BMB-101

Novel 5-HT_{2C}
Selective Agonist

Breaking through

Drug resistant epilepsies

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Agenda

Investor Presentation Agenda: Announcement of the BREAKTHROUGH Study

1. **Welcome and Introduction**
Ian McDonald, Chief Executive Officer

2. **Understanding Absence Epilepsy**
Dr. Dennis Dlugos, Key Opinion Leader (KOL)

3. **Deep Dive into Developmental Epileptic Encephalopathy (DEE)**
Dr. Joe Sullivan, Key Opinion Leader (KOL)

4. **BMB-101: Preclinical and Clinical Rationale**
Jan Torleif Pedersen, MSc PhD, Chief Scientific Officer

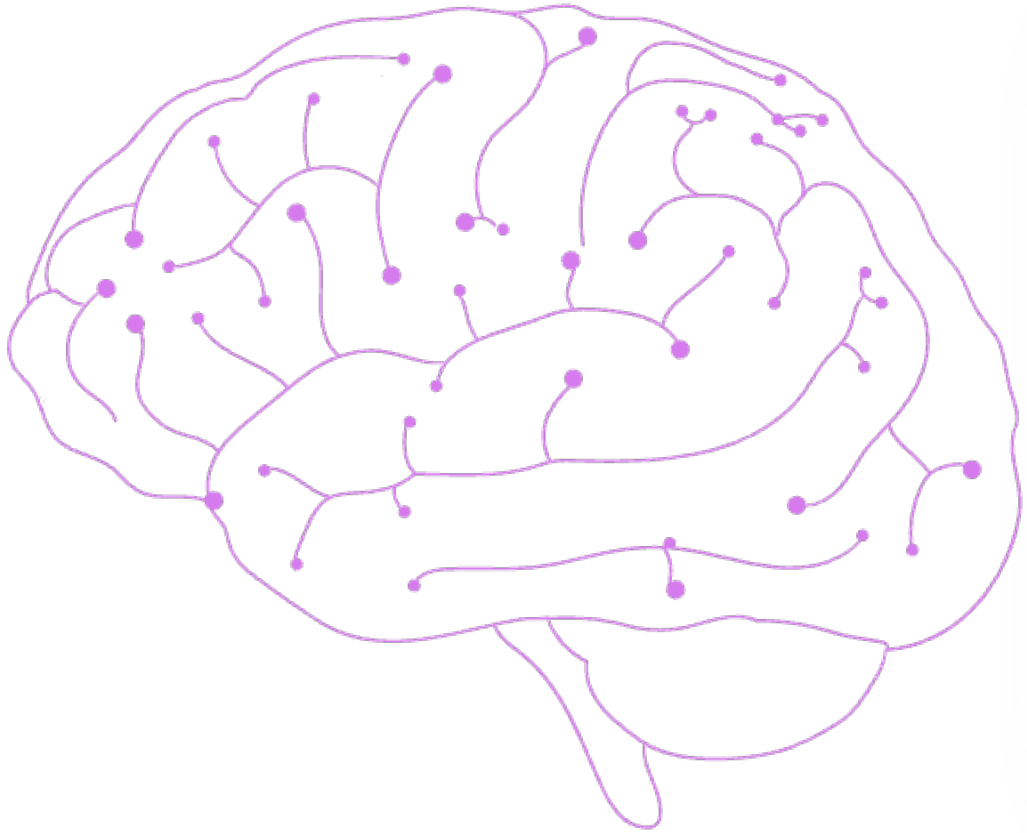
5. **The BREAKTHROUGH Study: Trial Design and Objectives.**
Dr. Jo Sourbron, Key Opinion Leader (KOL)

6. **Market Potential and Strategic Positioning**
Ian McDonald, Chief Executive Officer

BMB-101

Novel 5-HT_{2C}
Selective Agonist

About Bright Minds Biosciences



Healing the central nervous system & brain through regulation of serotonin

New approaches to neuroscience create Bright Minds

Pipeline

Rich and diverse portfolio in neurology and psychiatry with multiple programs

Lead	Features	Research	Ph-1	Ph-2	Indications
5-HT$_{2C}$ agonists for CNS disorders					
BMB-101	• Selective and biased 2C agonist, low 5-HT$_{2A/2B}$ • Biased agonism with minimal arrestin recruitment • Suitable for chronic dosing		Clinical Studies – Phase 2		Rare epilepsies
BMB-xxx	• Selective 5-HT$_{2C}$ agonist compound • Biased agonist		ADME/PK profiling		Obesity and feeding behaviour
Non-hallucinogenic psychoplastogens					
BMB-201	• Promotes neuroplasticity • Low or absent psychedelic activity • Devoid of 5-HT$_{2B}$ activity		IND-enabling studies		Treatment-resistant depression
5-HT$_{2A}$ agonists for the treatment of depression					
BMB-202	• Selective 5-HT$_{2A}$ "Fast-On-Fast-Off" compound • High C_{max} and short plasma half-life • 2-fold more potent than psilocin at 5-HT$_{2A}$		IND-enabling tox		Depression (Fast-onset)
BMB-xxx	• Mixed 5-HT$_{2A/2C}$ compound • 10-fold more potent than psilocin at 5-HT$_{2A}$		ADMEPK profiling		Neurology / Neuropsychiatric Indication

Creating New Chemical Entities That Target Serotonin Agonism

Serotonin (5-HT) is the most prominent neurotransmitter in the brain and modulates many functions

Key 5-HT_2 Receptors Targets

5-HT_{2A} Agonists

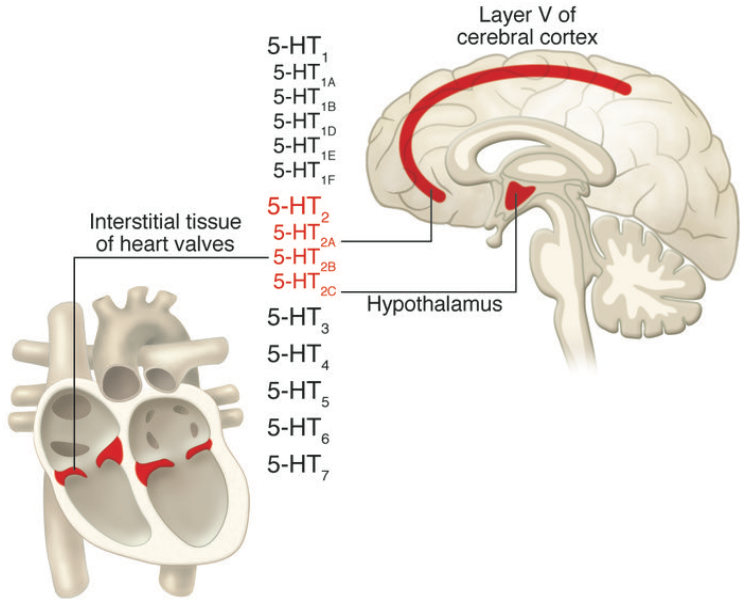
Depression, PTSD

5-HT_{2C} Agonists

Epilepsy, Impulsivity Control Disorders

5-$HT_{2A/2C}$ Agonists

Depression, Generalized Anxiety Disorder

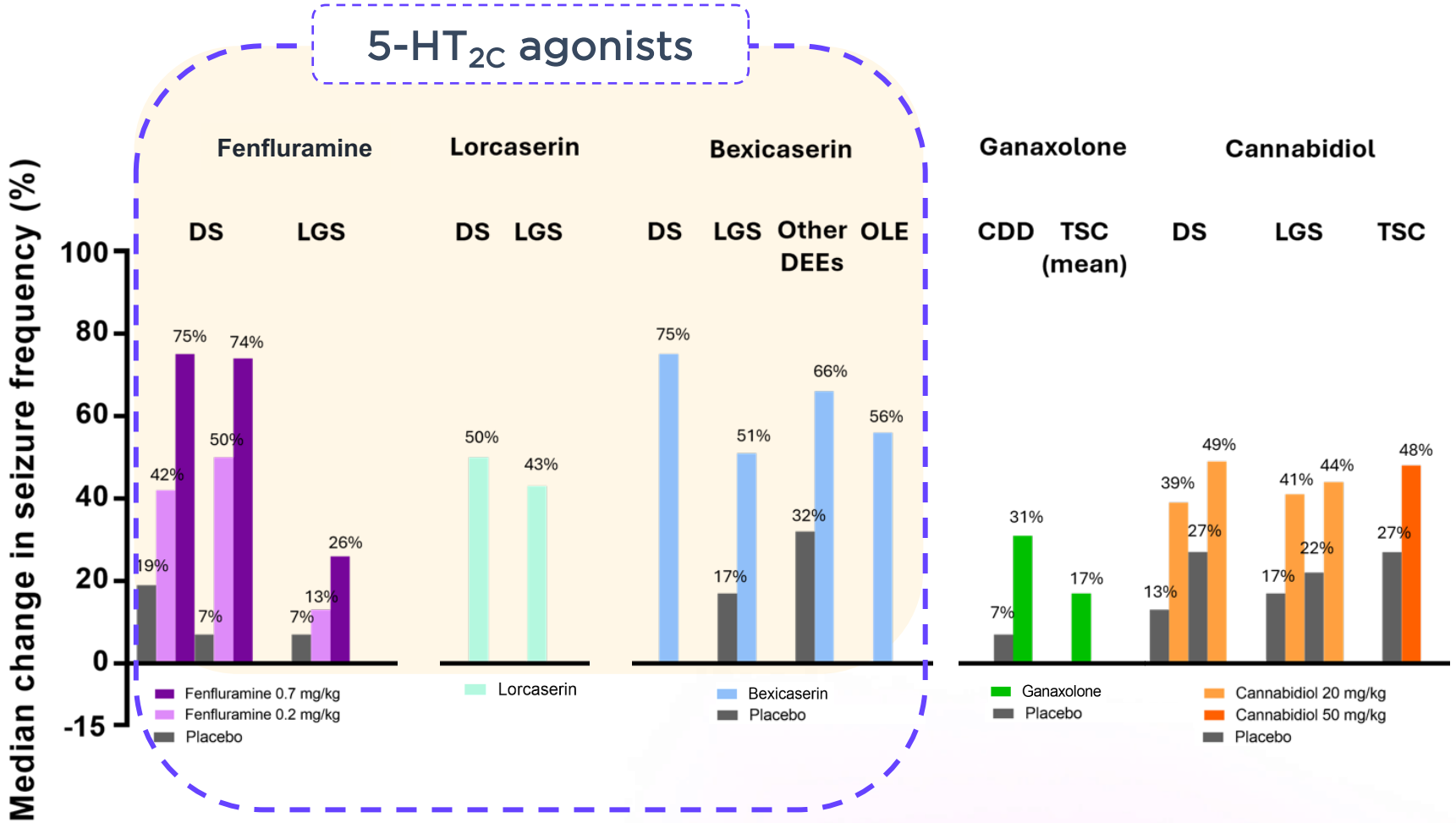


Based on a proprietary chemistry platform Bright Minds have developed highly selective 5-HT_{2A} and 5-HT_{2C} agonists without 5-HT_{2B} activity

5-HT_{2B} activation is associated with undesirable cardiac valvulopathy

J Clin Invest. 2013;123(12):4986-4991

5-HT_{2C} agonism provides superior efficacy in DEE epilepsies



DEE - Developmental and Epileptic Encephalopathy
DS – Dravet Syndrome
LGS – Lennox Gastaut Syndrome
TSC - Tuberous sclerosis
CDD - CDKL5 deficiency disorder
OLE – Open-Label Extension

