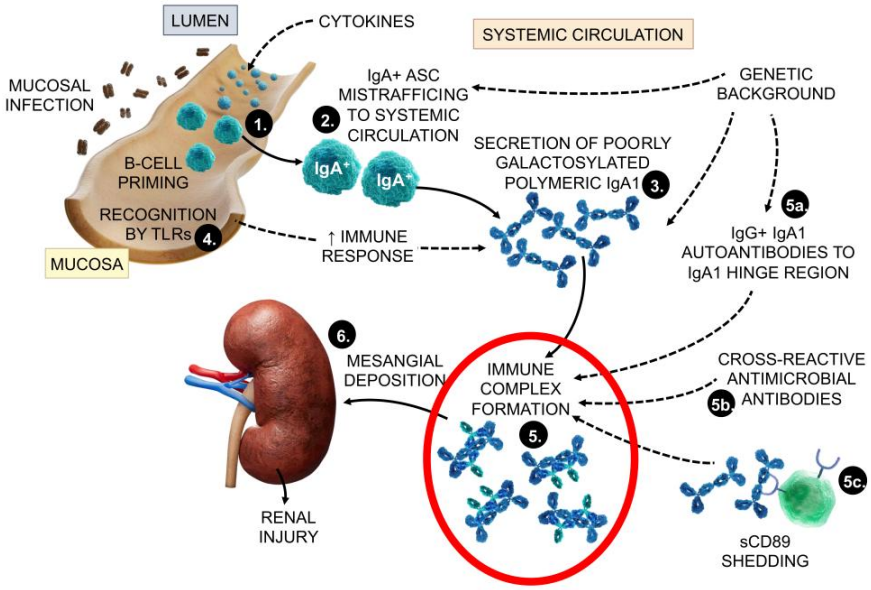
RENAL INJURY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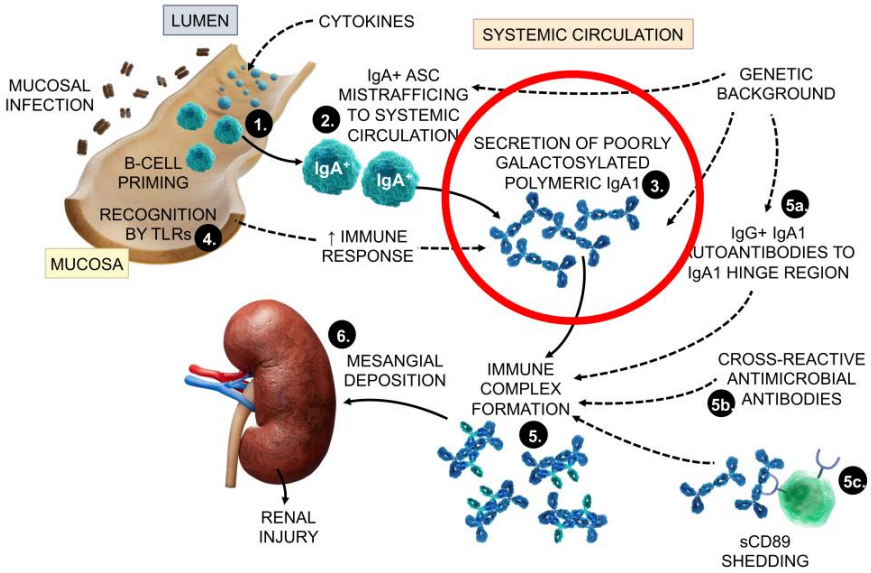
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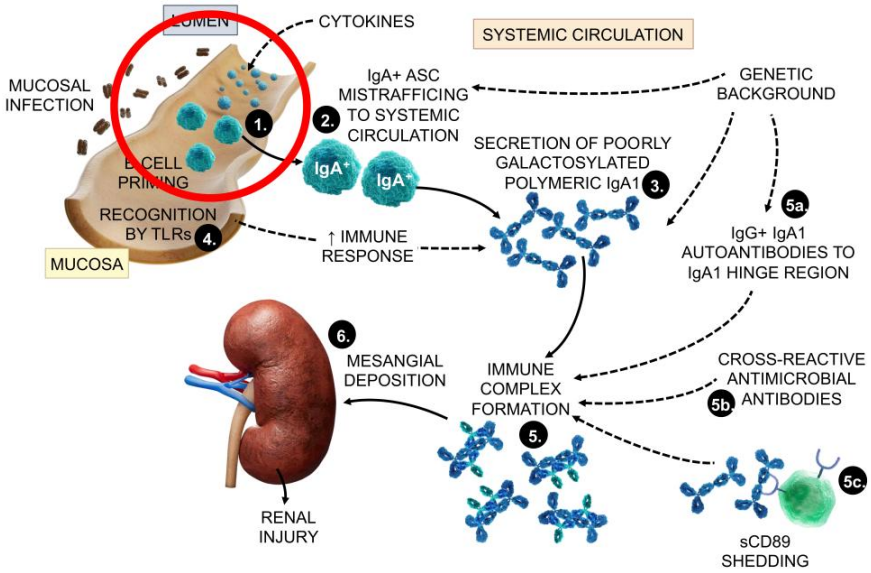
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sCD89 SHEDDING

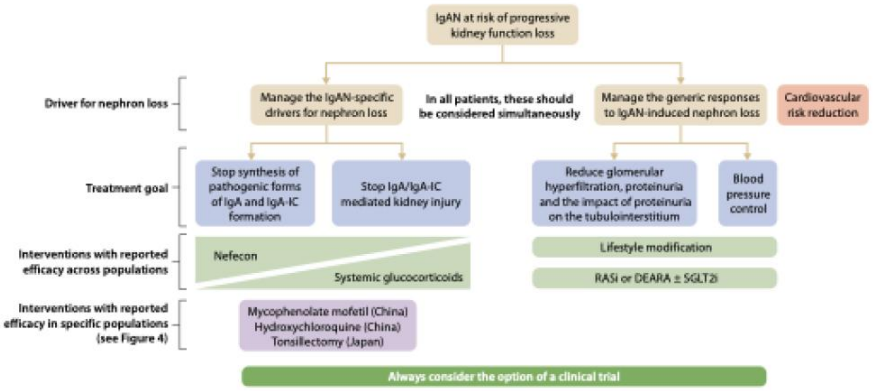
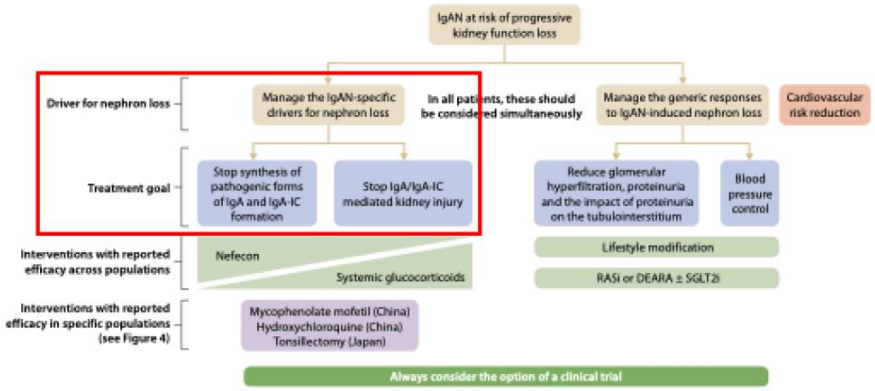


Figure 3 | Treatment targets in immunoglobulin A nephropathy (IgAN) and the positioning of drugs included in this guideline. Reflecting current understanding, Nefecon is shown as having a predominant effect on the production of pathogenic forms of IgA and IgA-containing immune complexes (IgA-ICs), with an undetermined direct effect of systemically absorbed budesonide on the kidneys. Systemic glucocorticoids have a well-documented anti-inflammatory effect within the kidneys and an undetermined direct effect on the production of pathogenic forms of IgA and IgA-ICs. Strategies to manage the generic response to IgAN-induced nephron loss may also include the use of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors in selected patients. DEARA, dual endothelin angiotensin receptor antagonist; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor.



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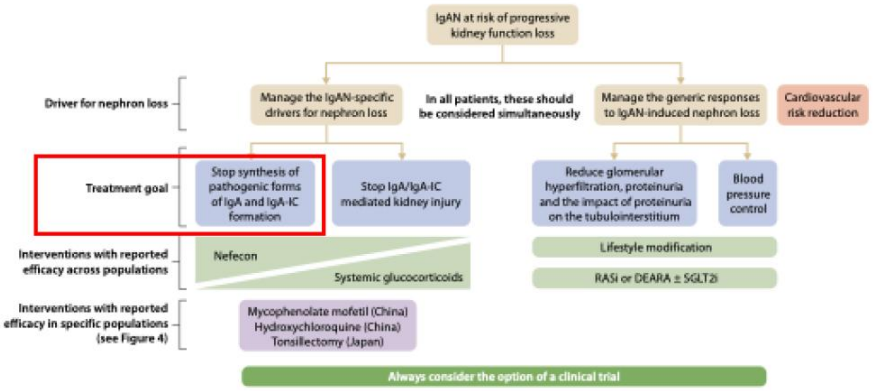

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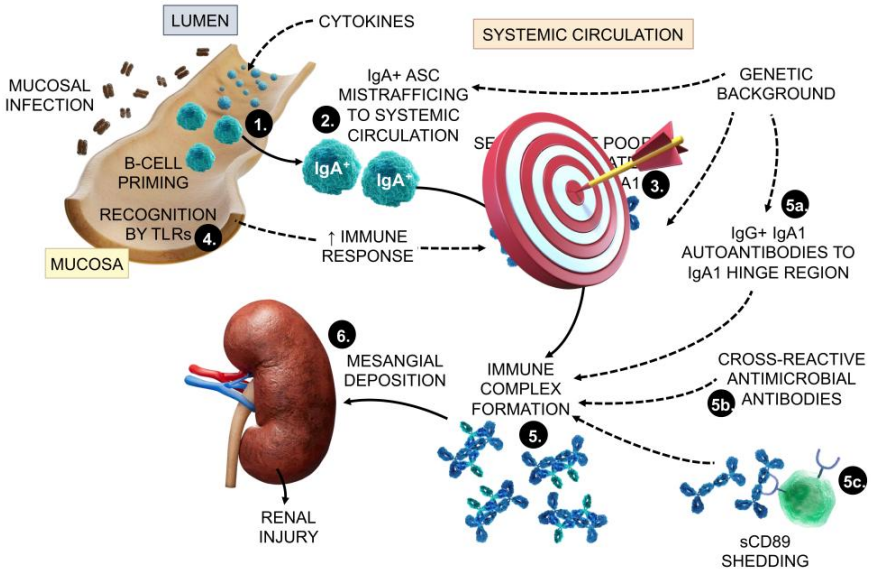
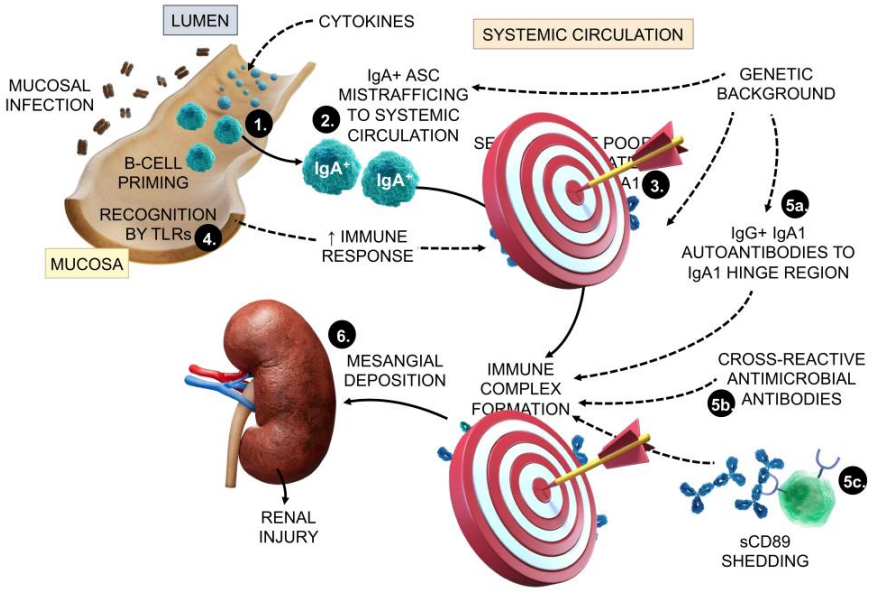

