BRIGHT MINDS

Novel Drugs for Targeted Treatment of

CNS & Neuropsychiatric Disorders

June 2025

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Bright Minds Biosciences (NASDAQ: DRUG)

2041
BMB-101
IP Protection

$2Bn
DEE
Market opportunity

$2Bn
Absence epilepsies
Market opportunity

2027
Cash Runway

5-HT_{2C}

Best-in-class mechanism in DEE epilepsies

Relevant M&A deals

GW pharmaceuticals — $ 7.2 Bn (2021) → Jazz Pharmaceuticals

ZOGENIX — $ 1.9 Bn (2022) → UCB

LONGBOARD PHARMACEUTICALS — $ 2.6 Bn (2024) → Lundbeck

Pipeline

Rich and diverse portfolio in neurology and psychiatry with multiple programs

Lead	Indications	Research	Ph-1	Ph-2
5-HT$_{2C}$ agonists for CNS disorders				
BMB-101	DEE Absence epilepsy			Clinical Studies – Phase 2
BMB-10x	Obesity and feeding behaviour		ADME/PK profiling	
Non-hallucinogenic psychoplastogens				
BMB-201	Treatment-resistant depression		IND-enabling studies	
5-HT$_{2A}$ agonists for the treatment of depression				
BMB-202	Depression (Fast-onset)		IND-enabling tox	
BMB-xxx	Neurology / Neuropsychiatric Indication		ADMEPK profiling	

Drug-resistant epilepsy is still a significant issue

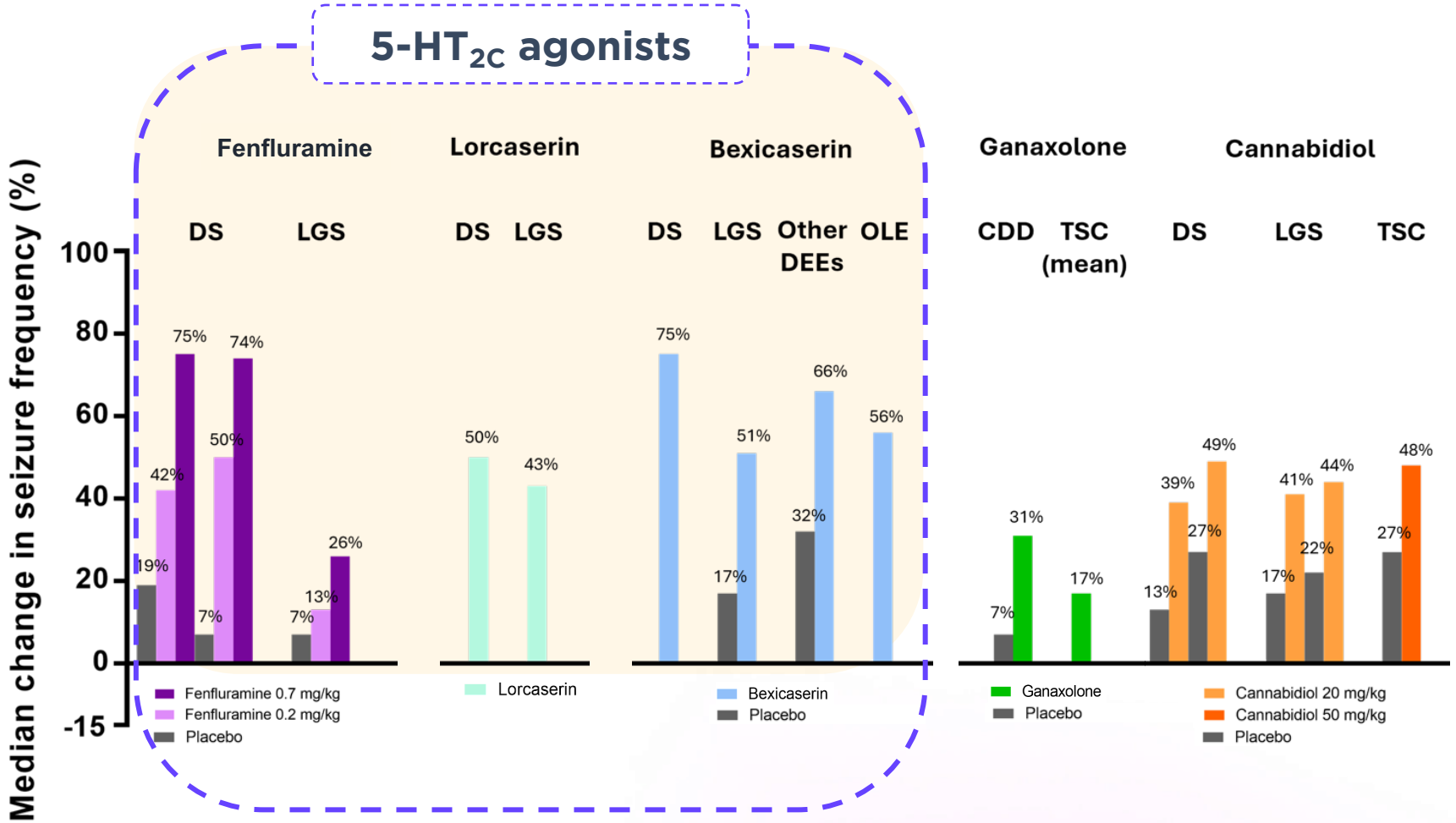
~30%
of Epilepsy patients develop drug resistance