Drug-resistant epilepsy is still a significant issue

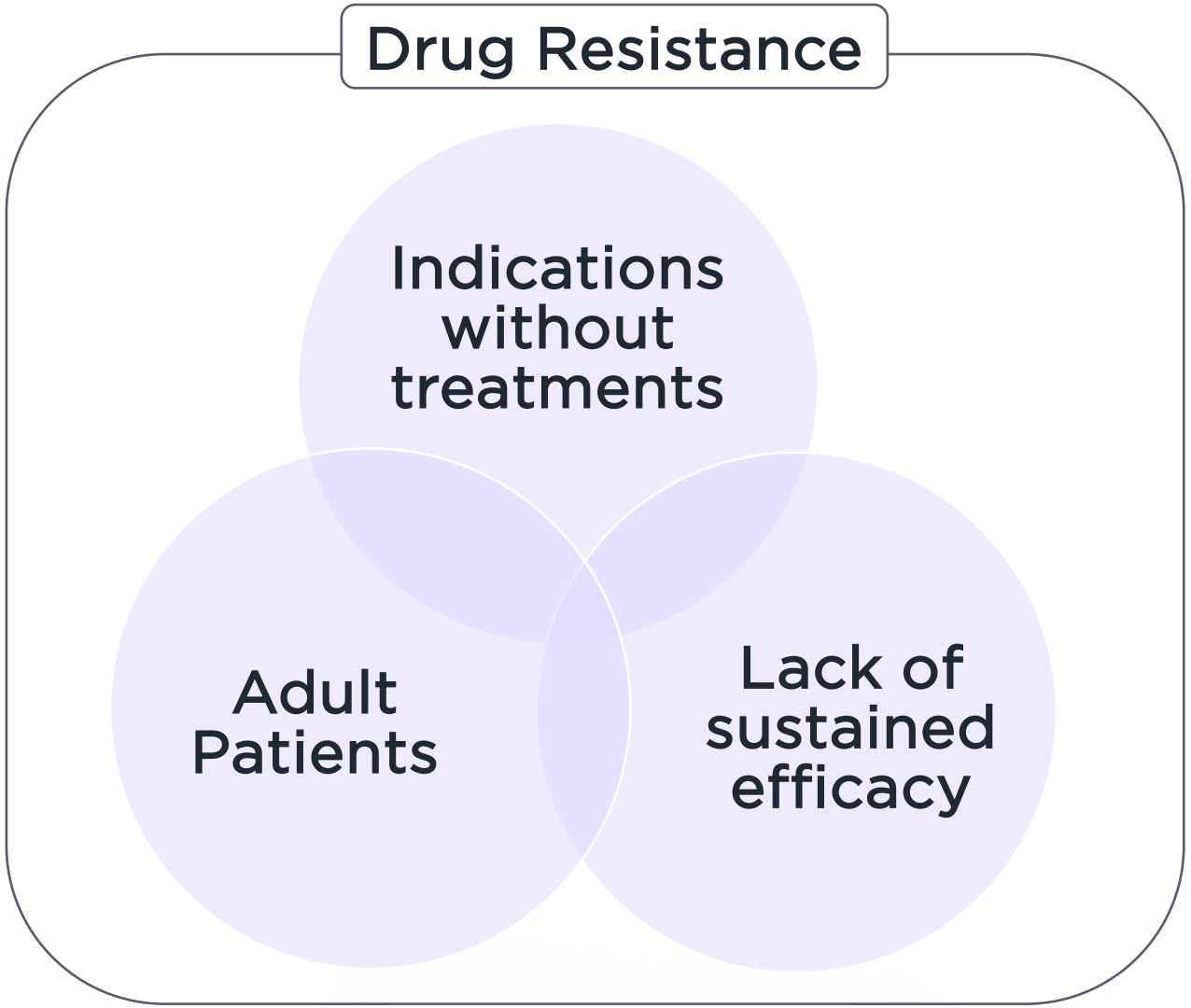
~30%
of Epilepsy patients develop drug resistance

Definition:
Drug-resistant epilepsy is characterized by the persistence of seizures despite the use of at least two appropriate antiseizure medications (ASMs) at effective doses

Despite the availability of over 20 ASMs, achieving seizure control in DRE patients remains difficult.

Woldman W, Cook MJ, Terry JR. Evolving dynamic networks: An underlying mechanism of drug resistance in epilepsy? Epilepsy Behav. 2019 May;94:264-268. doi: 10.1016/j.yebeh.2019.03.003.

Drug Resistance



Treatment of Drug-Resistant Epilepsies

Recent drug development focused on Dravet Syndrome, LGS and other DEEs

Semah F, et al. Is the underlying cause of epilepsy a major prognostic factor for recurrence? Neurology. 1998;(51):1256-1262
Brenner T et al. Prevalence of neurologic autoantibodies in cohorts of patients with new and established epilepsy. Epilepsia. 2013;54(6):1028–1035
Image credits: UCB

BMB-101

Novel 5-HT_{2C}
Selective Agonist

Breaking through

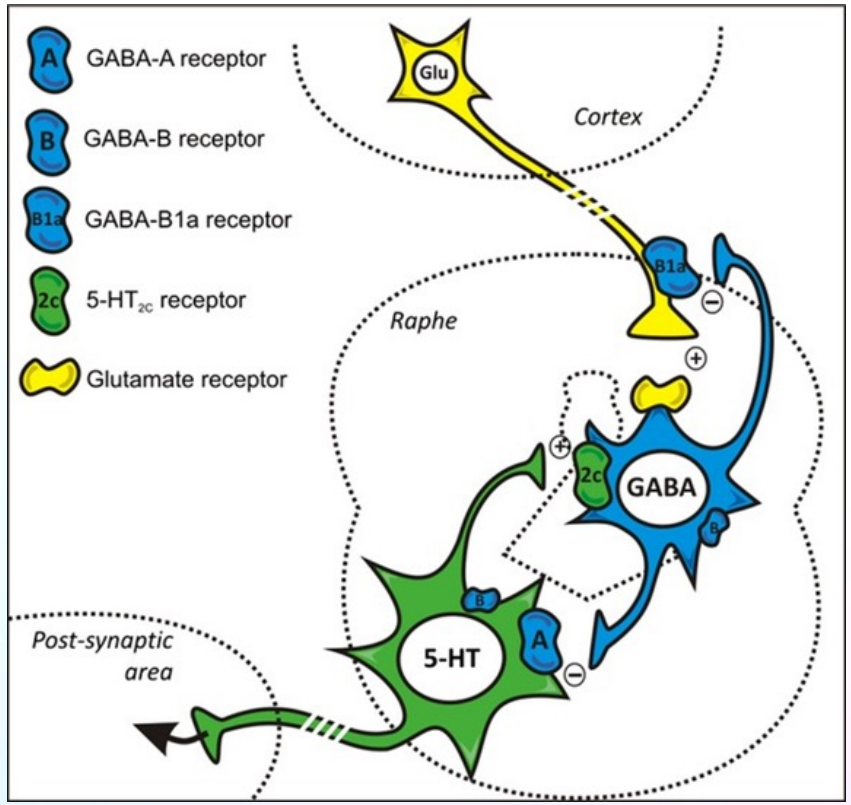
Drug resistant epilepsies

Novel mechanism to address major unmet need

Jan Torleif Pedersen, MSc PhD

Chief Scientific Officer
Bright Minds Biosciences

5-HT_{2C} Agonists – Putting a brake on Seizures



- Epileptic Seizures are caused by hypersynchronous neuronal discharges that can be alleviated by enhancing GABAergic inhibition.
- 5-HT2C receptors are expressed on the surface of GABAergic interneurons pre-synaptic to dopamine and serotonin cell bodies.
- Activation of 5-HT2C receptors via Gq will release GABA and increase firing threshold of serotonergic and dopaminergic neurons.

Effect of genetic and pharmacological blockade of GABA receptors on the 5-HT2C receptor function during stress
Cédric B. P. Martin, Martin Gassmann, Caroline Chevarin, Michel Hamon, Uwe Rudolph, Bernhard Bettler, Laurence Lanfumey, Raymond Mongeau. J. Neurochem. (2014) 131, 566–572

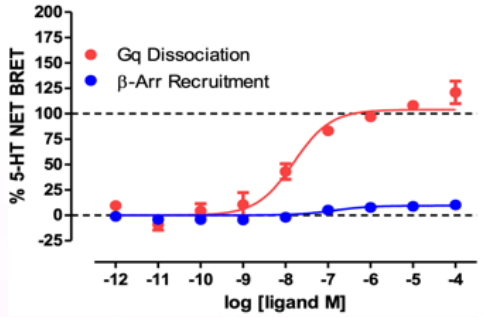
BMB-101 is uniquely positioned to address major unmet needs

Highly selective 5-HT2C agonist

Compound	5-HT$_{2A}$	5-HT$_{2B}$	5-HT$_{2C}$
BMB-101	2280	>10000	16.2
Nor-Fenfluramine	82.8	11.6	2.5
Lorcaserin	50.1	67.4	2.4
Bexicaserin	>10000	>10000	120

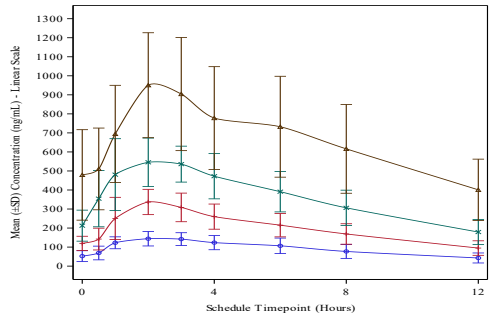
- Validated mechanism of action in DEEs
- Improved safety profile

G-protein biased agonist



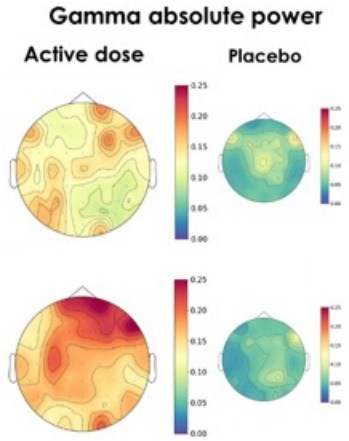
- Sustained chronic effect
- Reduced tolerance

Safety and PK/PD properties validated in Phase 1



- Potential for a more convenient once daily formulation

Proof of mechanism demonstrated in Ph.1 Increased gamma-power on qEEG



- Additional behavioral/cognitive benefits

BMB-101 – Preclinical validation

Highly selective and potent 5-HT_{2C} agonist with favorable preclinical profile

5-HT_2 Gq dissociation

Absolute EC_{50} (nM)

Compound	5-HT_{2A}	5-HT_{2B}	5-HT_{2C}
BMB-101	2280	>10000	16.2
Nor-Fenfluramine	82.8	11.6	2.5
Lorcaserin	50.1	67.4	2.4
Bexicaserin	>10000	>10000	120