LUMEN
CYTOKINES
SYSTEMIC CIRCULATION
MUCOSAL INFECTION
IgA+ ASC MISTRAFFICING TO SYSTEMIC CIRCULATION
GENETIC BACKGROUND
1.
2.
B-CELL PRIMING
IgA+
IgA+
3.
RECOGNITION BY TLRs
4.
↑ IMMUNE RESPONSE
MUCOSA
5a.
IgG+ IgA1 AUTOANTIBODIES TO IgA1 HINGE REGION
6.
MESANGIAL DEPOSITION
IMMUNE COMPLEX FORMATION
5.
CROSS-REACTIVE ANTIMICROBIAL ANTIBODIES
5b.
5c.
RENAL INJURY
sCD89 SHEDDING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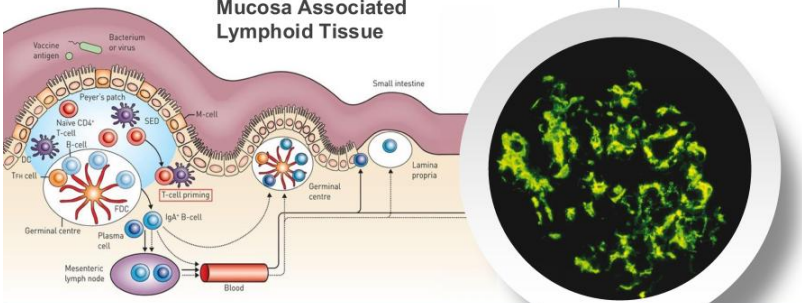
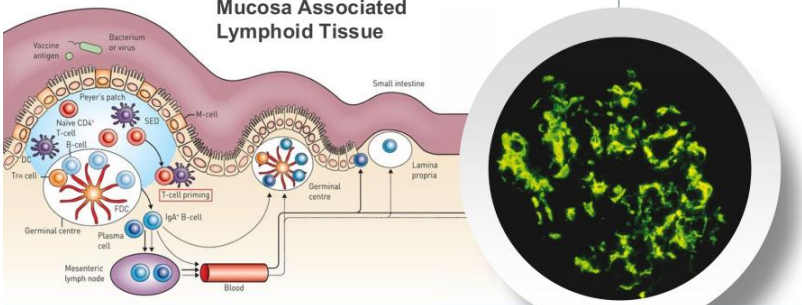
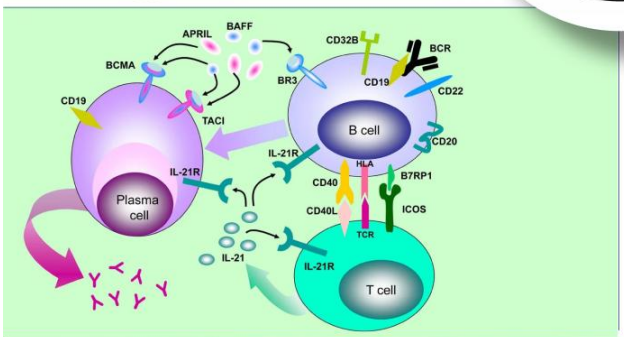
5c.
RENAL INJURY
sCD89 SHEDDING

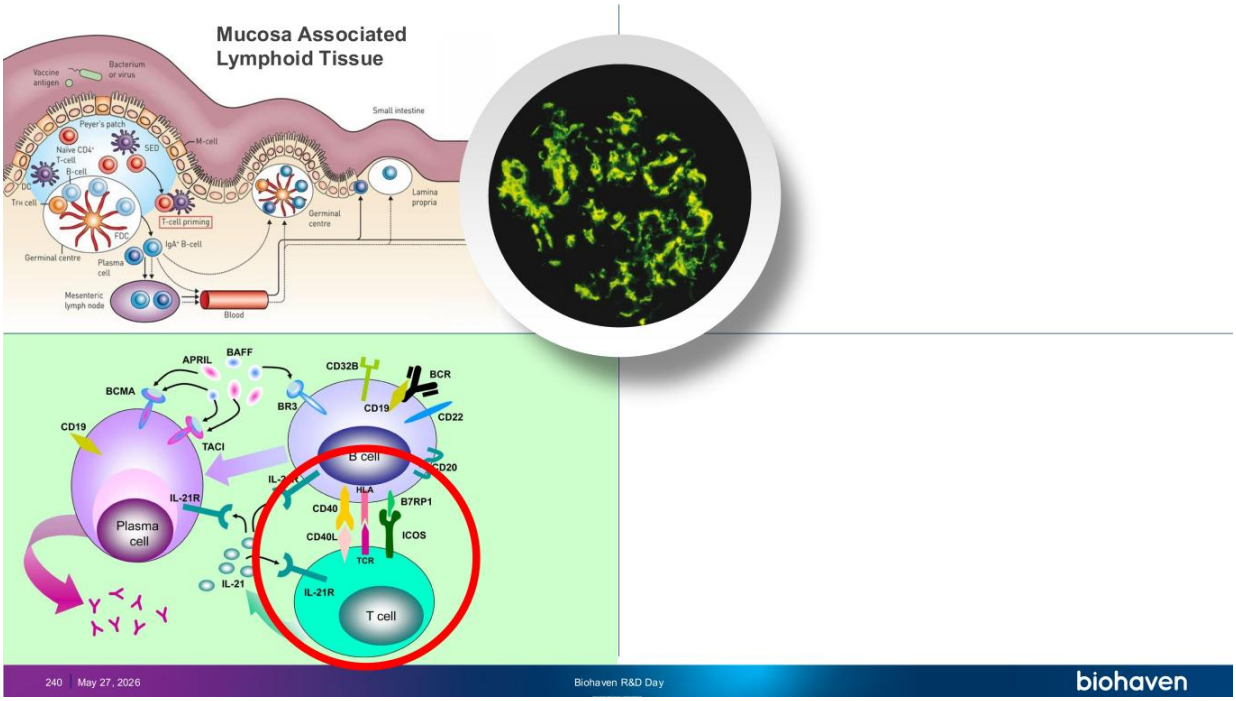
Mucosa Associated Lymphoid Tissue



Mucosa Associated Lymphoid Tissue

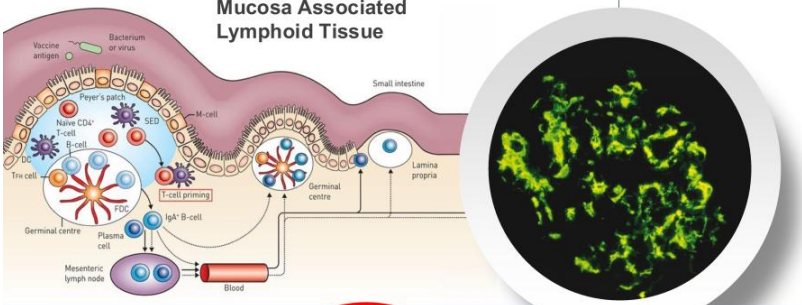


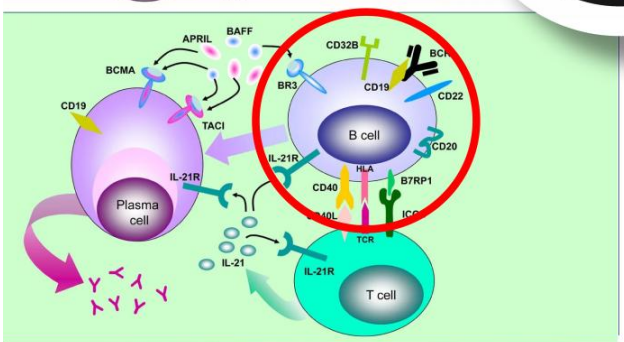



Mucosa Associated
Lymphoid Tissue
Vaccine antigen
Bacterium or virus
Small intestine
Peyer's patch
Naive CD4+ T-cell
B-cell
SED
M-cell
DC
Thy cell
T-cell priming
FDC
Germinal centre
Plasma cell
IgA+ B-cell
Germinal centre
Lamina propria
Mesenteric lymph node
Blood

APRIL
BAFF
BCMA
BR3
CD32B
BCR
CD19
CD22
TACI
B cell
CD20
IL-21R
HLA
B7RP1
CD40
CD40L
ICOS
TCR
Plasma cell
IL-21
IL-21R
T cell

Mucosa Associated Lymphoid Tissue





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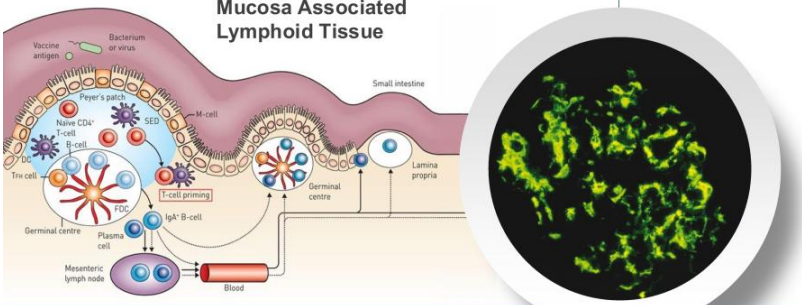