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

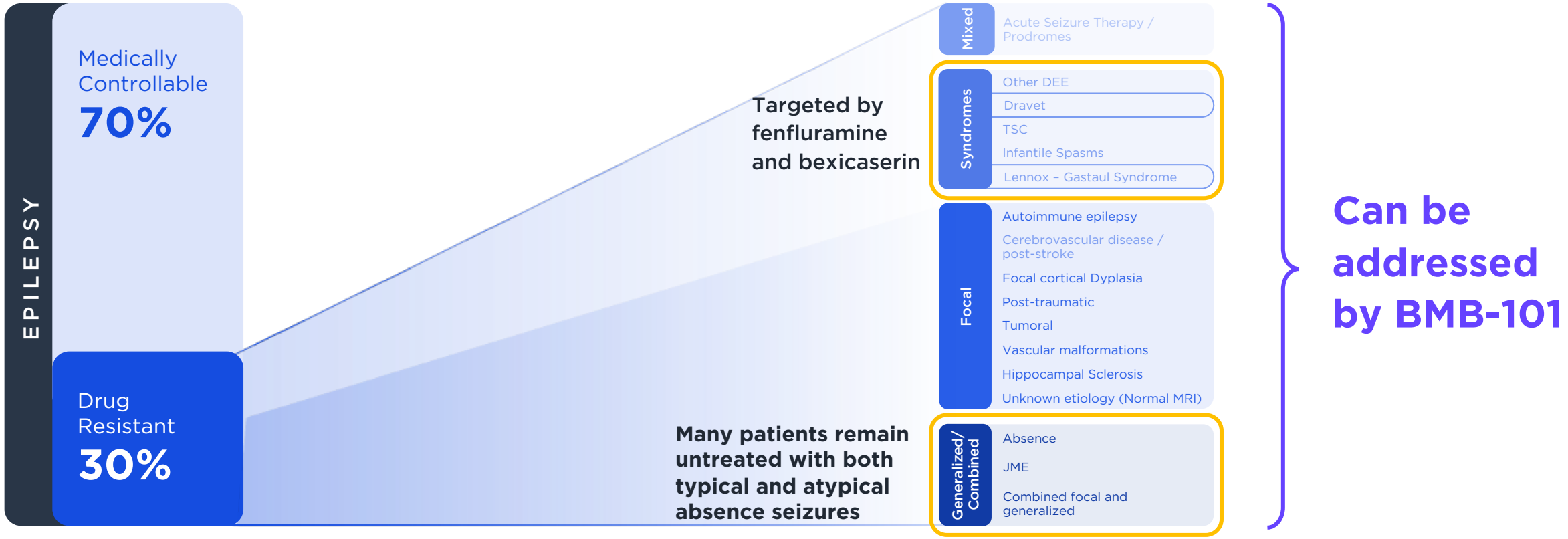
5-HT$_{2C}$ agonism provides superior efficacy in DEE epilepsies