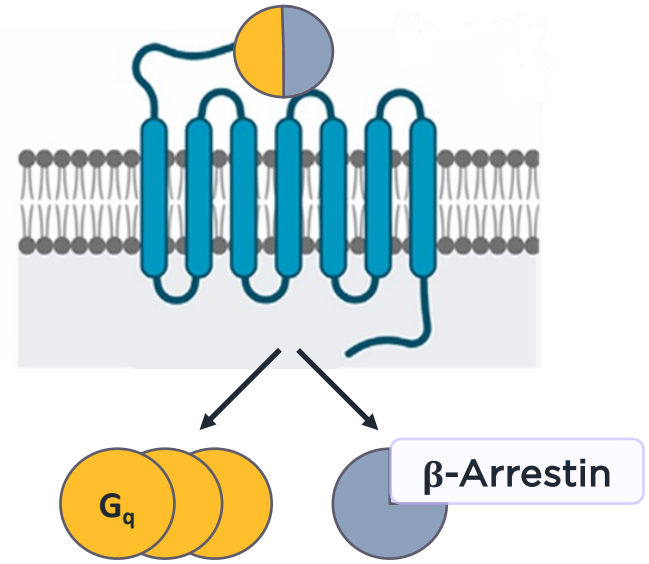
Internal data for BMB-101, fenfluramine, lorcaserin.
Bexicaserin data from Longboard corporate deck

Preclinical validation summary

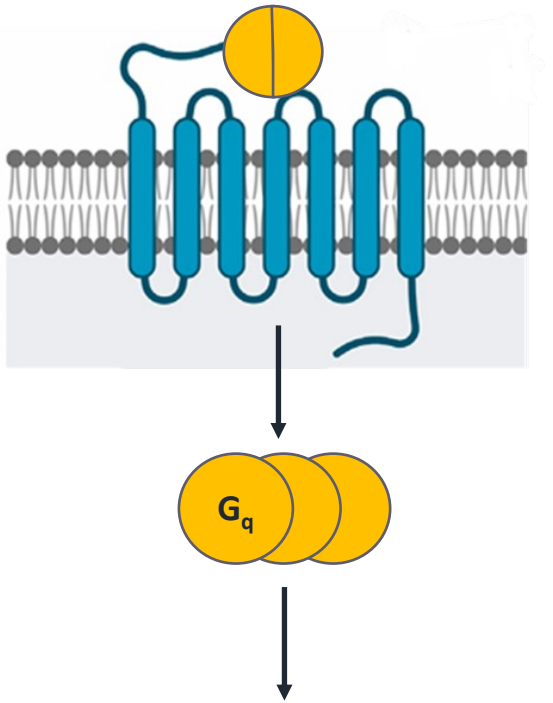
- ✓ Reduces locomotion and duration of epileptiform discharges in zebrafish model of Dravet syndrome
- ✓ Reduces duration of seizures in the mouse 6Hz model of epilepsy (similar to other anti-epileptics)
- ✓ Oral bioavailability ~90%
- ✓ Low potential for drug-drug interactions
- ✓ High solubility and permeability, typical BCS Class 1 compound

Novel 5-HT$_{2C}$ mechanism
One receptor – multiple modes of activation

Balanced Agonism

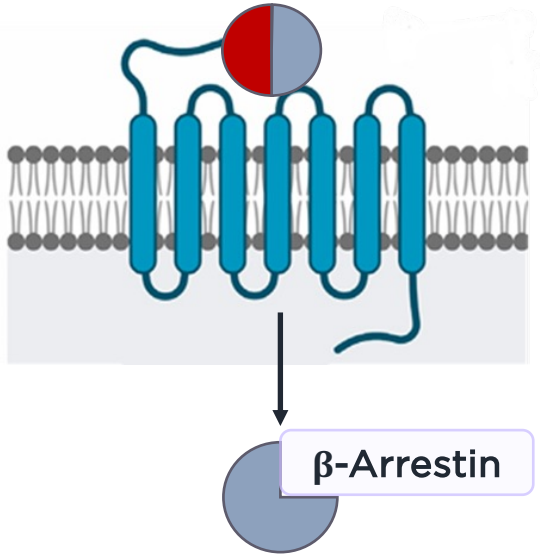


G-protein biased Agonism



Anti-Epileptic Effect

β-Arrestin biased Agonism



Receptors removed from cell surface

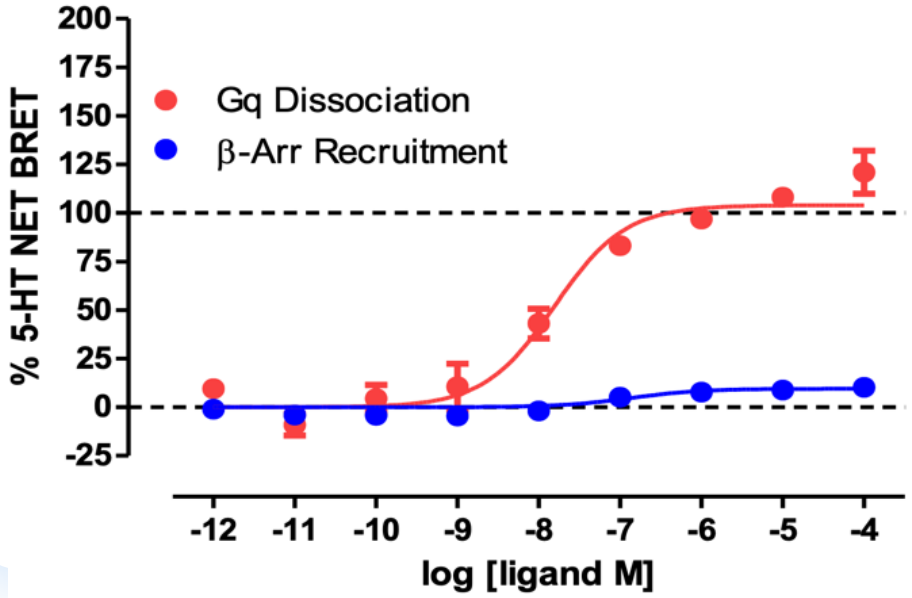
Reduced sensitivity
Tolerance

BMB-101 a Novel 5-HT_{2C} mechanism

- BMB-101 does not recruit β-arrestin
- Cells to stay “healthy” and maintains the response to the drug over time