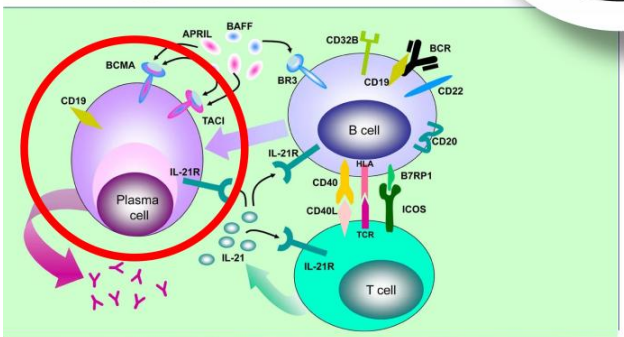

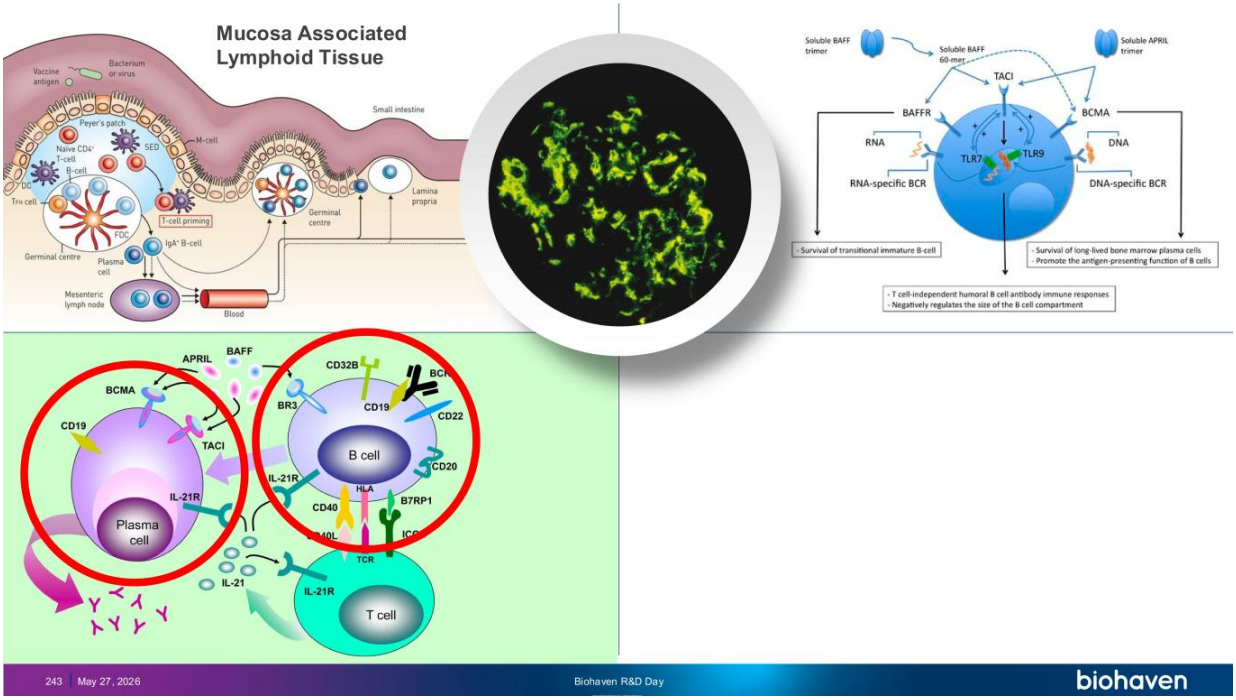
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Mesenteric lymph node
Blood
Small intestine
Germinal centre
Lamina propria
Soluble BAFF trimer
Soluble BAFF 60-mer
Soluble APRIL trimer
TACI
BAFFR
BCMA
RNA
DNA
TLR7
TLR9
RNA-specific BCR
DNA-specific BCR
- Survival of transitional immature B-cell
- Survival of long-lived bone marrow plasma cells
- Promote the antigen-presenting function of B cells
- T cell-independent humoral B cell antibody immune responses
- Negatively regulates the size of the B cell compartment
APRIL
BAFF
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CD22
B cell
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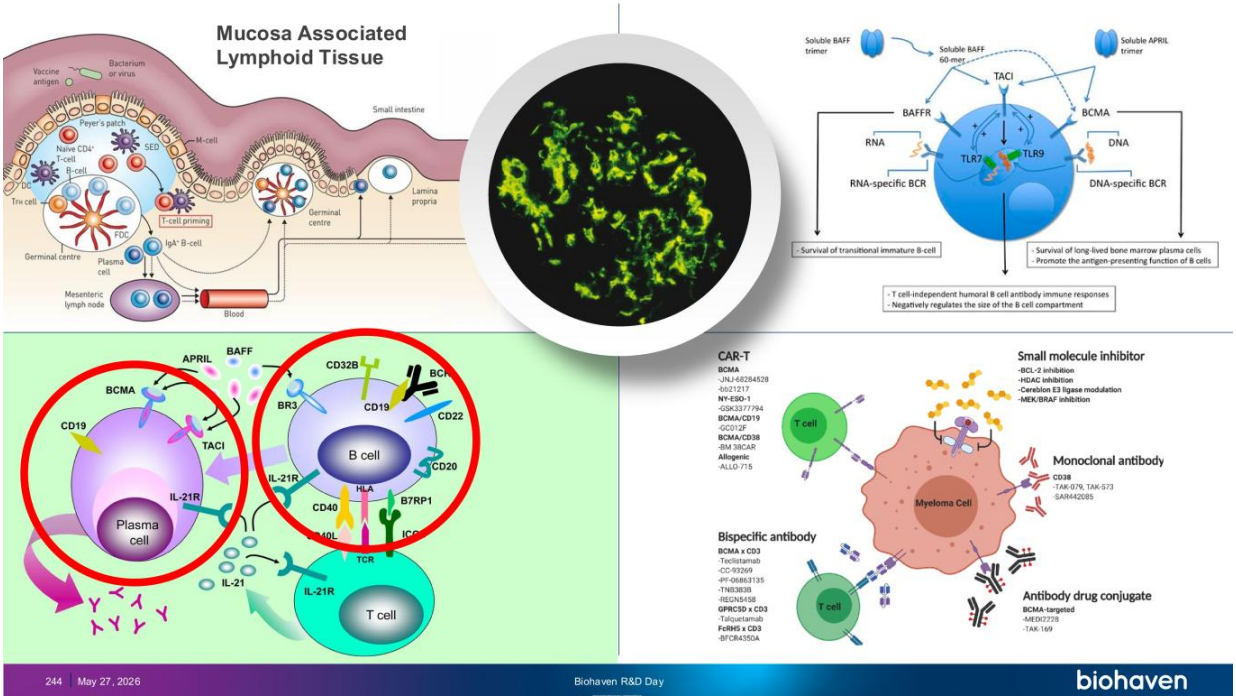
CD40
B7RP1
TCR
IL-21
IL-21R
T cell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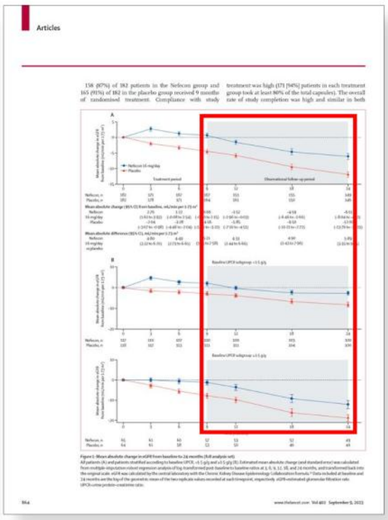
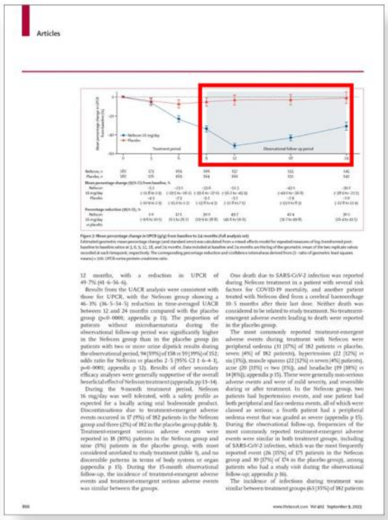
IL-21
IL-21R
T cell
CAR-T
BCMA
-JNJ-68284528
-bb21217
NY-ESO-1
-GSK3377794
BCMA/CD19
-GC012F
BCMA/CD38
-BM 38CAR
Allogenic
-ALLO-715
Small molecule inhibitor
-BCL-2 inhibition
-HDAC inhibition
-Cereblon E3 ligase modulation
-MEK/BRAF inhibition
T cell
Myeloma Cell
Monoclonal antibody
CD38
-TAK-079, TAK-573
-SAR442085
Bispecific antibody
BCMA x CD3
-Teclistamab
-CC-93269
-PF-06863135
-TNB383B
-REGN5458
GPRC5D x CD3
-Talquetamab
FcRH5 x CD3
-BFCR4350A
T cell
Antibody drug conjugate
BCMA-targeted
-MEDI2228
-TAK-169

KEY POINT

In all immune modulating therapies approved or in development, disease recurs upon cessation of therapy


Articles
Efficacy and safety of a targeted-release formulation of budesonide in patients with primary IgA nephropathy (NefIgArd): 2-year results from a randomised phase 3 trial
Summary
Introduction


Articles


Articles

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology

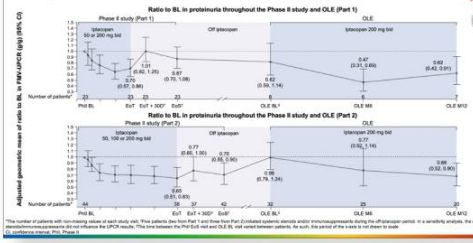
in collaboration with
Österreichische Gesellschaft für Nephrologie

Effect of iptacopan discontinuation on proteinuria and complement biomarkers in patients with immunoglobulin A nephropathy (IgAN): a *post hoc* analysis from a Phase II trial

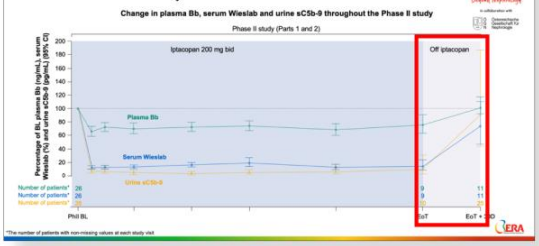
Jonathan Barratt,[1,2] Dana V. Rizk,[3] Hong Zhang,[4] Bart Maes,[5] Naoki Kashihara,[6] Brad Rovin,[7] Hernán Trimarchi,[8] Dmitrij Kollins,[9] Manasi Desai,[9] Olympia Papachristofi,[9] Evanthia Koukouli,[9] Vlado Perkovic[10]

[1]*The Mayer IgA Nephropathy Laboratories, University of Leicester, Leicester, UK;* [2]*The John Walls Renal Unit, Leicester General Hospital, Leicester, UK;* [3]*University of Alabama at Birmingham, Birmingham, AL, USA;* [4]*Peking University First Hospital, Beijing, China;* [5]*AZ Delta, Roeselare, Belgium;* [6]*Kawasaki Medical School, Okayama, Japan;* [7]*The Ohio State University Wexner Medical Center, Columbus, OH, USA;* [8]*Hospital Británico de Buenos Aires, Buenos Aires, Argentina;* [9]*Novartis Pharma AG, Basel, Switzerland;* [10]*University of New South Wales, Sydney, NSW, Australia*

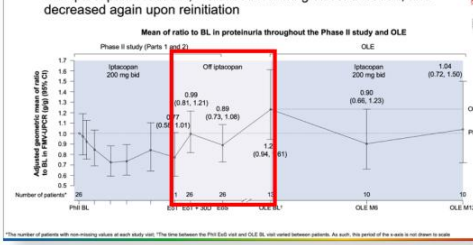
Proteinuria increased after iptacopan discontinuation, and decreased upon its reinitiation to a similar extent as during initial treatment

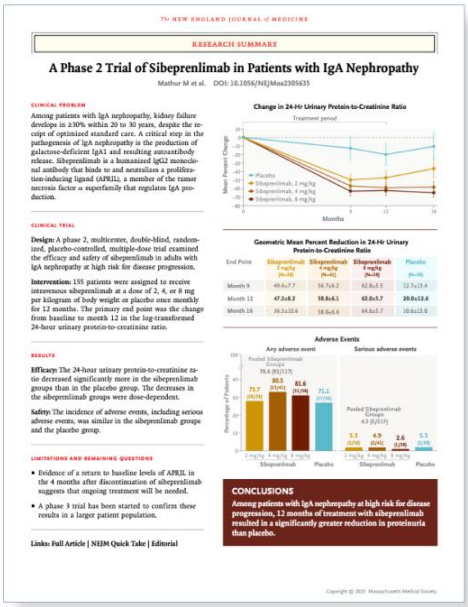


When iptacopan 200 mg bid was discontinued, there was an increase in AP biomarker activity



In the pooled iptacopan 200 mg bid arms, proteinuria decreased with iptacopan treatment, increased following discontinuation, and decreased again upon reinitiation





The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

A Phase 2 Trial of Sibeprenlimab in Patients with IgA Nephropathy

Mathur M et al. DOI: 10.1056/NEJMoa2305635

CLINICAL PROBLEM

Among patients with IgA nephropathy, kidney failure develops in ≥30% within 20 to 30 years, despite the receipt of optimized standard care. A critical step in the pathogenesis of IgA nephropathy is the production of galactose-deficient IgA1 and resulting autoantibody release. Sibeprenlimab is a humanized IgG2 monoclonal antibody that binds to and neutralizes a proliferation-inducing ligand (APRIL), a member of the tumor necrosis factor α superfamily that regulates IgA production.

CLINICAL TRIAL

Design: A phase 2, multicenter, double-blind, randomized, placebo-controlled, multiple-dose trial examined the efficacy and safety of sibeprenlimab in adults with IgA nephropathy at high risk for disease progression.

Intervention: 155 patients were assigned to receive intravenous sibeprenlimab at a dose of 2, 4, or 8 mg per kilogram of body weight or placebo once monthly for 12 months. The primary end point was the change from baseline to month 12 in the log-transformed 24-hour urinary protein-to-creatinine ratio.

RESULTS

Efficacy: The 24-hour urinary protein-to-creatinine ratio decreased significantly more in the sibeprenlimab groups than in the placebo group. The decreases in the sibeprenlimab groups were dose-dependent.

Safety: The incidence of adverse events, including serious adverse events, was similar in the sibeprenlimab groups and the placebo group.

LIMITATIONS AND REMAINING QUESTIONS

- Evidence of a return to baseline levels of APRIL in the 4 months after discontinuation of sibeprenlimab suggests that ongoing treatment will be needed.
- A phase 3 trial has been started to confirm these results in a larger patient population.