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

High unmet need beyond Dravet

Addressable targets for BMB-101 range across multiple epilepsies



Today Suppression of seizures in Broad Epilepsy Population (~65 Million)

Future Focus on epilepsies without treatments

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

Best-in-class

5-HT_{2C} Selective Agonist

First-in-class

G-protein biased agonist

BMB-101 is uniquely positioned to address major unmet needs in epilepsy

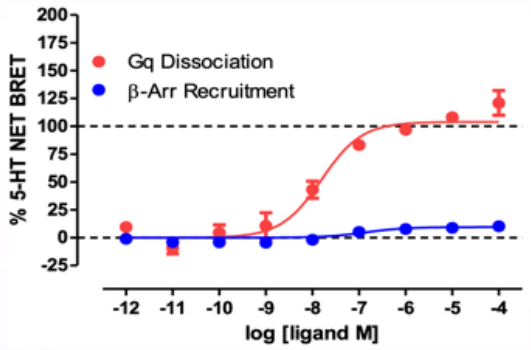
Highly selective 5-HT2C agonist

Compound	5-HT2A	5-HT2B	5-HT2C
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

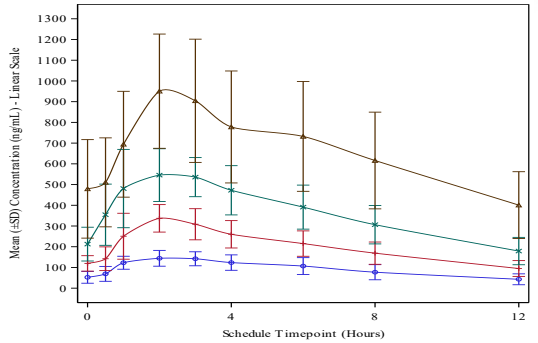
Improved safety profile

The only G protein-biased 5-HT2C agonist



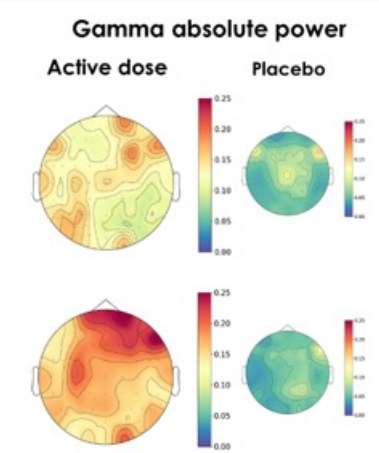
Sustained chronic effect via reduced tolerance