BMB-101

5-HT_{2C} receptor activation pathways



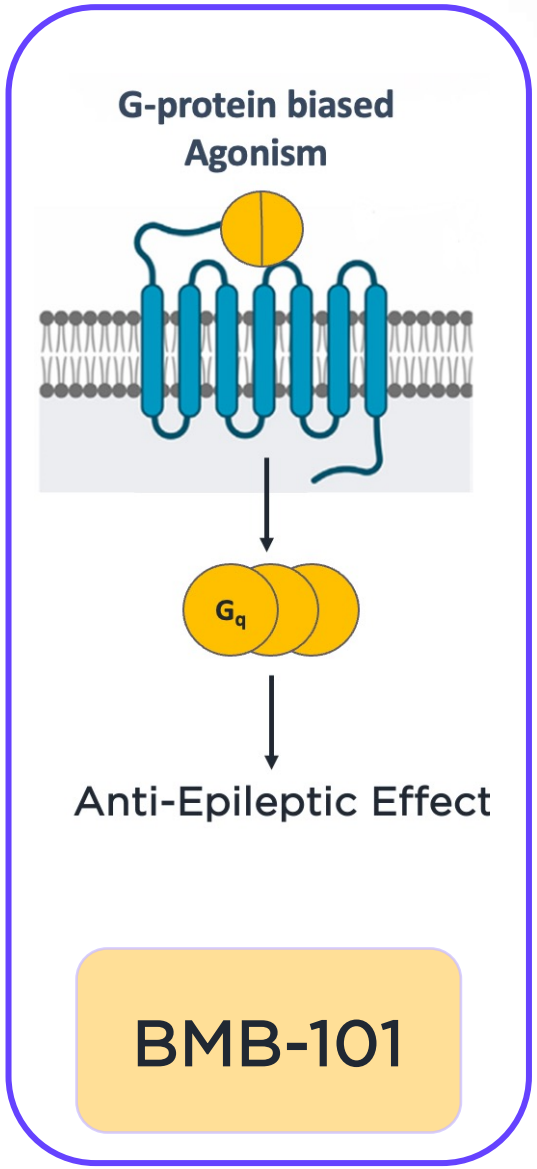
G-protein Pathway

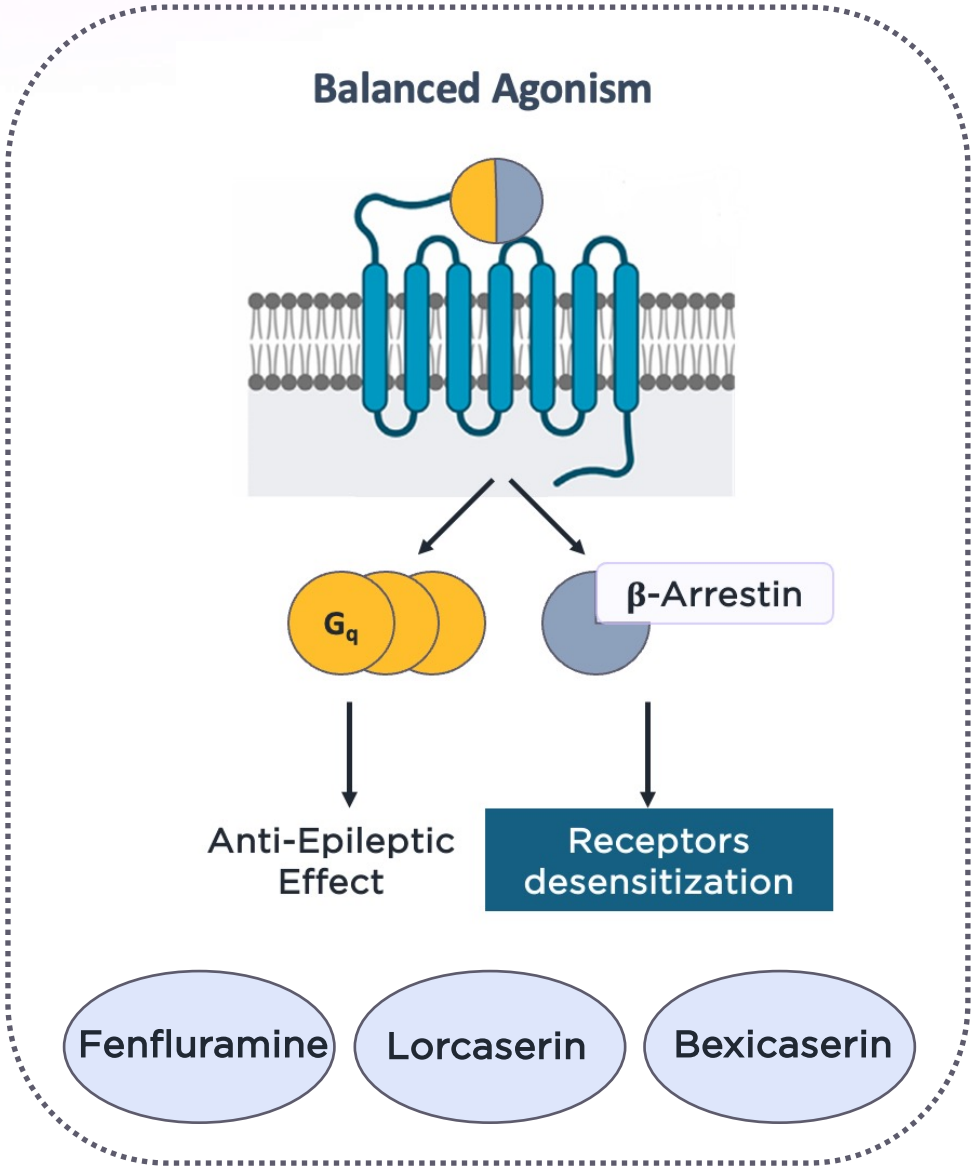
Associated with therapeutic effect

β-Arrestin pathway

Associated with tolerance

BMB-101 Exhibits Functional Selectivity

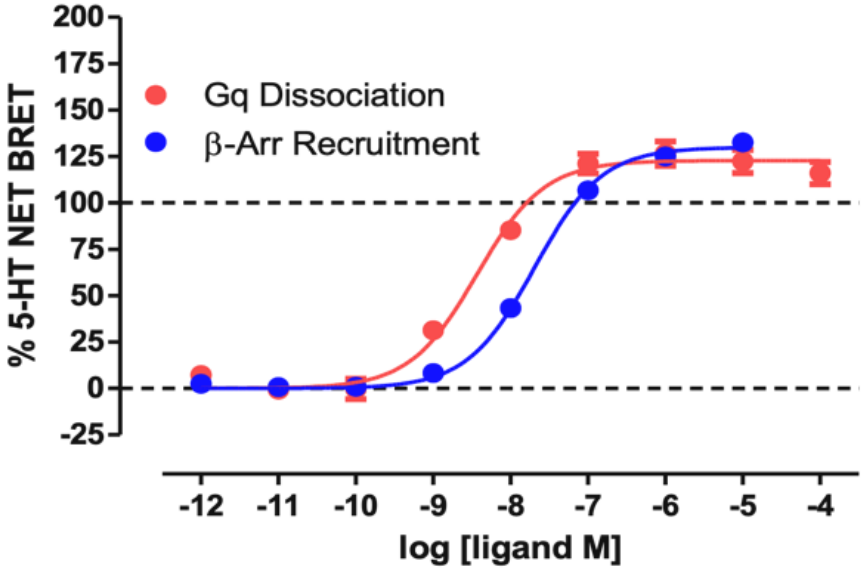




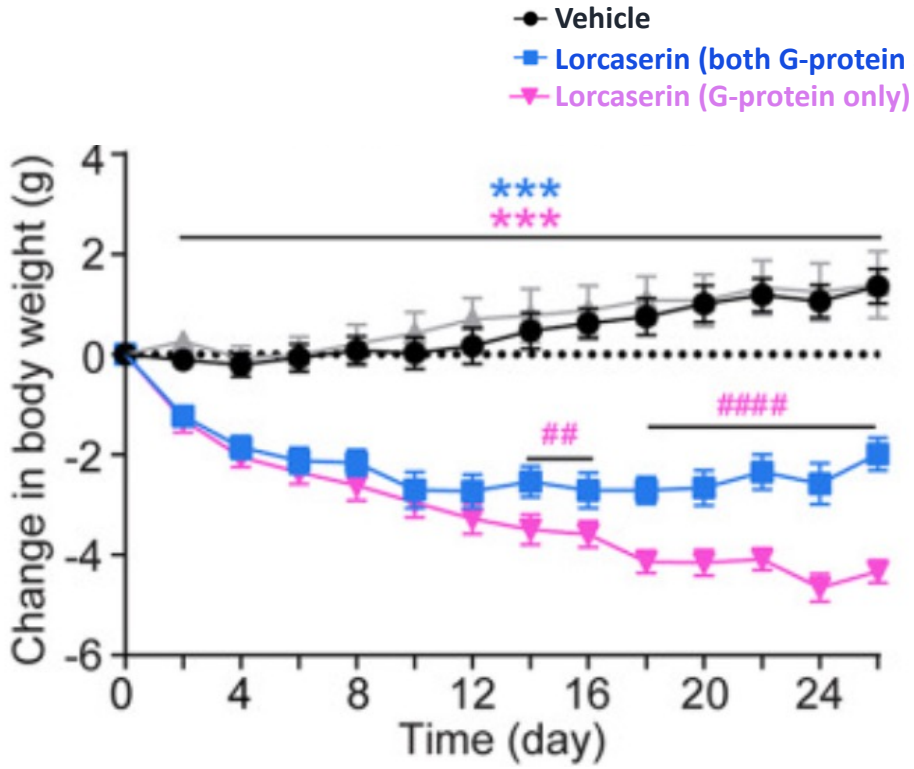
How does it translate to efficacy?

Lessons learned from Lorcaserin

Lorcaserin



- Balanced 5-HT_{2C} agonist
- Potent β-arrestin activator
- Had diminished effects after 6 months as a weight loss drug



+β-Arrestin inhibitor

Deactivation of β-arrestin produces a superior and sustained effect in long term Lorcaserin use (in vivo study)

He Y, et al. **Barbadin Potentiates Long-Term Effects of Lorcaserin on POMC Neurons and Weight Loss.** J Neurosci. 2021 Jun 30;41(26):5734-5746. doi: 10.1523/JNEUROSCI.3210-20.2021.

BMB-101 Phase 1 study - design

A 3-Part Study to Evaluate the Safety, Tolerability, PK, and Food Effect of BMB-101 in Healthy Volunteers
Protocol PR-BMB-101-101
Study was done in Adelaide, Australia with Syneos and CMAX

Single Ascending Dose	4 cohorts (6 drug and 2 placebo) single dose (oral solution)
Food Effects	12 subjects - crossover with and without breakfast
Multiple Ascending Dose	4 cohorts (6 drug and 2 placebo) – twice a day dosing for 7 days Quantitative electroencephalogram (qEEG) recording in Cohort 4 (dose 150 mg) Cardiac monitoring

BMB-101 Phase 1 – SAD/MAD

Favorable Safety & Tolerability Results Observed

40-80 mg BID

Expected Therapeutic dose

- Drug slightly better tolerated in fed state at 120 mg
- No SAEs observed, all AEs were transient

	Placebo (n=9)	20 mg (n=6)	60 mg (n=6)	120 mg (n=7)	180 mg (n=6)
Oral paresthesias	1 (11.1%)	1 (16.7%)	-	2 (28.6%)	5 (83.3%)
Nausea	-	-	2 (33.3%)	-	3 (50%)
Sedation	-	-	-	-	3 (50%)
Headache	1 (11.1%)	-	-	-	2 (33.3%)
Balance Disorder	-	-	-	-	2 (33.3%)
Photophobia	-	-	-	-	2 (33.3%)
Dizziness	-	-	-	-	1 (16.7%)
Decreased Appetite	-	-	-	1 (14.3%)	-
Euphoria	-	-	-	1 (14.3%)	-

Single Ascending Dose

	Placebo (n=8)	40 mg BID (n=6)	80 mg BID (n=6)	120 mg BID (n=6)	150 mg BID (n=6)
Headache	2 (25%)	-	1 (16.7%)	1 (16.7%)	3 (50%)
Balance Disorder	-	-	-	-	3 (50%)
Photophobia	-	-	-	-	3 (50%)
Visual Impairment	-	-	-	1 (16.7%)	-
Oscillopsia	-	-	-	-	1 (16.7%)
Oral Paresthesias	-	1 (16.7%)	1 (16.7%)	1 (16.7%)	-
Nausea	-	-	-	1 (16.7%)	1 (16.7%)
Somnolescence	-	-	-	1 (16.7%)	1 (16.7%)
Cognitive Disorder	-	-	-	-	1 (16.7%)
Dizziness	-	-	-	-	1 (16.7%)
Decreased Appetite	-	-	-	-	1 (16.7%)
Dysphoria	-	-	-	1 (16.7%)	-

Multiple Ascending Dose

BMB-101 – Clinical Data from Phase 1

Safety:

- ✓ Favorable safety & tolerability in Phase 1. All side effects transient, no severe adverse events. No side-effects observed before top dose was reached.
- ✓ Side effects at top dose (2-3x of predicted therapeutic dose) as expected for the CNS drug acting at 5-HT receptors.

Target engagement:

- ✓ Transient dose-dependent prolactin release
- ✓ Central target engagement by qEEG and Potential for improved cognitive performance (increase in gamma power)*

Favorable PK:

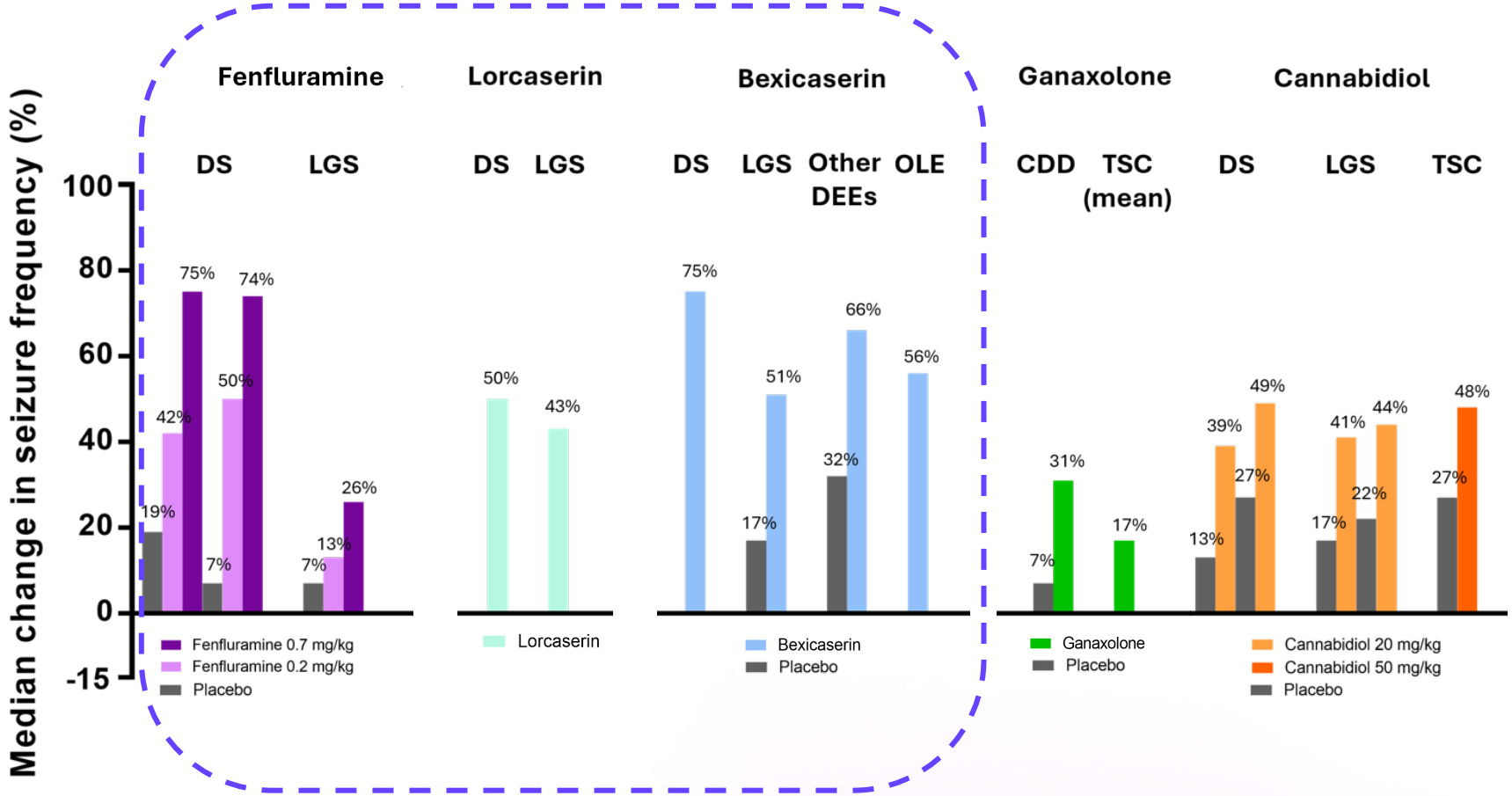
- ✓ Dose proportionality observed in SAD and MAD study. No significant food effects observed