Links: Full Article | NEJM Quick Take | Editorial

Change in 24-Hr Urinary Protein-to-Creatinine Ratio

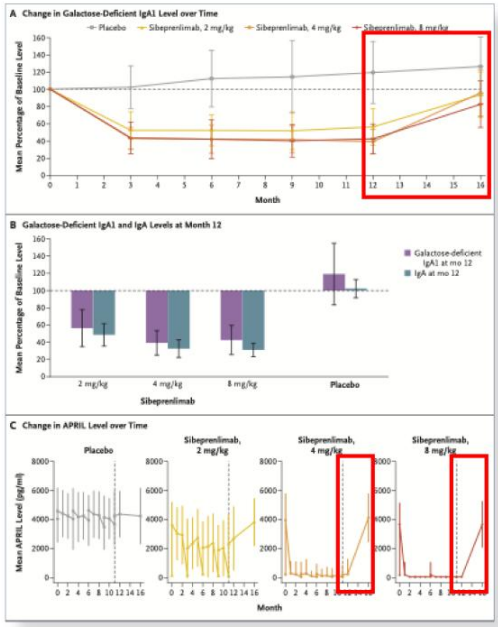
Geometric Mean Percent Reduction in 24-Hr Urinary Protein-to-Creatinine Ratio

End Point	Sibeprenlimab 2 mg/kg (N=39)	Sibeprenlimab 4 mg/kg (N=41)	Sibeprenlimab 8 mg/kg (N=18)	Placebo (N=18)
Month 9	49.6±7.7	56.7±6.2	62.8±3.5	12.7±15.4
Month 12	**47.2±8.1**	**58.8±6.1**	**62.0±5.7**	**20.0±12.6**
Month 16	36.1±12.6	58.8±6.6	64.6±5.7	10.6±13.9

Adverse Events

CONCLUSIONS

Among patients with IgA nephropathy at high risk for disease progression, 12 months of treatment with sibeprenlimab resulted in a significantly greater reduction in proteinuria than placebo.



Clinical Research

OPEN

Long-Term Results from an Open-Label Extension Study of Atacicept for the Treatment of IgA Nephropathy

Jonathan Barratt,[1] Sean J. Barbour,[2] Robert M. Brenner,[3] Kerry Cooper,[3] Xuelian Wei,[3] Necmi Eren,[4] Jürgen Floege,[5] Vivekanand Jha,[6,7,8] Sung Gyun Kim,[9] Bart Maes,[10] Richard K.S. Phoon,[11,12] Harmeet Singh,[13] Vladimír Tesař,[14] and Richard Lafayette,[15] on behalf of the ORIGIN Phase 2b Investigators*

Key Points

- Participants who completed a 36-week double-blind study of atacicept were eligible for a 60-week, open-label extension study.
- Atacicept 96-week treatment resulted in sustained reductions in galactose-deficient IgA1, hematuria, and urine protein-creatinine ratio.
- The slope of the eGFR was similar to that observed in the general population without kidney disease.

Abstract

Background B-cell activating factor (BAFF) and A proliferation-inducing ligand (APRIL) play key roles in the pathogenesis of IgA nephropathy. Atacicept is a novel fully humanized fusion protein, self-administered at home by subcutaneous injection, that binds and inhibits BAFF and APRIL. By inhibiting BAFF and APRIL, atacicept targets the underlying B-cell–mediated pathogenesis driving disease progression. This study evaluated the long-term efficacy and safety of atacicept in patients with IgA nephropathy over 96 weeks.

Methods Participants with IgA nephropathy who received atacicept (25, 75, or 150 mg) or placebo in a 36-week phase 2b, randomized, blinded trial were enrolled in an open-label extension study and received atacicept 150 mg for an additional 60 weeks. Key efficacy outcomes were changes in galactose-deficient IgA1 (Gd-IgA1), percentage of participants with hematuria, urine protein-creatinine ratio (UPCR), and eGFR over 96 weeks. Long-term safety data were also evaluated.

Results There were 113 participants (67 [59%] male; 46 [41%] female) who ranged in age from 18 to 67 years who received ≥1 atacicept dose. Over 96 weeks, safety data demonstrated that atacicept was generally well tolerated. There were also sustained reductions (mean±SEM) in Gd-IgA1 (−66%±2%), percentage of participants with hematuria (−75%; 95% confidence intervals, −87 to −59; in participants with baseline hematuria), and UPCR (−52%±5%). The mean annualized slope of eGFR was −0.6±0.5 ml/min per 1.73 m^2 through 96 weeks.

Conclusions Atacicept was well tolerated over the duration of the study. Atacicept treatment reduced Gd-IgA1, hematuria, and UPCR with stabilization of eGFR through 96 weeks.

Clinical Trial registry name and registration number: Atacicept in Subjects with IgA Nephropathy (ORIGIN 2), NCT04716231.

JASN 00: 1–9, 2024. doi: https://doi.org/10.1681/ASN.0000000541

Introduction

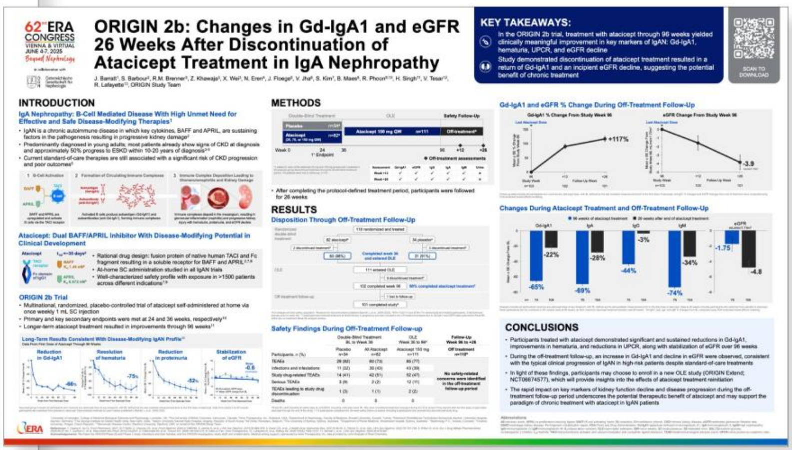
IgA nephropathy, predominantly diagnosed in young adults, represents a critical challenge in nephrology because of its progressive nature and significant effect on life expectancy and quality.[1–3] At least 50% of patients with IgA nephropathy develop kidney failure within 10–20 years of initial diagnosis.[4–6] Although currently available therapies provide benefit, they fail to stop an unrelenting decline in kidney function.[7–9] Unless the rate of eGFR decline can be minimized, most patients are likely to experience kidney

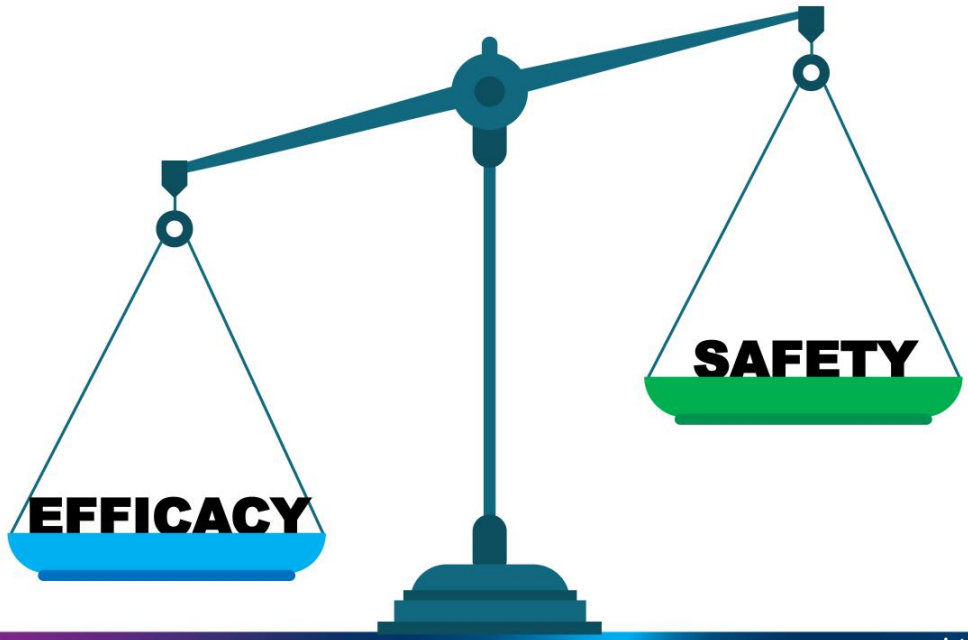
Due to the number of contributing authors, the affiliations are listed at the end of this article.

Correspondence: Dr. Richard Lafayette, email: czar@stanford.edu

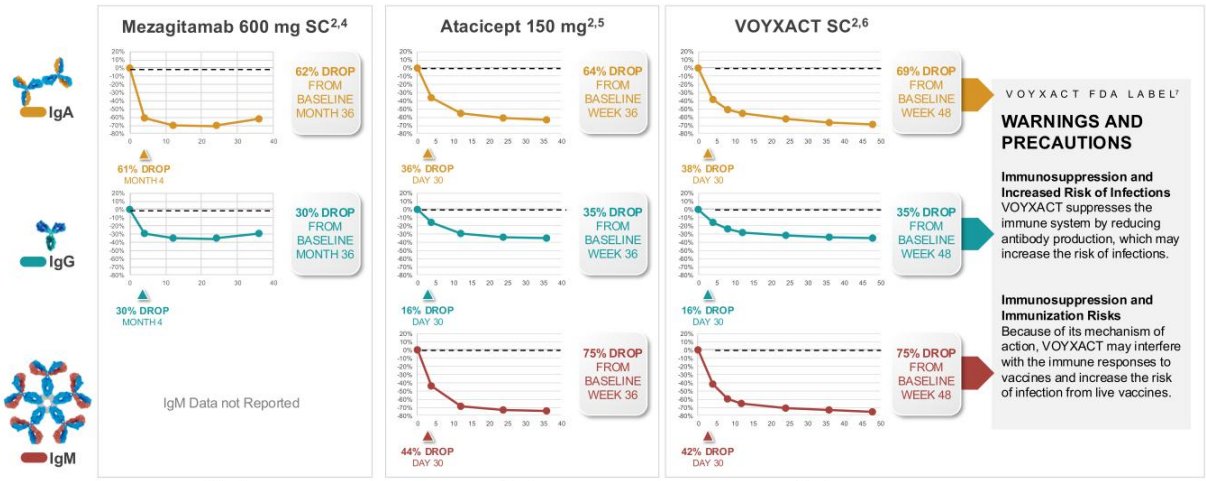
Received: September 13, 2024 **Accepted:** October 9, 2024
Published Online Ahead of Print: October 26, 2024

*A list of investigators and collaborators for the ORIGIN phase 2b study is provided in the Supplemental Material.