Safety and PK/PD properties validated in Phase 1



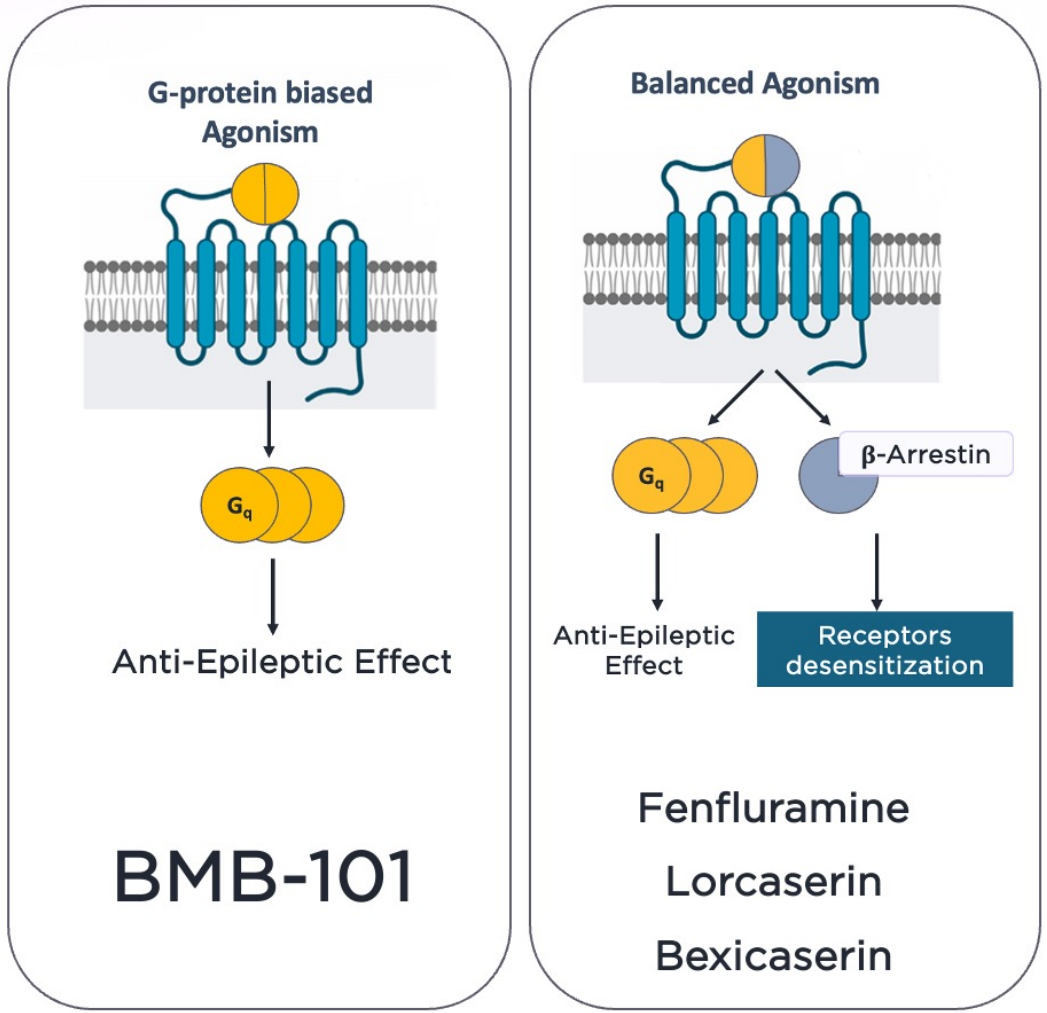
Potential for a more convenient once daily formulation

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



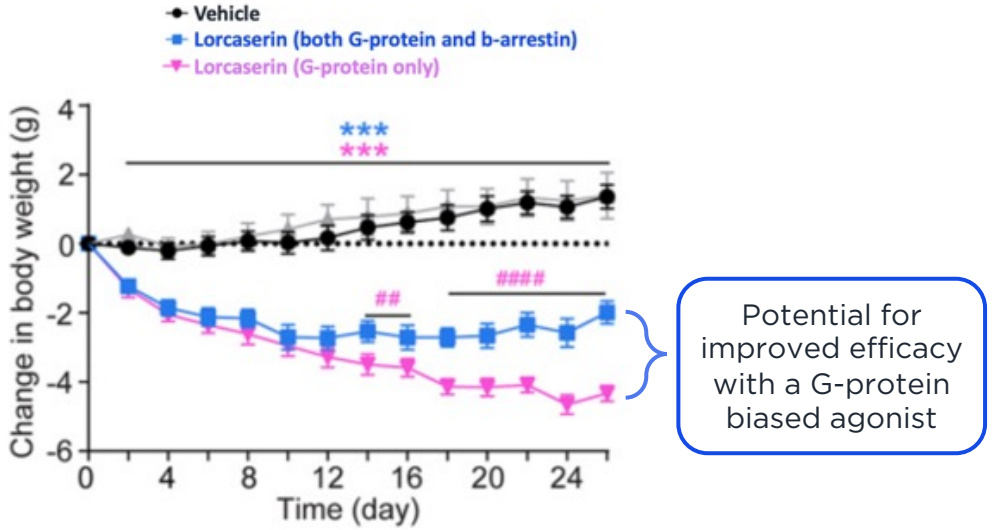
Additional behavioral/cognitive benefits

Novel 5-HT$_{2C}$ mechanism to avoid tolerance pathways



Beta-arrestin activation is associated with receptor desensitization and the development of tolerance.

BMB-101 is designed to avoid b-arrestin activation and produce sustained effect.