Changes in absolute power pre/post-dose

	Delta	Alpha	Beta	Gamma
Broad spectrum ASMs				
Valproate	⇩	⇩	⇩	⇩
Leviracetam	⇩	⇩	⇩	NA
Carbamazepine	⇧	⇩	⇩	NA
Lacosamide	⇧	⇩	⇩	NA
5-HT$_{2C}$ agonists				
Bexicaserin	⇧	⇩	⇩	Not reported
BMB-101	⇧	⇩	⇩	⇧

*Increases in gamma power can be related to increased cognitive demands, higher attention, better processing of attended stimuli, and response inhibition

5-HT_{2C} agonism provides superior efficacy in DEE disorders



DEE - Developmental and Epileptic Encephalopathy
DS – Dravet Syndrome
LGS – Lennox Gastaut Syndrome
TSC - Tuberous sclerosis
CDD - CDKL5 deficiency disorder
OLE – Open-Label Extension

BMB-101 – a next-generation 5-HT_{2C} agonist for chronic treatment

Potency and Selectivity

- Very potent and selective at 5-HT_{2C} receptor
- No significant activity at other 5-HT receptors

Safety in clinical trials Phase 1

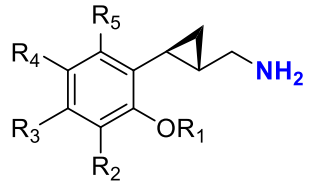
- Safe and tolerable at all tested doses
- Excellent PK/PD properties and central target engagement

Optimized for chronic treatment

- Potential for once-a-day formulation
- Designed to have sustained efficacy without tolerance

Strong IP

- Granted patent until 2036
- Possible extension to 2041



BMB-101

Novel 5-HT_{2C}
Selective Agonist

Jo Sourbron
MD, PhD, PharmD

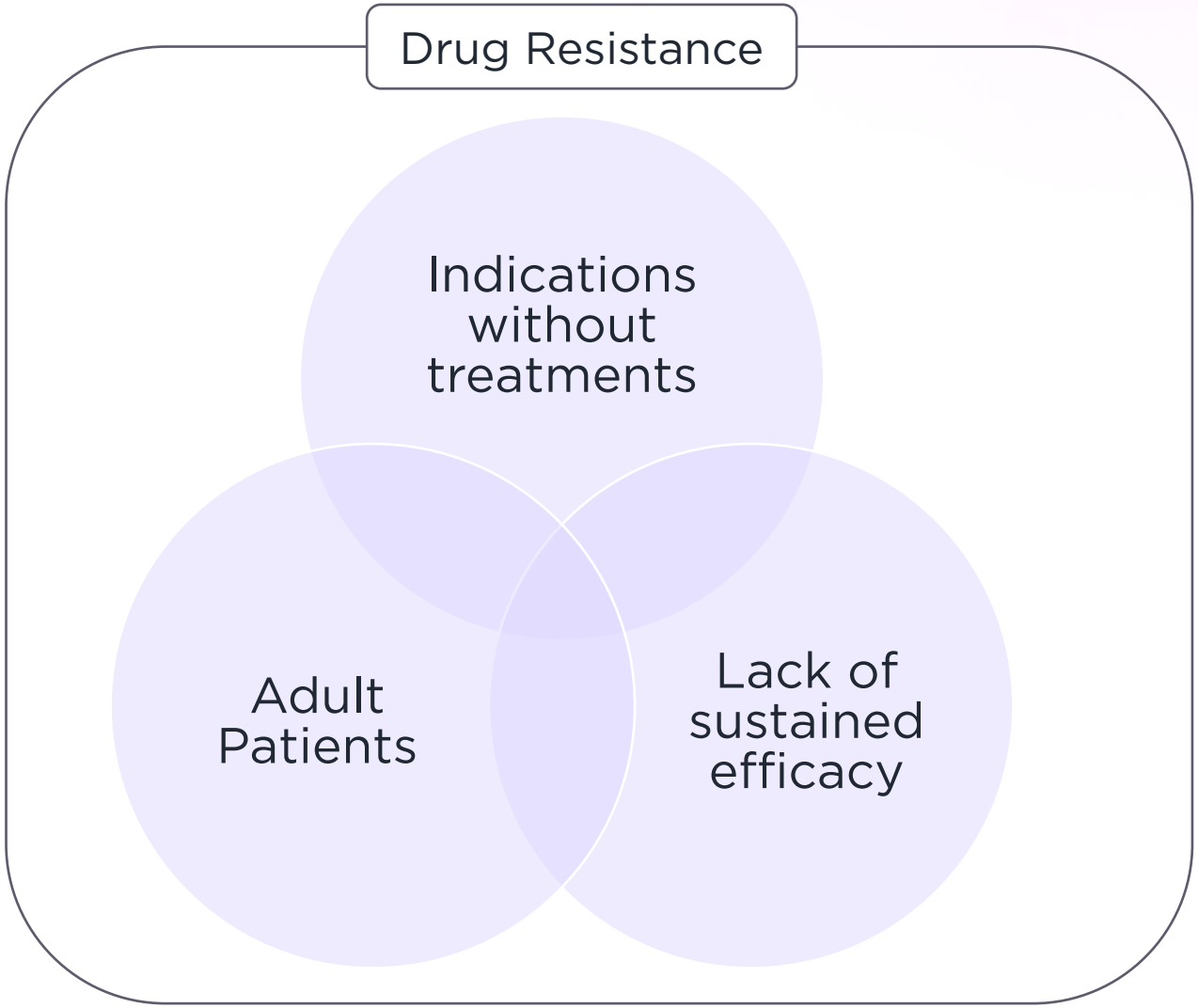
Breaking through

Drug-resistant epilepsies

Unmet need in epilepsy

Unmet needs in epilepsy

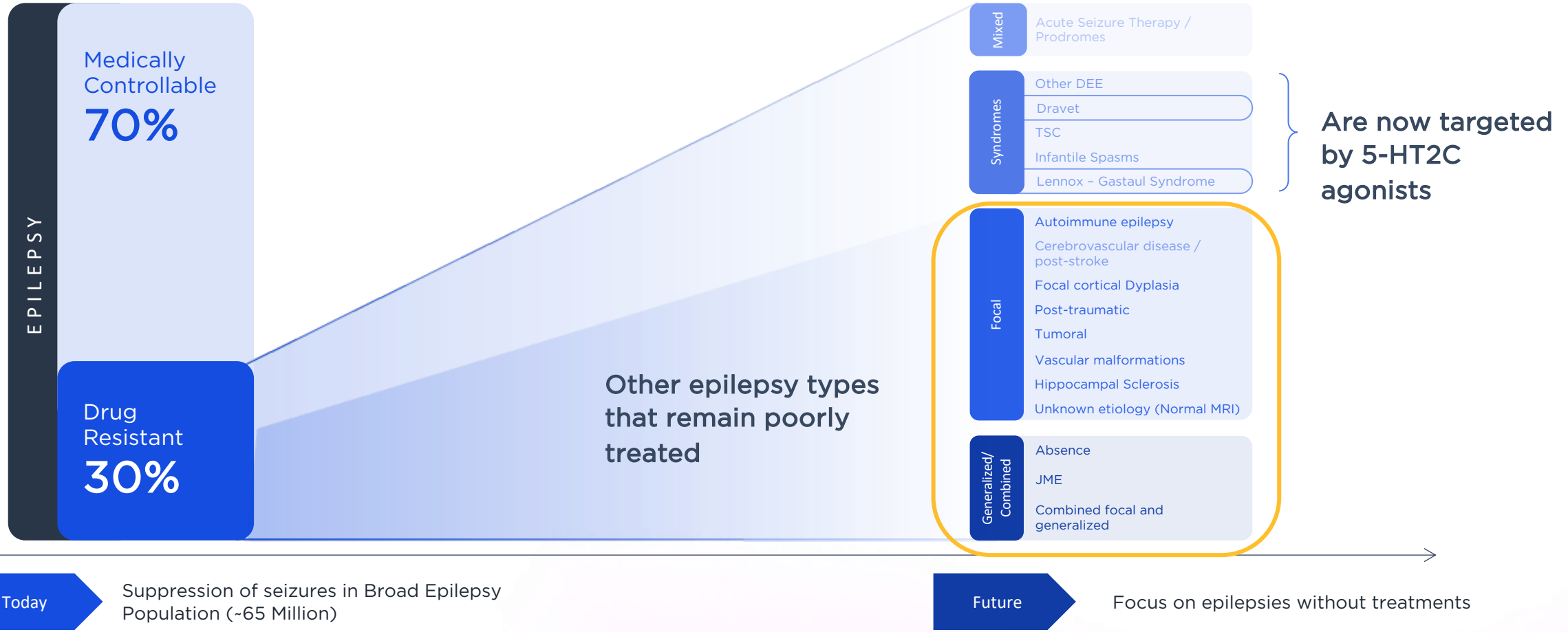
Patients need to shift the treatment paradigm



- Some patients spend years searching for an optimal combination of medications
- But instead, experiencing a new set of side effects with limited efficacy
- Some groups remain underserved (e.g. adult patients)

Recent drug development focus on Dravet, LGS and DEEs

High Unmet Need Beyond DEE



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Brenner T et al. Prevalence of neurologic autoantibodies in cohorts of patients with new and established epilepsy. Epilepsia. 2013;54(6):1028–1035

Image credits: UCB

Adult Patients are Underserved

Case of Fenfluramine in DEEs

Over **80%** patients will require care in adult age

Have a higher degree of drug resistance

Some have onset in childhood, but newly diagnosed

SUDEP (Sudden Unexpected Death in Epilepsy) remains a risk in adulthood

Fenfluramine has a dose cap (due to 5-HT_{2B} activity)

Without Stiripentol	0.7 mg/kg/day 26 mg/day
With Stiripentol	0.4 mg/kg/day 17 mg/day

Hashmi SA, Sachdeva S, Sindhu U, Tsai C, Bonda K, Keezer M, Zawar I, Punia V. The implications of frailty in older adults with epilepsy. Epilepsia Open. 2024 Sep 9.
Wirrell EC, Lagae L, Scheffer IE, Cross JH, Specchio N, Strzelczyk A. Practical considerations for the use of fenfluramine to manage patients with Dravet syndrome or Lennox-Gastaut syndrome in clinical practice. Epilepsia Open. 2024 Jul 4

Epilepsy with Eyelid Myoclonia patients have high degree of drug resistance

No approved drugs

Generalized epilepy
- Photosensitive/reflex epilepsy
- Subgroup: with handwaving: "Sunflower syndrome"

~90,000 patients in the USA
- 2:1 female predominance
- 6-8 years childhood onset
- Seizures persist in adulthood

Drug-resistant epilepsy

First line:
Valproic acid, levetiracetam, lamotrigine

Second line:
Ethosuximide, clobazam

Dietary changes (ketogenic diet)

Avoid
Sodium channels blocking medications (except lamotrigine). CBD even worsens seizures in EEM patients

Need for **novel** treatments

Nilo A, Crespel A, Genton P, Macorig G, Gigli GL, Gélisse P. Prognostic factors in epilepsy with eyelid myoclonia (Jeavons syndrome). Rev Neurol (Paris). 2023 Dec;179(10):1081-1085. doi: 10.1016/j.neurol.2023.04.005.