62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
ORIGIN 2b: Changes in Gd-IgA1 and eGFR 26 Weeks After Discontinuation of Atacicept Treatment in IgA Nephropathy
KEY TAKEAWAYS:
In the ORIGIN 2b trial, treatment with atacicept through 96 weeks yielded clinically meaningful improvement in key markers of IgAN: Gd-IgA1, hematuria, UPCR, and eGFR decline
Study demonstrated discontinuation of atacicept treatment resulted in a return of Gd-IgA1 and an incipient eGFR decline, suggesting the potential benefit of chronic treatment
SCAN TO DOWNLOAD
INTRODUCTION
IgA Nephropathy: B-Cell Mediated Disease With High Unmet Need for Effective and Safe Disease-Modifying Therapies
Atacicept: Dual BAFF/APRIL Inhibitor With Disease-Modifying Potential in Clinical Development
ORIGIN 2b Trial
METHODS
After completing the protocol-defined treatment period, participants were followed for 26 weeks
RESULTS
Disposition Through Off-Treatment Follow-Up
Safety Findings During Off-Treatment Follow-up
Gd-IgA1 and eGFR % Change During Off-Treatment Follow-Up
+117%
-3.9
Changes During Atacicept Treatment and Off-Treatment Follow-Up
Gd-IgA1
IgA
IgG
IgM
eGFR
-65%
-22%
-69%
-28%
-44%
-3%
-74%
-34%
-1.75
-4.8
CONCLUSIONS
Participants treated with atacicept demonstrated significant and sustained reductions in Gd-IgA1, improvements in hematuria, and reductions in UPCR, along with stabilization of eGFR over 96 weeks
During the off-treatment follow-up, an increase in Gd-IgA1 and decline in eGFR were observed, consistent with the typical clinical progression of IgAN in high-risk patients despite standard-of-care treatments
In light of these findings, participants may choose to enroll in a new OLE study (ORIGIN Extend; NCT06674577), which will provide insights into the effects of atacicept treatment reinitiation
The rapid impact on key markers of kidney function decline and disease progression during the off-treatment follow-up period underscores the potential therapeutic benefit of atacicept and may support the paradigm of chronic treatment with atacicept in IgAN patients


SAFETY
EFFICACY

Competitors Show Long-Term Immunosuppression[1,2]



VOYXACT FDA LABEL[7]

WARNINGS AND PRECAUTIONS

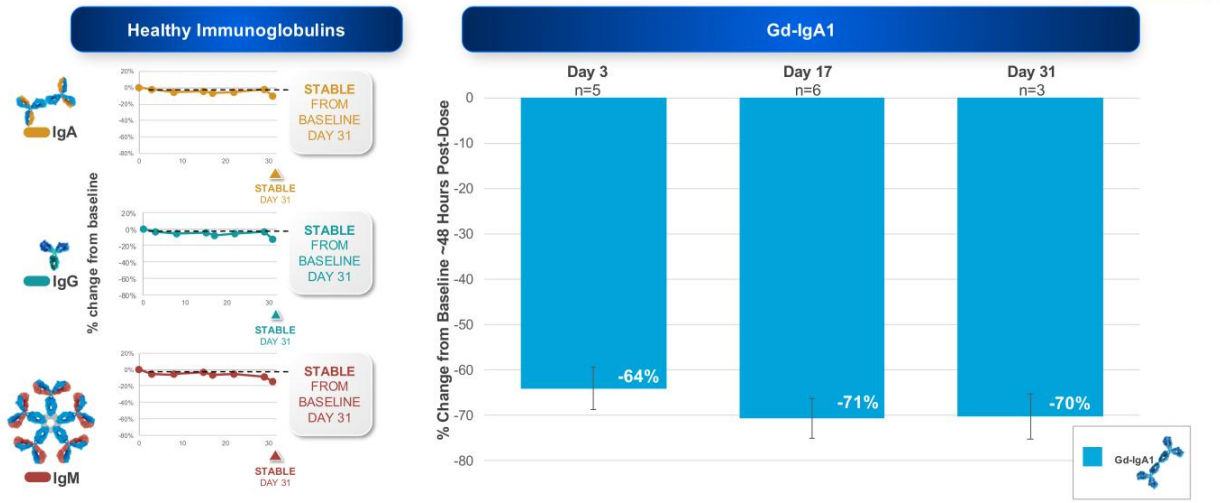
Immunosuppression and Increased Risk of Infections
VOYXACT suppresses the immune system by reducing antibody production, which may increase the risk of infections.

Immunosuppression and Immunization Risks
Because of its mechanism of action, VOYXACT may interfere with the immune responses to vaccines and increase the risk of infection from live vaccines.

1. Competitors did not report IgE. 2. All competitor data presented herein are derived from publicly available sources only. Certain data points have been reconstructed or estimated from published graphical information. No confidential, non-public, or proprietary information was used. This analysis has not been reviewed or validated by the referenced companies. 3. Solid dots represent the mean of the maximal total IgG % change from baseline 4. Barratt. American Society of Nephrology Kidney Week 2025. Poster FRPO0808. 5. Lafayette. Kidney International. 2024 6. Lafayette. NEJM. 2025. 7. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761434s000lbl.pdf

BHV-1400 500 mg SC Bi-Monthly Deeply and Selectively Removes Gd-IgA1 Without Suppression of Normal Healthy IgA in Patients With IgAN

DEGRADERS



Preliminary data from ongoing study. Data represents mean % change in immunoglobulins in patients with IgAN administered one month of BHV-1400 500 mg every two weeks. Error bars represent standard error.

KDIGO

Practice Point 1.4.2.2: Treatment of patients with IgAN who are at risk of progressive loss of kidney function and do not have a variant form (Section 1.5) of primary IgAN (Figure 3):

- The focus of management in most patients should be to *simultaneously*:
  - Prevent or reduce immunoglobulin A–containing immune complex (IgA-IC) formation and IgA-IC–mediated glomerular injury (whether this requires lifelong or intermittent therapy is currently unknown)
  - Manage the consequences of existing IgAN-induced nephron loss (likely lifelong)
- Reduction or prevention of IgA-IC formation should incorporate treatments that have been proven to reduce pathogenic forms of IgA (commonly measured as galactose-deficient IgA1 [gd-IgA1]).
- Prevention of IgA-IC–mediated injury should incorporate treatments with proven anti-inflammatory and/or antifibrotic effects and ideally should be used in combination with, and not as a replacement for, treatments that prevent or reduce IgA-IC formation.
- Management of the consequences of IgAN-induced nephron loss should include:
  - Lifestyle advice, including information on dietary sodium restriction (<2 g/d), smoking and vaping cessation, weight control, and endurance exercise, as appropriate
  - Control of blood pressure with a target of ≤120/70 mm Hg
  - Measures to reduce glomerular hyperfiltration and the impact of proteinuria on the tubulointerstitium, using renin-angiotensin system (RAS) blockade or dual endothelin angiotensin receptor antagonism, ... hibitor (SGLT2i)
  - A thorough cardiovasc... as per local guidelines...
- Enrollment in a clini... increase in the... from the... dard...

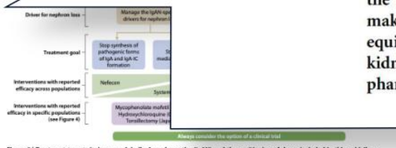
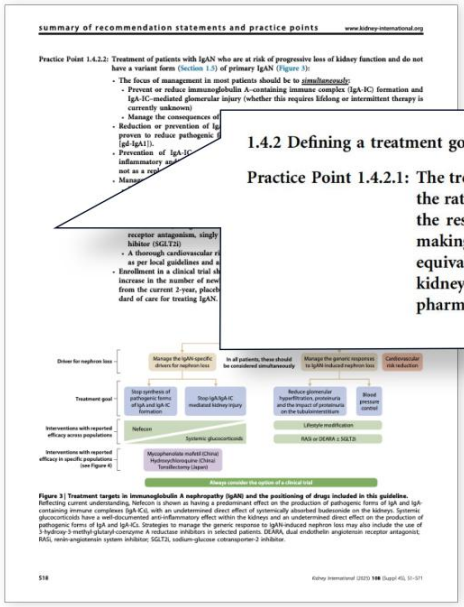


Figure 3 | Treatment targets in immunoglobulin A nephropathy (IgAN) and the positioning of drugs included in this guideline. Reflecting current understanding, Nefecon is shown as having a predominant effect on the production of pathogenic forms of IgA and IgA-containing immune complexes (IgA-ICs), with an undetermined direct effect of systemically absorbed budesonide on the kidneys. Systemic glucocorticoids have a well-documented anti-inflammatory effect within the kidneys and an undetermined direct effect on the production of pathogenic forms of IgA and IgA-ICs. Strategies to manage the generic response to IgAN-induced nephron loss may also include the use of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors in selected patients. DEARA, dual endothelin angiotensin receptor antagonist; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

1.4.2 Defining a treatment goal in patients with IgAN at risk of progressive loss of kidney function

Practice Point 1.4.2.1: The treatment goal in patients with IgAN at risk of progressive loss of kidney function is to reduce the rate of loss of kidney function to the physiological state (i.e., <1 ml/min/yr for most adults) for the rest of the patient's life. The only validated early biomarker to help guide clinical decision-making is urine protein excretion, which should be maintained at a minimum of <0.5 g/d (or equivalent), and ideally at <0.3 g/d (or equivalent), accepting that in some patients with extensive kidney scarring, this may not be possible and that multiple treatment strategies, including non-pharmacologic interventions, may be needed to achieve this.

KDIGO


summary of recommendation statements and practice points www.kidney-international.org

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- Reduction or prevention of
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inhibitor (SGLT2i)
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- Enrollment in a clinical trial
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from the current 2-year, placeb
dard of care for treating IgAN.

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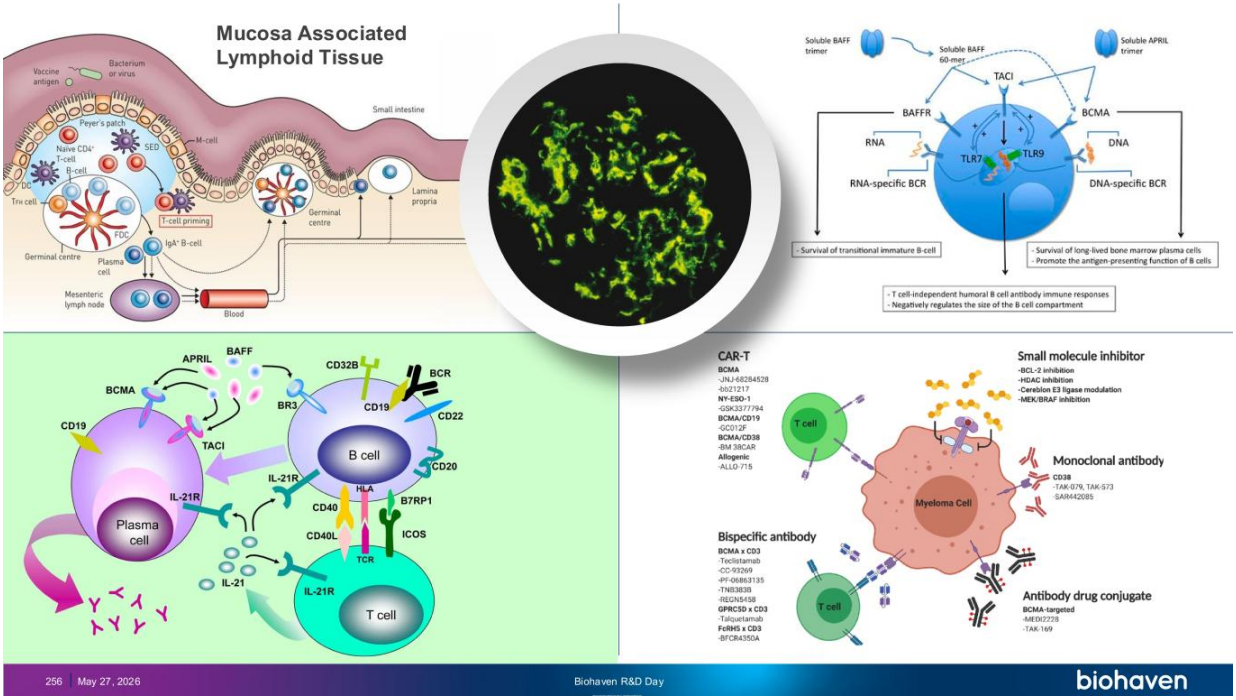
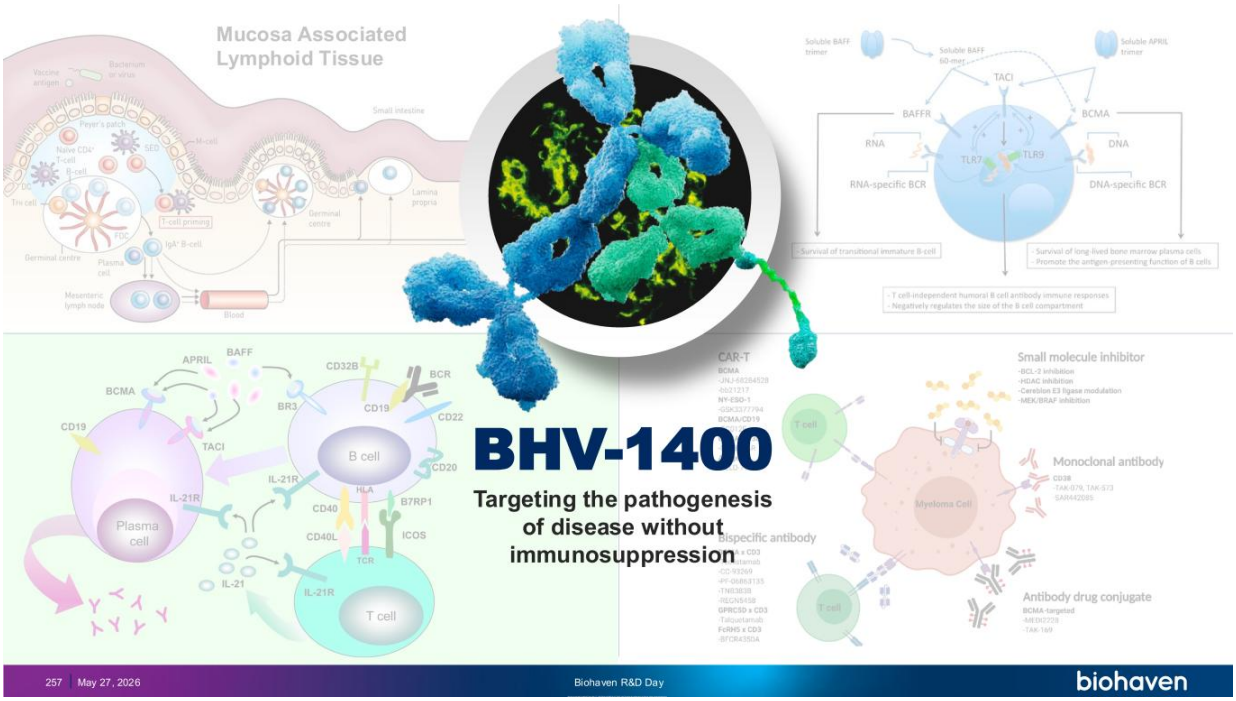
In few patients, competitors achieve guideline proteinuria threshold goal

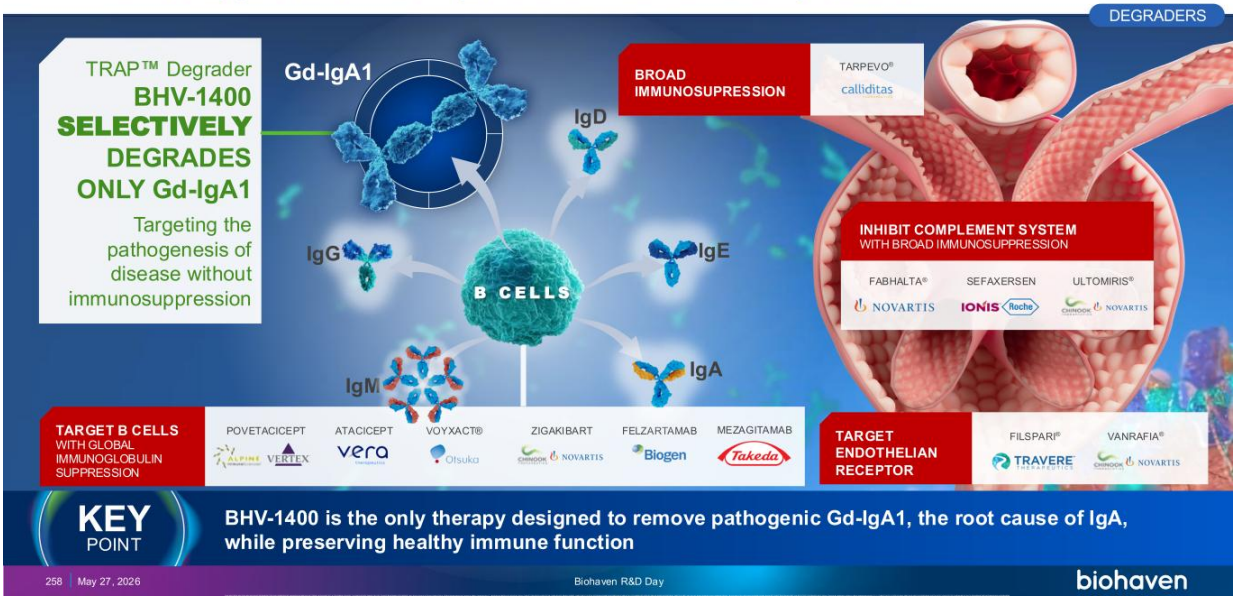
VOYXACT®[1]	FILSPARI®[2]
Sibeprenlimab	Sparsentan
By month 12, 34.3%	By month 9, 11%
vs 12.7% placebo	<0.3 g/d
<0.5 g/d	


UNMET
NEED

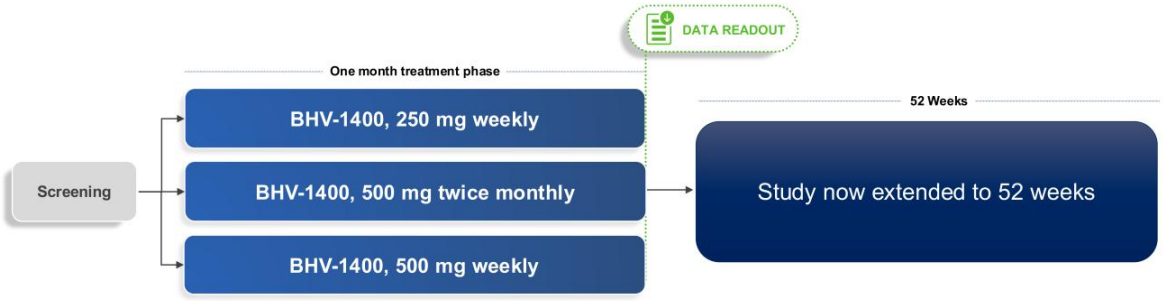

Mucosa Associated Lymphoid Tissue
Vaccine antigen
Bacterium or virus
Small intestine
Peyer's patch
Naive CD4+ T-cell
SED
M-cell
B-cell
DC
Tfh cell
T-cell priming
FDC
Germinal centre
Plasma cell
IgA+ B-cell
Germinal centre
Lamina propria
Mesenteric lymph node
Blood
Soluble BAFF trimer
Soluble BAFF 60-mer
Soluble APRIL trimer
TACI
BAFFR
BCMA
RNA
DNA
TLR7
TLR9
RNA-specific BCR
DNA-specific BCR
- Survival of transitional immature B-cell
- Survival of long-lived bone marrow plasma cells
- Promote the antigen-presenting function of B cells
- T cell-independent humoral B cell antibody immune responses
- Negatively regulates the size of the B cell compartment
APRIL
BAFF
BCMA
CD32B
BCR
BR3
CD19
CD22
CD19
TACI
B cell
CD20
IL-21R
HLA
IL-21R
CD40
B7RP1
Plasma cell
CD40L
ICOS
TCR
IL-21
IL-21R
T cell
CAR-T
BCMA
-JNJ-68284528
-bb21217
NY-ESO-1
-GSK3377794
BCMA/CD19
-GC012F
BCMA/CD38
-BM 38CAR
Allogenic
-ALLO-715
Small molecule inhibitor
-BCL-2 inhibition
-HDAC inhibition
-Cereblon E3 ligase modulation
-MEK/BRAF inhibition
T cell
Myeloma Cell
Monoclonal antibody
CD38
-TAK-079, TAK-573
-SAR442085
Bispecific antibody
BCMA x CD3
-Teclistamab
-CC-93269
-PF-06863135
-TNB383B
-REGN5458
GPRC5D x CD3
-Talquetamab
FcRH5 x CD3
-BFCR4350A
T cell
Antibody drug conjugate
BCMA-targeted
-MEDI2228
-TAK-169
256 | May 27, 2026
Biohaven R&D Day
biohaven


Mucosa Associated Lymphoid Tissue
BHV-1400
Targeting the pathogenesis of disease without immunosuppression
B cell
Plasma cell
T cell
Myeloma Cell
Small molecule inhibitor
Monoclonal antibody
Bispecific antibody
Antibody drug conjugate
CAR-T
BAFFR
TACI
BCMA
TLR7
TLR9
RNA
DNA
RNA-specific BCR
DNA-specific BCR

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



IgAN Patient Expansion Cohort Study Design

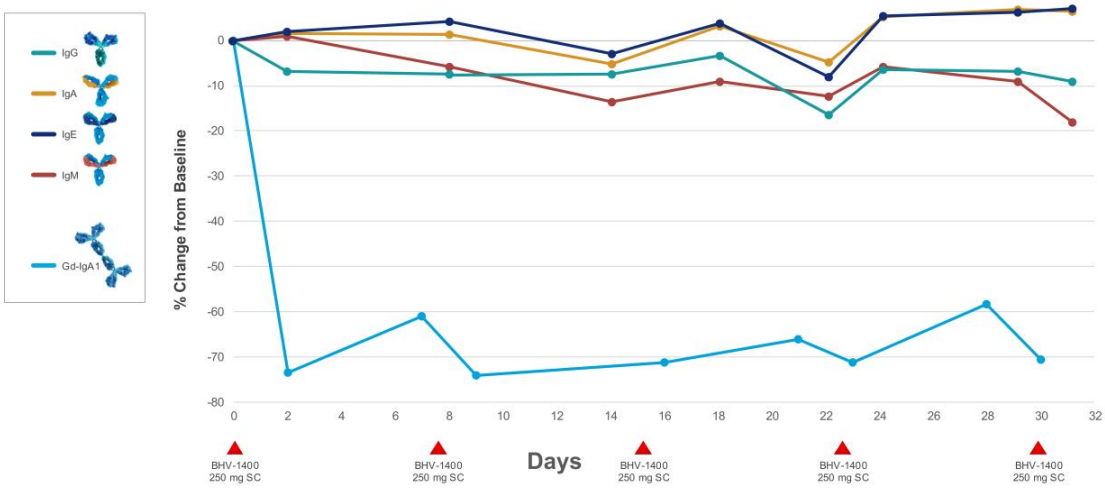


KEY STUDY DETAILS

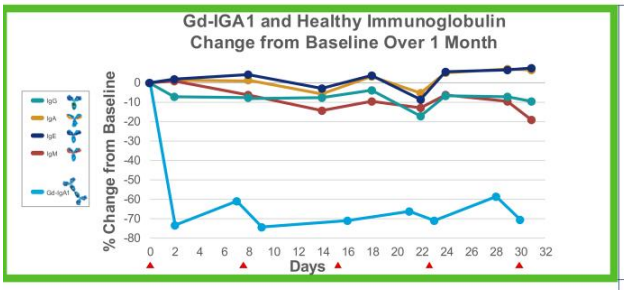
Study Design: Open-label, n=10, potential to increase
Population: Male and female adults with biopsy proven IgAN, UPCR ≥ 0.5 g/d, eGFR ≥ 30
Endpoints: Primary safety, pharmacodynamic measures

IgAN Patient Expansion Cohort Site Map

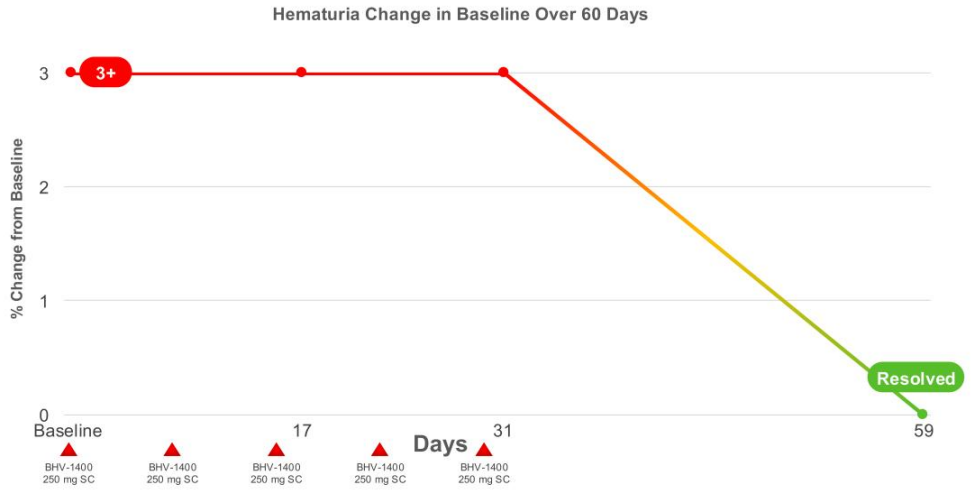
Dr. Barratt's First Patient With IgAN Dosed: BHV-1400 SC Delivers Rapid, Selective, Deep and Sustained Removal of Gd-IgA1 Over First Month