Possible mechanism also in broader epilepsy populations

5-HT2C agonism can be promising in reflex (e.g. photosensitive/EEM) and/or absence epilepsy disorders

Clinical

- ✓ Clinical data on **pathogenesis** of these epilepsies indicate:
  - ✓ Local hyperexcitability of the primary visual cortex
  - ✓ Impaired intra-cortical inhibition
  - ✓ Increased thalamic activity (absence)
- ✓ 5HT2C agonists are effective in some photosensitive epilepsies:
  - ✓ Hypothesis: other photosensitive epilepsies could benefit?
  - ✓ **Broader treatment indications**? Multiply the market?

Zawar I, Knight EP. Epilepsy With Eyelid Myoclonia (Jeavons Syndrome). Pediatr Neurol 2021;121:75–80.
Forcelli PA. Serotonin in the Dorsal Raphe: As I Live and Breathe. Epilepsy Curr 2018;18:191–3.
Vaudano AE, Ruggieri A, Tondelli M, Avanzini P, Benuzzi F, Gessaroli G, et al. The visual system in eyelid myoclonia with absences. Ann Neurol 2014;76:412–27.
Martin CBPCBP, Gassmann M, Chevarin C, Hamon M, Rudolph U, Bettler B, et al. Effect of genetic and pharmacological blockade of GABA receptors on the 5-HT2C receptor function during stress. J Neurochem 2014;131:566–72.

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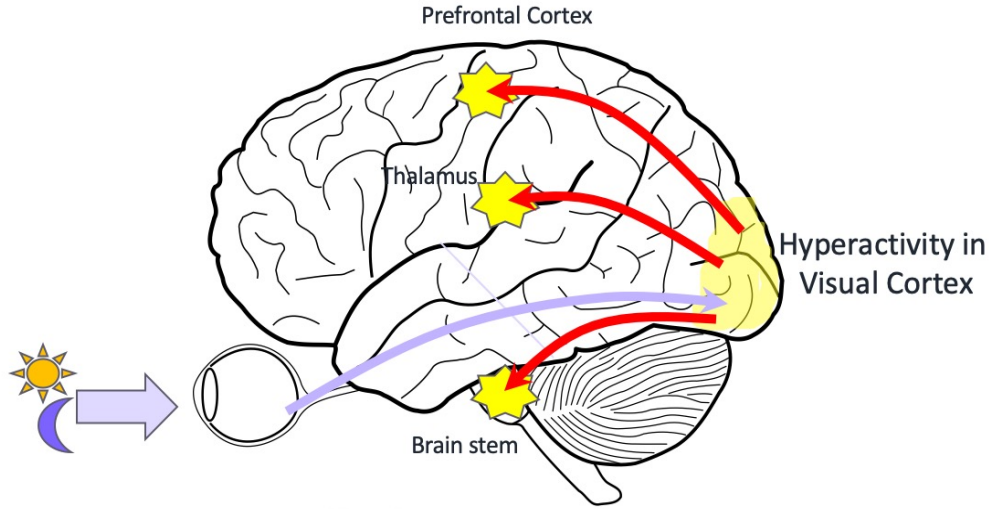
5-HT2C agonism can be promising in reflex (e.g. photosensitive/EEM) and/or absence epilepsy disorders

Clinical



Pathogenesis

- In **reflex/photosensitive** epilepsy: hyperactivity in visual cortex
  => hypersynchronous discharges in specific areas=> propagation throughout brain
- In **absence** epilepsy: thalamus as origin of electric firing

Zawar I, Knight EP. Epilepsy With Eyelid Myoclonia (Jeavons Syndrome). Pediatr Neurol 2021;121:75–80.
Forcelli PA. Serotonin in the Dorsal Raphe: As I Live and Breathe. Epilepsy Curr 2018;18:191–3.
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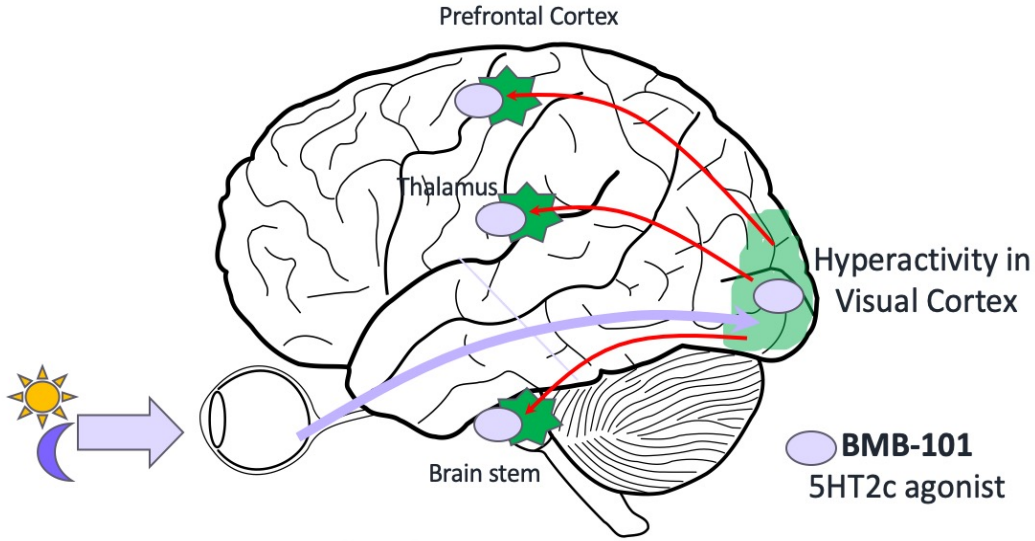

5-HT2C agonists act as a **break on hyperactivity** in

- Visual cortex => targeting source **reflex/photosensitive** epilepsy
- Thalamus => targeting source **absence** epilepsy

Targeting underlying pathogenesis = novel mechanism

Zawar I, Knight EP. Epilepsy With Eyelid Myoclonia (Jeavons Syndrome). Pediatr Neurol 2021;121:75–80.
Forcelli PA. Serotonin in the Dorsal Raphe: As I Live and Breathe. Epilepsy Curr 2018;18:191–3.
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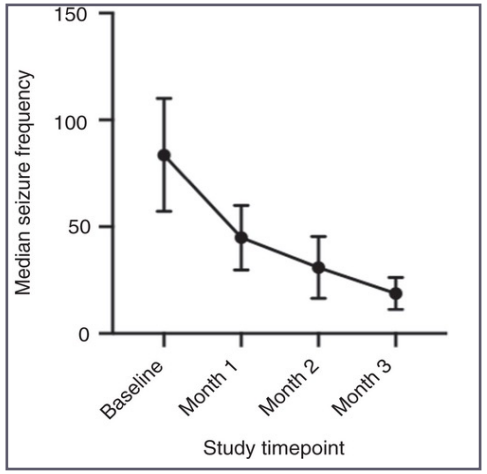
Proven mechanism also in broader epilepsy populations

5-HT2C agonists demonstrate promise in DEE and absence epilepsy disorders

Clinical

Fenfluramine

- ✓ Dravet Syndrome (DEE): Observed antiseizure effects on focal and absence seizures.
- ✓ Sunflower Syndrome (subtype EEM): seizure reduction of >70% in the first cohort



Median hand-waving episode frequency Fenfluramine study with Sunflower Syndrome

Lagae et al. Lancet 2019 Dec 21;394(10216):2243-2254
Geenen KR, Doshi SP, Patel S, Sourbron J, Falk A, Morgan A, Vu U, Bruno PL, Thiele EA. Fenfluramine for seizures associated with Sunflower syndrome. Dev Med Child Neurol. 2021 Dec;63(12):1427-1432.
Patel S, Geenen KR, Dowless D, Bruno PL, Thiele EA. Follow-up to low-dose fenfluramine for Sunflower syndrome: A non-randomized controlled trial. Dev Med Child Neurol. 2023 Jul;65(7):961-967.

Preclinical

- ✓ Fenfluramine in 6Hz mice (model of drug-resistant seizures)
- ✓ Lorcaserin in GAERS (rat model of absence epilepsies)
- ✓ Fenfluramine and lorcaserin in *scn1Lab* zebrafish (model of Dravet syndrome/DEE/DRE)

Venzi M, David F, Bellet J, Cavaccini A, Bombardi C, Crunelli V, Di Giovanni G. Role for serotonin2A (5-HT2A) and 2C (5-HT2C) receptors in experimental absence seizures. Neuropharmacology. 2016 Sep;108:292-304.
Silenieks LB, Carroll NK, Van Niekerk A, Van Niekerk E, Taylor C, Upton N, Higgins GA. Evaluation of Selective 5-HT2C Agonists in Acute Seizure Models. ACS Chem Neurosci. 2019 Jul 17;10(7):3284-3295.

Proven mechanism also in broader epilepsy populations

BMB-101 demonstrates preclinical efficacy in DEE and DRE

Locomotor behavior

Locomotor behavior
EEG

Preclinical

BMB-101
- ✓ in 6Hz mice (model of drug-resistant seizures)
- ✓ in *scn1Lab* zebrafish (model of Dravet syndrome/DEE/DRE)

Internal documentation (2023-2024)

Safety and tolerability demonstrated in phase 1

BMB-101 demonstrates clinical safety and tolerability by **Phase 1 Study**

Clinical

- ✓ SAD (*highest dose 2.5 mg/kg*) and MAD (*highest dose 2.14 mg/kg*)
- ✓ No SAEs observed
- ✓ All AEs were transient
- ✓ Most common side effects (*mostly solely in high dose group*)
  - ✓ Oral paresthesias (possibly formulation taste); n=8 SAD; n=3 MAD
  - ✓ Nausea; n=5 SAD; n=2 MAD
  - ✓ Sedation; n=3 SAD; n=0 MAD
- ✓ No clinically significant shifts in laboratory parameters, vital signs, or EKG

Study Details

Drug-placebo ratio 3:1

N=76
18 years and older

BMB-101
- ✓ **Effects**: at 1 mg/kg (transient prolactin increase and qEEG changes)
- ✓ **Safety**: up to 2.14 mg/kg (MAD: 150 mg/70 kg)

Kim SH, Lee H, Kim DW. Switching antiepileptic drugs to once-daily dosing regimens in epilepsy patients. Acta Neurol Scand. 2021 Jan;143(1):51-55. doi: 10.1111/ane.13333. Epub 2020 Aug 26. PMID: 32762074.