Dr. Jonathan Barratt's First Patient With IgAN Dosed: BHV-1400 SC Delivers Rapid, Selective, Deep and Sustained Removal of Gd-IgA1 Over First Month



Dr. Jonathan Barratt's First Patient With IgAN Dosed: Removal of Gd-IgA1Translating Into Rapid Resolution of Hematuria



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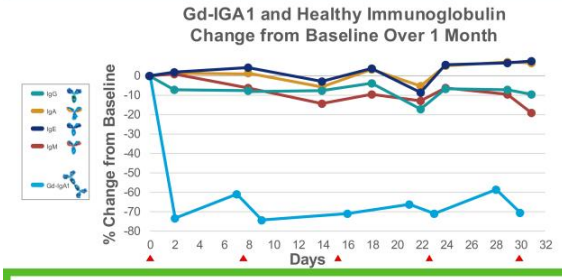
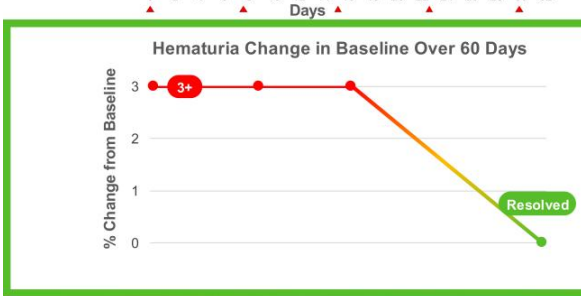
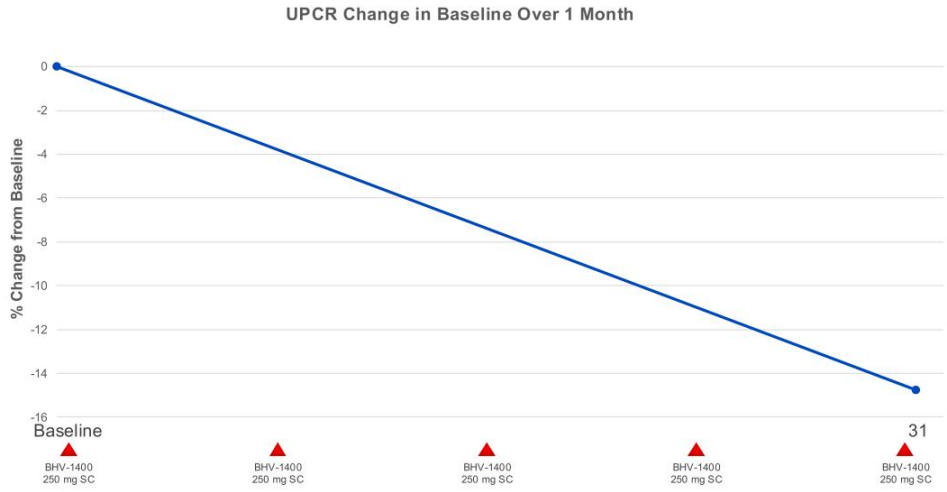




Dr. Jonathan Barratt's First Patient With IgAN Dosed: BHV-1400 SC Delivers Rapid Removal of Gd-IgA1Translating Into Rapid Improvement of Proteinuria



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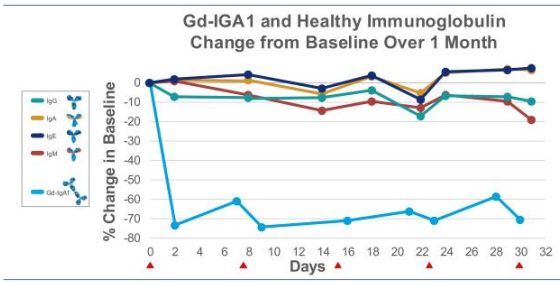
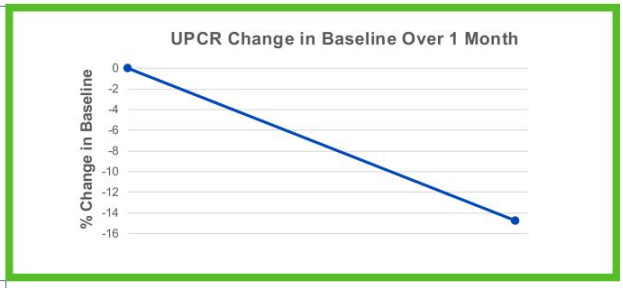
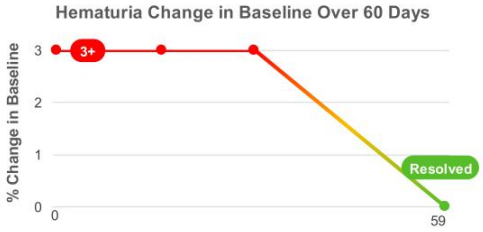
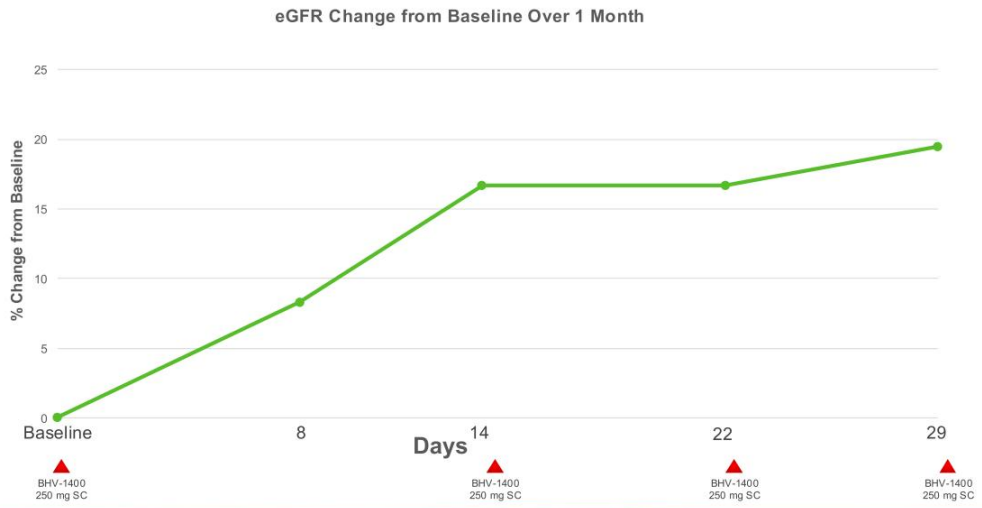






Dr. Jonathan Barratt's First Patient With IgAN Dosed: BHV-1400 SC Delivers Rapid Removal of Gd-IgA1Translating Into Rapid Improvement in Kidney Function (eGFR)



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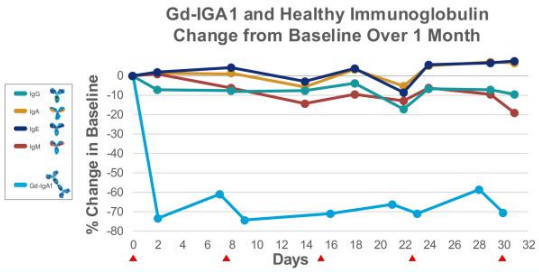
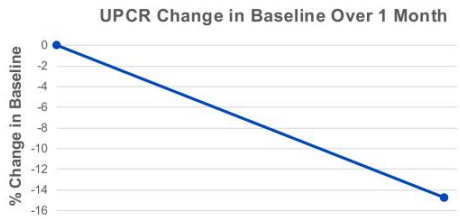
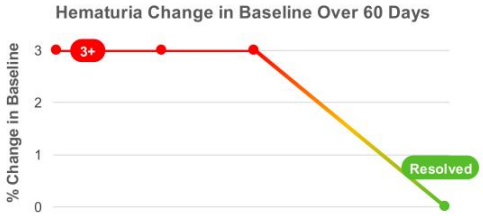






Demographic and Clinical Characteristics of the Patients Receiving BHV-1400 at Baseline

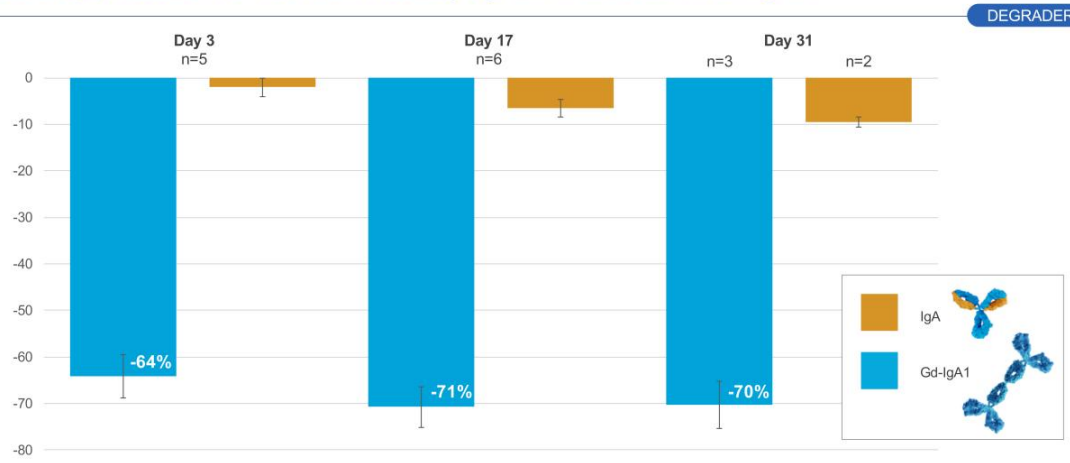
DEGRADERS

Characteristics	Overall (n=10)
Age (yrs) Mean [Min, Max]	43.6 [27, 65]
Sex n (%) Male Female	 6 (60%) 4 (40%)
Race n (%) Asian White Unknown	 3 (30%) 6 (60%) 1 (10%)
Spot UPCR* (mg/g) Mean [Min, Max]	766.4 [213–2144]
eGFR** (ml/min/1.73 m^2) Mean [Min, Max]	67 [33–124]
Hematuria (1+, 2+, or 3+) n (%)	2 (20%)
Time from Biopsy (yrs) Mean [Min, Max]	3.03 [0.3, 8.9]

UPCR, urinary protein-to-creatinine ratio. **eGFR:** estimated glomerular filtration rate.

BHV-1400 500 mg SC Q2WK Deeply and Selectively Removes Gd-IgA1 Without Suppression of Normal Healthy IgA in Patients With IgAN

DEGRADERS



Preliminary data from ongoing study. Graph represents the mean and standard error of % change in Gd-IgA1 from baseline at each time-point in patients with IgAN receiving BHV-1400 500 mg every two weeks.

BREAKING NEWS

Patients with IgAN administered BHV-1400 achieved deep lowering within hours and 70% lowering within one month of dosing.

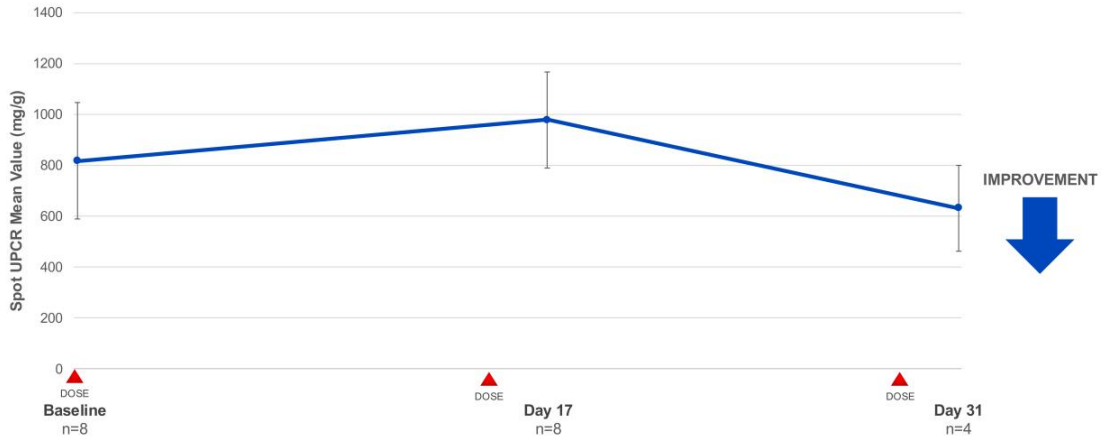
Hematuria Change With One Month of Dosing BHV-1400 SC

DEGRADERS

Preliminary data from ongoing study. Graph represents hematuria values for participants with IgAN (n=10) receiving BHV-1400 SC for one month of dosing.