Proven mechanism also in broader epilepsy populations

BMB-101 demonstrate promise for treatment of numerous epilepsies:
DRE, DEE, absence and reflex (e.g. photosensitive/EEM) epilepsy disorders

Clinical

BMB-101

- ✓ **Phase 1 Study** completed: safety, tolerability, proof of mechanism
- ✓ **Phase 2 Study** initiated (exploratory: DRE: Absence and EEM)
- ✓ **Future studies?**
  - ✓ Cfr. pathogenesis: other reflex/photosensitive epilepsies
  - ✓ Cfr. preclinical data: expanding to other DEEs/DRE

Preclinical

BMB-101

- ✓ in 6Hz mice (rodent model of **drug-resistant** seizures)
- ✓ in *scn1Lab* zebrafish (model of **Dravet syndrome/DRE**)

Internal documentation (2023-2024)

BMB-101

Novel 5-HT_{2C}
Selective Agonist

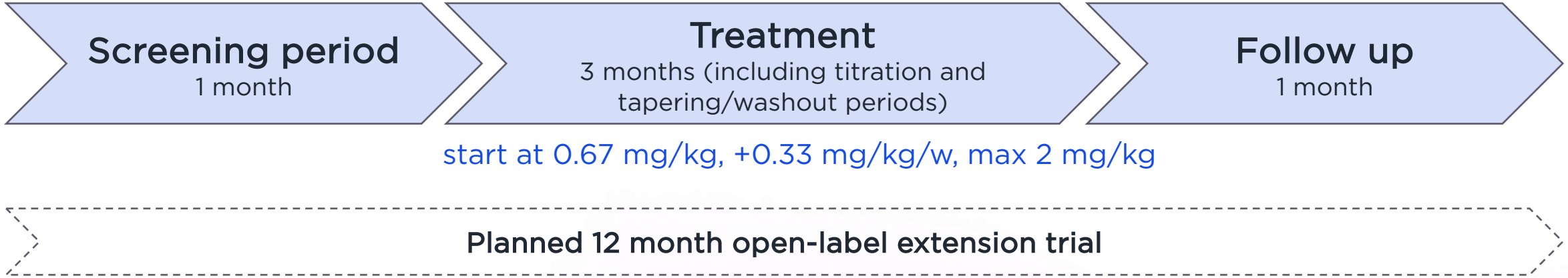
BREAKTHROUGH:
Bridging Resistance in Epilepsy with Advanced Therapies

BREAKTHROUGH Trial Design

An Open-Label Phase 2 Study

To Evaluate the Efficacy, Safety and Tolerability of BMB-101 in Adults:

- Absence Epilepsy (with or without Eyelid Myoclonia (Jeavons syndrome))
- Developmental Epileptic Encephalopathy (DEE)



BREAKTHROUGH Trial Design

An Open-Label Phase 2 Study

	INCLUSION criteria	EXCLUSION criteria
	DRUG-RESISTANT - Absence Epilepsy with or without eyelid myoclonia (Jeavons Syndrome) - Developmental and Epileptic Encephalopathy (DEE)	Cardiovascular disease (e.g. valvulopathy, EKG anomalies,…) Cerebrovascular disease Degenerative neurological disease Other disease/symptoms that can negatively impact the study or pose a risk to the subject
	If **Absence** epilepsy: 4 or > episodes of 3-4/s SWD (3s each) in 24h EEG (baseline)	Hepatic impairment Renal impairment
	If **DEE**: typical EEG pattern • 4 or > seizures on EEG (5s or >) in 24h EEG (baseline) • 4 or > seizures (baseline)	Participation in other clinical trial past 30 days or on an investigational medicinal product
	Tried 1 or > ASM at recommended dose/duration Stable dose current ASM for 4 or > weeks prior to baseline	Serotonergic therapies: fenfluramine, lorcaserin, SSRI,… Felbamate <1 year
	Male/female 18-65 years (Adult)	Drug or alcohol abuse

Focus on harder to treat epilepsies
Looking for higher impact

Absence Epilepsy
with or without Eyelid Myoclonia

Developmental Epileptic Encephalopathies **(DEEs)**

✓ **Phase 2** start at 0.67 mg/kg, +0.33 mg/kg/w, max 2 mg/kg

Study Details

Multi-center

N=20
18 years and older

- **Drug-resistant** population
- **Adult** epilepsy patients have higher rate of drug resistance & often harder to treat
- Extensive use of **EEG** for patient characterization & evaluation sustained efficacy

Focus on harder to treat epilepsies
Looking for higher impact

	Absence Epilepsy with or without Eyelid Myoclonia	Developmental Epileptic Encephalopathies (DEEs)
1 Endpoint	Number of generalized spike-wave discharges (GSWD) seen on EEG	Seizure frequency based on seizure diary

Study Details

- Multi-center
- N=20
  18 years and older

Focus on harder to treat epilepsies
Looking for higher impact

	Absence Epilepsy with or without Eyelid Myoclonia	Developmental Epileptic Encephalopathies (DEEs)
2 and 3 Endpoints	Seizure frequency based on seizure diary Quality of Life (QOLIE-31)	Number of electrographic seizures seen on EEG Quality of Life (QOLIE-31)

Study Details

Multi-center

N=20
18 years and older

- Safety objective: safety and tolerability
- Epilepsy is **more** than seizures (Quality of Life*)

*Chiang S, Moss R, Stern JM, Hughes I, Josephson SA, Pearce JR, Kopald BE, Patel AD, Rao VR. Development of a core outcome set for quality of life for adults with drug-resistant epilepsy: A multistakeholder Delphi consensus study. Epilepsia. 2023 Jan;64(1):170-183.

BREAKTHROUGH: Novel approach to use EEG as primary endpoint in Absence Epilepsy

	Absence Epilepsy with or without Eyelid Myoclonia	Developmental Epileptic Encephalopathies (DEEs)
EEG	GSWD (inter)ictal 3-6 Hz	E.g. DS and LGS: GSWD E.g. LGS: ictal 1.5-2.5 Hz

Seizures

- **Seizure diary**
- **EEG**

- Golden standard for clinical trials: seizure diary*
- Large uncertainty when using seizure diary
  - Underreporting (not witnessed and/or patient is not aware)
  - Subtle seizures
  - Nocturnal seizures (24h EEG)
- EEG is a **better** and **accepted** **endpoint****

*Egenasi CK, Moodley AA, Steinberg WJ, Adefuye AO. Current norms and practices in using a seizure diary for managing epilepsy: A scoping review. South African Fam Pract Off J South African Acad Fam Pract Care 2022;64:e1–9. https://doi.org/10.4102/safp.v64i1.5540.

**Buchhalter J, Neuray C, Cheng JY, D'Cruz O, Datta AN, Dlugos D, French J, Haubenberger D, Hulihan J, Klein P, Komorowski RW, Kramer L, Lothe A, Nabbout R, Perucca E, der Ark PV. EEG parameters as endpoints in epilepsy clinical trials - An expert panel opinion paper. Epilepsy Res. 2022 Nov;187:107028.

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	Absence Epilepsy with or without Eyelid Myoclonia	Developmental Epileptic Encephalopathies (DEEs)
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Seizures

- **Seizure diary**
- **EEG**

- Large uncertainty when using seizure diary
  - Underreporting (not witnessed and/or patient is not aware) e.g. absence epilepsy
  - **Subtle** seizures e.g. absence epilepsy
  - **Nocturnal** seizures (24h EEG): e.g. in DEEs
    - Dravet syndrome: predominant seizure in adults: **nocturnal TC** seizures
    - Lennox Gastaut syndrome: **nocturnal T** seizures

  Poor sleep quality can provoke seizures + seizure activity impacts sleep
- EEG is (**more recently**) being used for **treatment effect***

*Dömötör J, Clemens B, Puskás S, Fekete I. Decrease of global current source density predicts successful treatment in absence and juvenile myoclonic epilepsies. Epilepsy Res 2017;133:1–5.

BMB-101: Potential for Ideal Drug

A clinical trial is designed to explore several hypotheses and inform the direction of future pivotal trials:

- Short-term & long-term efficacy of G-protein biased 5-HT_{2C} agonist in epilepsy patients
  - In DEE
  - In Absence epilepsies
- BID, with potential to once-a-day formulation
- Assess the effects in adult patients (unmet need)
- Endpoints
  - Golden standard (seizure diary)
  - "Harder" endpoint (24h EEG; nocturnal events)
  - "Beyond" seizures (e.g. Quality of Life)

Topline results expected in Q2 2025

BMB-101: Potential for Ideal Drug

Potency and Selectivity

- Very potent and selective at 5-HT_{2C} receptor
- No significant activity at other 5-HT receptors

Safety in clinical trials Phase 1

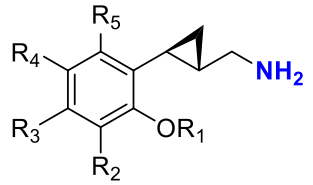
- Safe and tolerable at all tested doses
- Excellent PK/PD properties and central target engagement

Optimized for chronic treatment

- Potential for once-a-day formulation
- Designed to have sustained efficacy without tolerance

Strong IP

- Granted patent until 2036
- Possible extension to 2041



BMB-101

Novel 5-HT_{2C}
Selective Agonist

Business case

Market potential

BMB-101 – Novel scaffold 5-HT_{2C} agonist

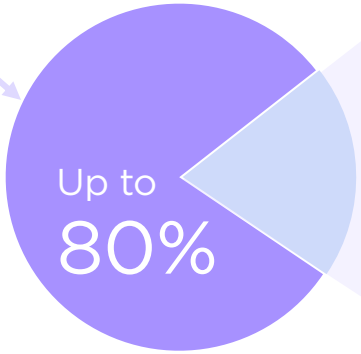
	BMB-101	Lorcaserin	Fenfluramine/ Norfenfluramine	LP352/ Bexicaserin
Lack of 5-HT_{2B} liability *(related to cardiac toxicity)*	✓	✓	x	✓
5-HT_{2C} Biased Agonism *(Sustained efficacy)*	✓	x	x	x
No 5-HT_{2A} Dose limiting effects	✓	x	x	✓
Can be Dose-optimized	✓	x	x	✓
Increased Frontal Gamma power on qEEG	✓	Not reported	Not reported	Not reported
Dosing	Once/Twice daily	Twice daily	Twice daily	Three times daily
Development Stage	Phase 2	Phase 3	Approved	End of Phase 2
Indications	EEM/DEE→ Absence Epilepsy	Dravet Syndrome	Dravet Syndrome LGS	Dravet Syndrome/LGS → Broad DEE

Epilepsy with Eyelid Myoclonia

Absence Epilepsy with high drug resistance and without approved drugs

BMB-101
Potential for the first approved drug

- ~90,000 patients in the USA
- 2:1 female predominance
- 6-8 years childhood onset. Diagnosis is often delayed to adolescence and adulthood
- Seizures persist in adulthood



Drug-resistant epilepsy

First line:
Valproic acid, levetiracetam, lamotrigine

Second line:
Ethosuximide, clobazam

Dietary changes (keto-diet)

Avoid
Sodium channels blocking medications (except lamotrigine). CBD even worsens seizures in EEM patients