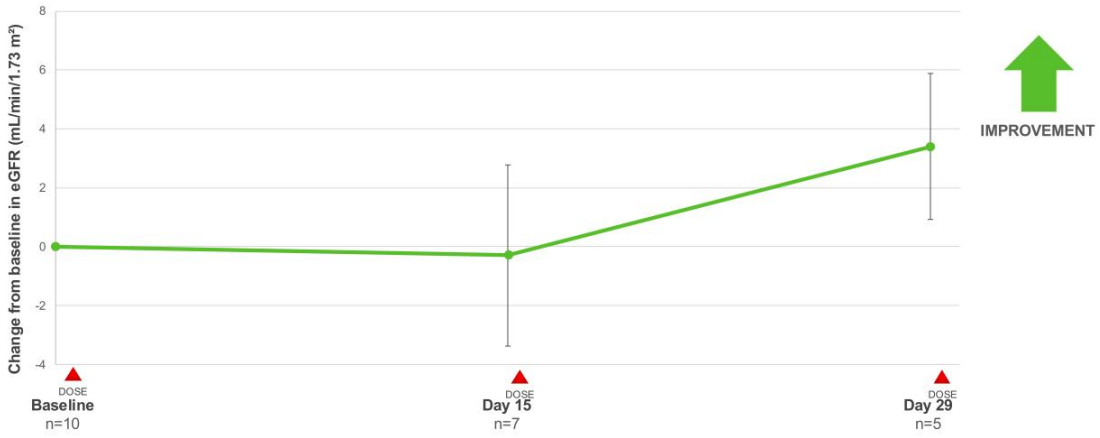
UPCR Change With One Month of Dosing BHV-1400 SC

DEGRADERS



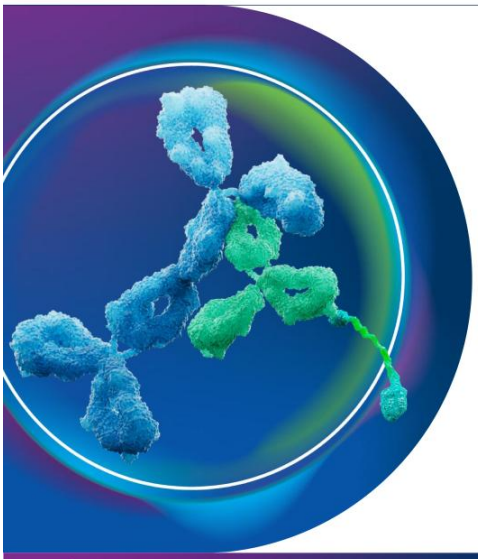
Preliminary data from ongoing study. Graph represent mean and standard error of spot UPCR in participants with IgAN (n=8) receiving BHV-1400 SC for one month of dosing.

eGFR Change With One Month of Dosing BHV-1400 SC



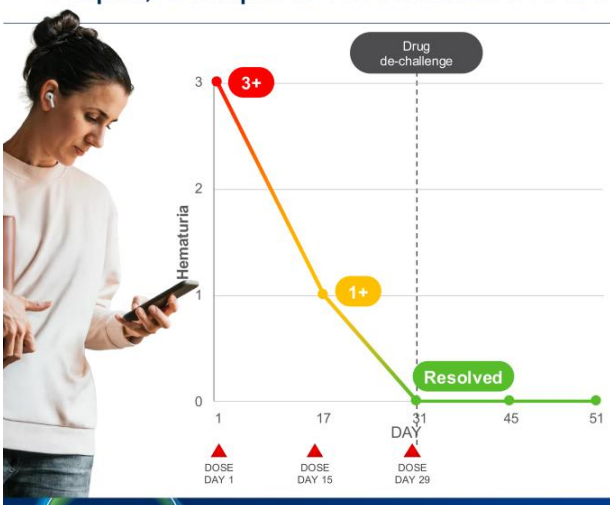
Preliminary data from ongoing study. Graph represent mean and standard error of eGFR in participants with IgAN (n=10) receiving BHV-1400 SC for one month of dosing.

BHV-1400 Phase 1/2 IgAN Patient Cohort — Safety Summary



- 10 participants with IgA Nephropathy
- Most AEs were mild and self-resolving
- No treatment discontinuations for adverse events
- No clinically significant trends in vitals, ECGs, or labs (including AST/ALT/Tbili)
- No clinical evidence of cardiovascular, renal, hepatic, or hematologic toxicity
- Preservation of IgA, IgG, IgM, IgE
- No SAEs, severe AEs, or AEs resulting in discontinuation of therapy

BHV-1400 Early Disease Clinical Experience: Rapid, Complete Resolution of Hematuria Within Weeks of Initial Dosing

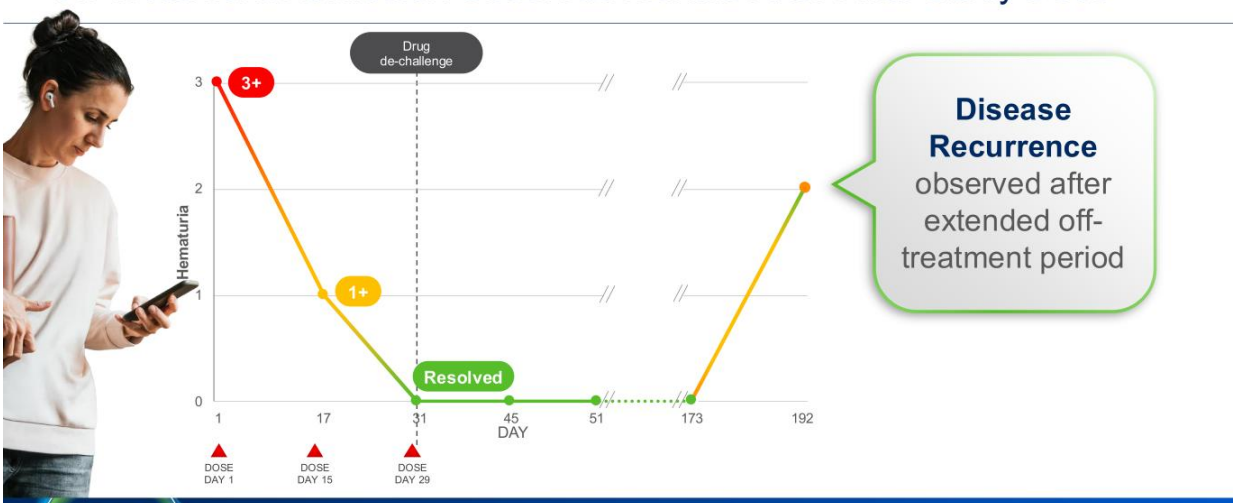


CASE REPORT:
Initial IgAN Patient Dosed

- Young female patient
- Normal eGFR
- Chronic hematuria
- Active lifestyle
- Significant fatigue
- Comorbid diabetes

KEY POINT BHV-1400 500 mg SC every other week delivers rapid and complete resolution of hematuria

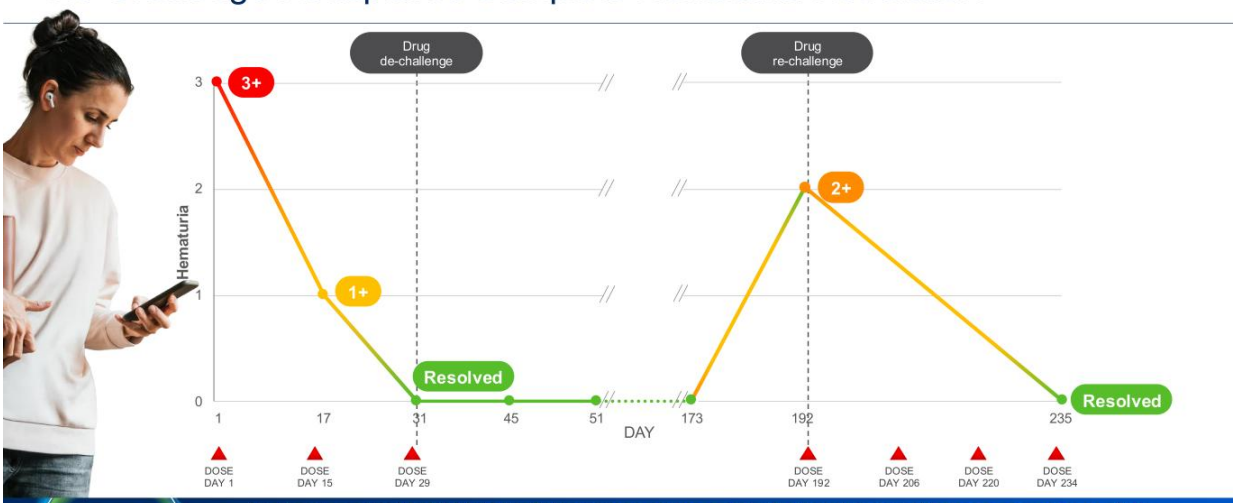
BHV-1400 Durable Response:
Off-Treatment Remission Observed Months After Final Study Dose



KEY POINTS

- Re-treatment initiated upon disease recurrence after extended off-treatment period
- Durability observed well beyond active treatment window

BHV-1400 Re-Treatment:
Re-Challenge Recaptures Complete Hematuria Resolution

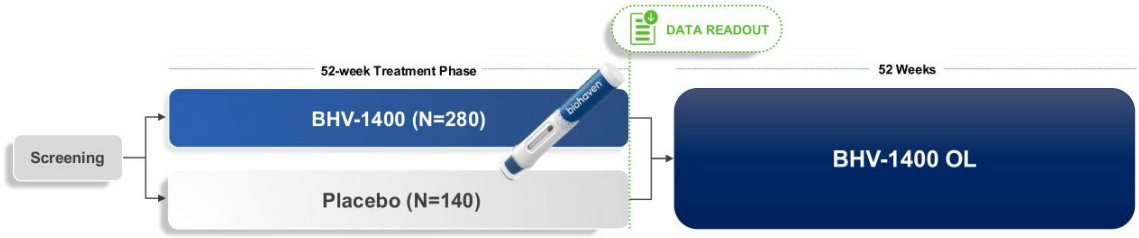


KEY POINTS

- **Re-treatment with BHV-1400 500 mg every two weeks initiated upon disease recurrence after extended off-treatment period**
- **Complete resolution of hematuria re-achieved within weeks of reinitiation**

Lead TRAP Degrader BHV-1400 Enters Phase 3

DEGRADERS



KEY STUDY DETAILS

Study Design: Randomized, double-blind, placebo-controlled trial
Population: Male and female adults with biopsy proven IgAN
Dose: 500 mg bimonthly, at home administration
Endpoints: Δ UPCR, Δ in eGFR, Δ in Gd-IgA1 at week 52

ATD, antithyroid drugs

KEY POINT

BHV-1400 pivotal trial in IgA nephropathy to commence in the coming weeks

Panel

MODERATOR

Corine Johnson
Equity Analyst
Goldman Sachs

PANELISTS

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

Malini Gupta, MD, ECNU, FACE, FITS
Director
G2Endo Endocrinology & Metabolism
2025 AACE Chair Thyroid DSN

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

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

Tova Gardin, MD, MPP
Chief Translational Officer
Biohaven

Brian McGuire, MD
Medical Director
Biohaven

David Pirman, PhD
SVP & Head of Drug Discovery
Biohaven

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Key Milestones Anticipated in 2026


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