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Market potential

Projected US market

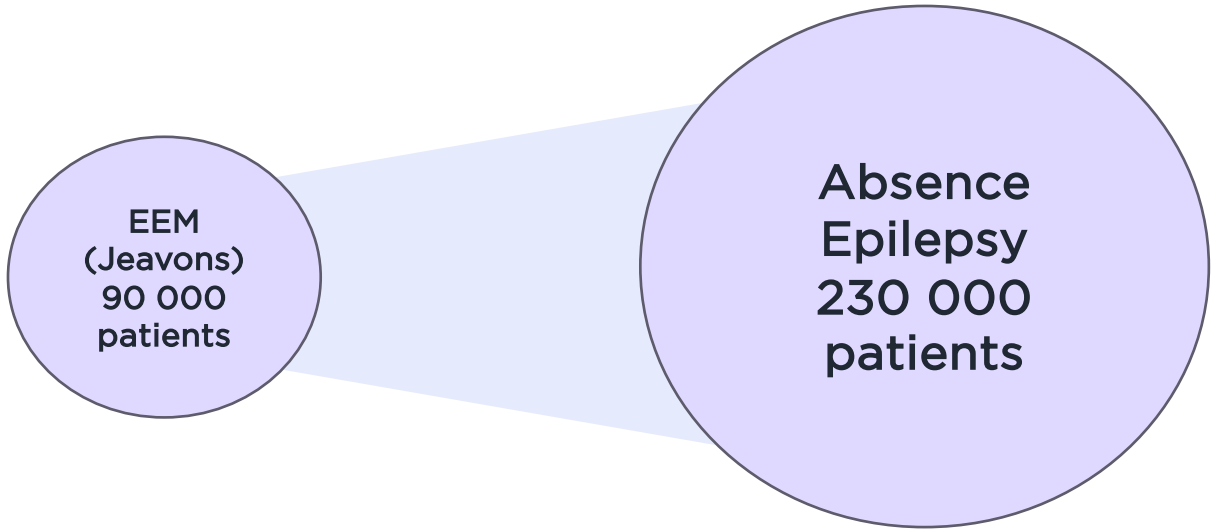
Strong IP protection until

2041*

*Including PTE extensions

Additional patent applications made to further extend market exclusivity

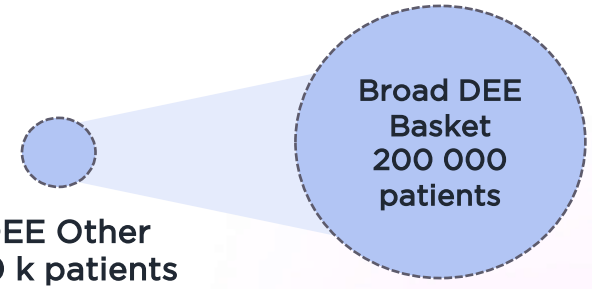
Jeavons->Absence epilepsy approach



~$2 Bn

Peak revenue potential

DEE approach



~$2 Bn

Peak revenue potential

Overcrowded drug development space

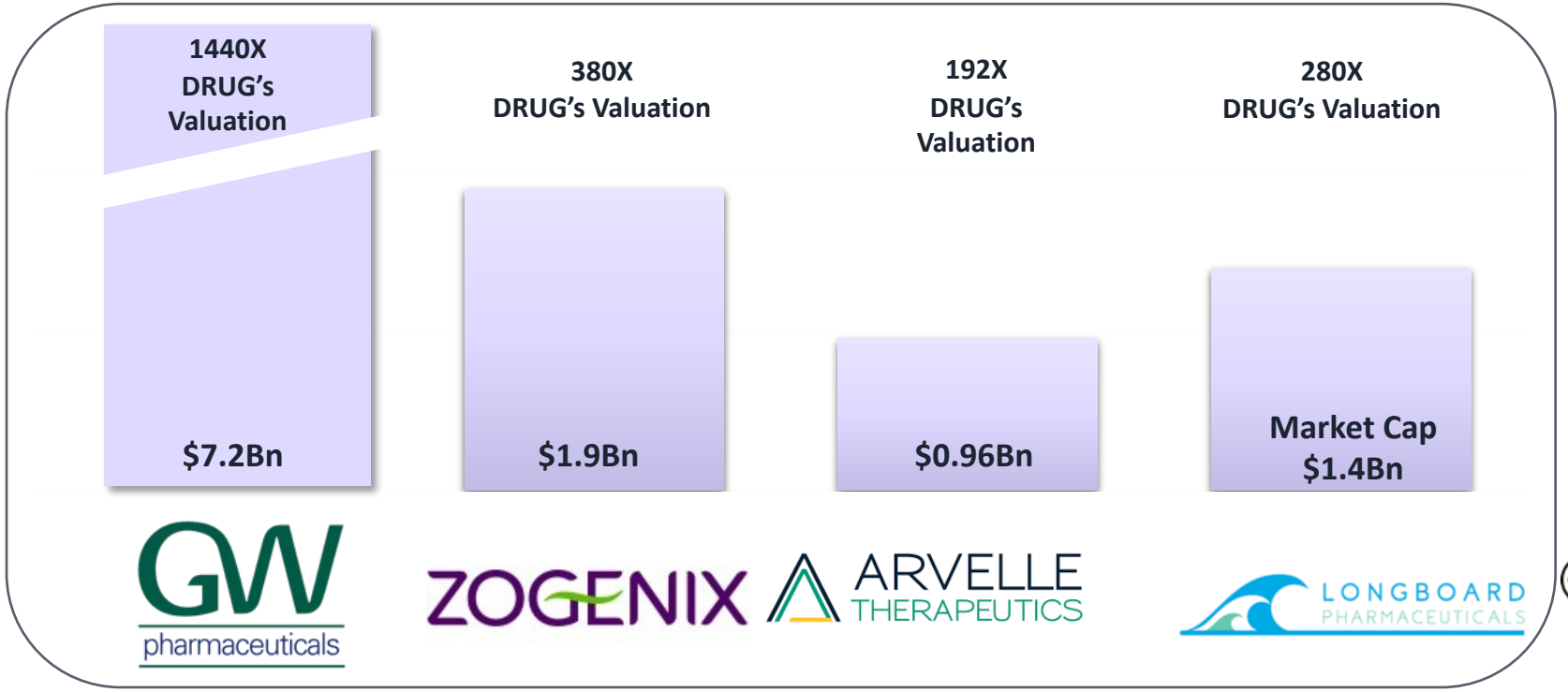
Dravet
Cannabidiol
Fenfluramine
Stiripentol
Clobazam
Topiramate
Bexicaserin
STK-001
other

LGS
Cannabidiol
Lamotrigine
Topiramate
Felbamate
Rufinamide
Fenfluramine
Bexicaserin
other

CDKL5
Ganaxolone

TSC
Epidiolex
Evirolimus
Ganaxolone

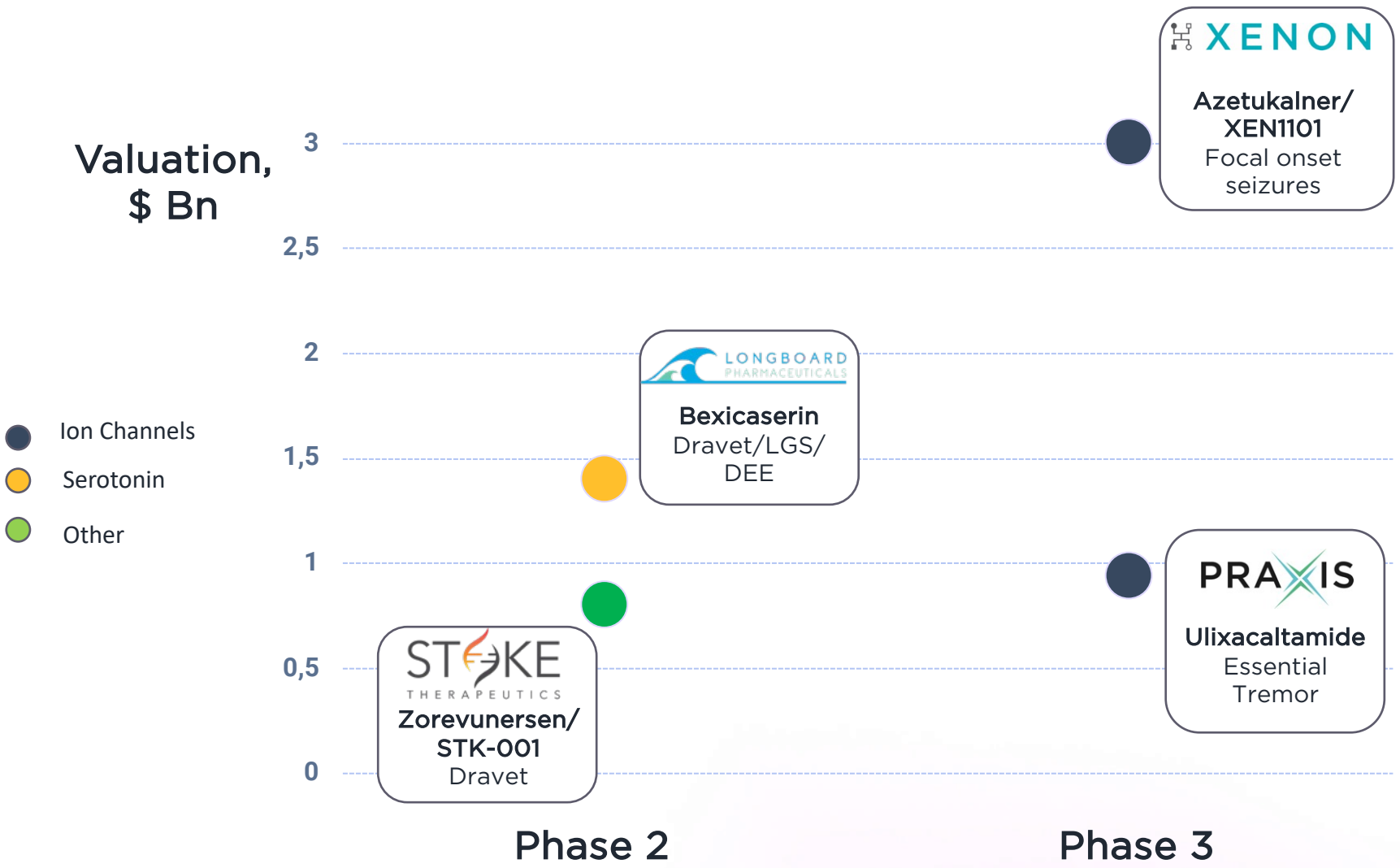
Undervalued relative to rare epilepsy peers



Transaction Value	$7.2Bn	$1.9Bn	$0.96Bn	$1.4Bn M CAP	$5M M CAP
Indication	Epidiolex (Childhood-onset epilepsy)	Fintepla (Dravet syndrome)	Cenobamate (Focal seizures) - EU Rights	Bexicaserin DEE basket	BMB-101 Absence/DEE basket
Date of Transaction	May, 2021	March, 2022	January, 2021	Public - NASDAQ:LBPH	Public - NASDAQ:DRUG
Stage of Development	Marketed	Marketed	Marketed	End of Phase 2	Initiating Phase 2
Acquirer Name	JAZZ Pharmaceuticals	UCB	Angelini Pharma		

*as of September 1, 2024

Biotech Companies in Rare CNS



Recent deals in 2023:

- **Karuna 14B** by **BMS** (Multiple CNS)
- **Cerevel 8.7 Bn by Abbvie** (Schizophrenia/Epilepsy/ Parkinson's)

*as of September 1, 2024

BMB-101

Novel 5-HT_{2C}
Selective Agonist

Breaking through

Drug resistant epilepsies

Q&A session