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

[1]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 – Novel scaffold 5-HT_{2C} agonist

	BMB-101	Fenfluramine/ Norfenfluramine	LP352/ Bexicaserin
Lack of 5-HT_{2B} liability *(related to cardiac toxicity)*	✓	x	✓
5-HT_{2C} Biased Agonism *(Sustained efficacy)*	✓	x	x
Can be Dose-optimized	✓	x	x
Increased Frontal Gamma power on qEEG	✓	Not reported	Not reported
Dosing	Once/Twice daily	Twice daily	Three times daily
Development Stage	Phase 2	Approved	Phase 3
Indications	**Broad DEE Absence Epilepsy**	Dravet Syndrome LGS	Dravet Syndrome/LGS → Broad DEE

BMB-101 Phase 1 study

Favorable Safety & Tolerability Results Observed

Single Ascending Dose
4 cohorts (6 drug and 2 placebo)

Food Effects
12 subjects

Multiple Ascending Dose
4 cohorts (6 drug and 2 placebo)
Quantitative electroencephalogram (qEEG) recording in Cohort 4

Safety and tolerability

- **No SAEs observed, all AEs were transient**
- **Most common adverse effect - oral paresthesias (related to the sweet taste of the drug product)**
- **Most common on target AE – Headache, Nausea and photophobia**
  - **Common AEs for serotonergic drugs**
  - **Only seen at the top dose (2-3x of predicted therapeutic dose)**
- **Lower incidence of somnolence and GI side effects than with other 5-HT_{2C} agonists**

BMB-101 Phase 1 study

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%)
Somnolence	-	-	-	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

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

BMB-101 Phase 2 BREAKTHROUGH Study

An Open-Label Phase 2 Study

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

- Absence Epilepsy
- Developmental and Epileptic Encephalopathy (DEE)

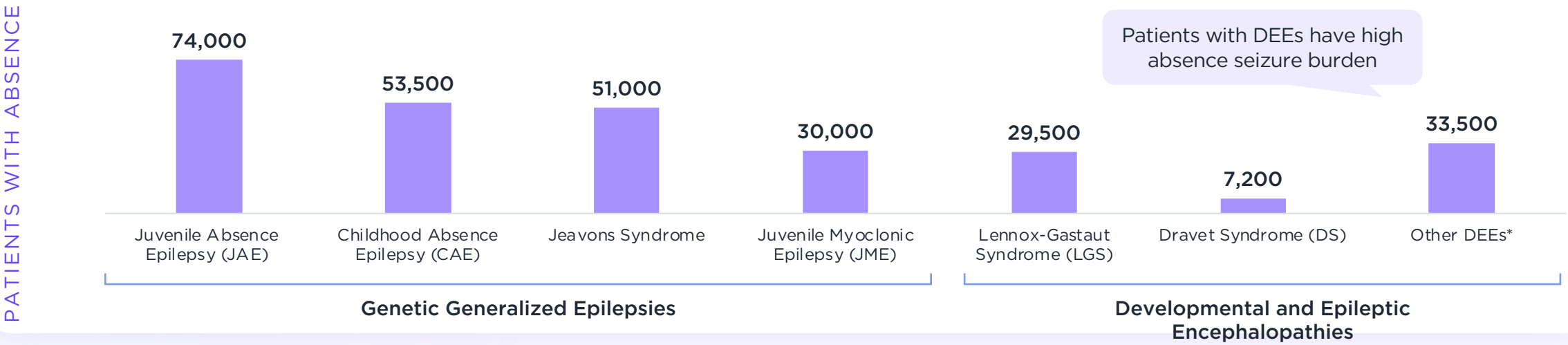
start at 0.67 mg/kg, +0.33 mg/kg/w, max 2 mg/kg

KEY ENDPOINTS:

- **Safety and tolerability of BMB-101**
- **Efficacy**
  - **Absence Epilepsy:**
    - Number of generalized spike-wave discharges seen on EEG
    - Seizure frequency based on seizure diary
    - Quality of Life (QOLIE-31)
  - **DEEs:**
    - Seizure frequency based on seizure diary
    - Number of electrographic seizures seen on EEG
    - Quality of Life (QOLIE-31)

Estimates indicate a total absence prevalence of at least 280K in the USA only

US Prevalence of Absence Across Common Epilepsy Syndromes



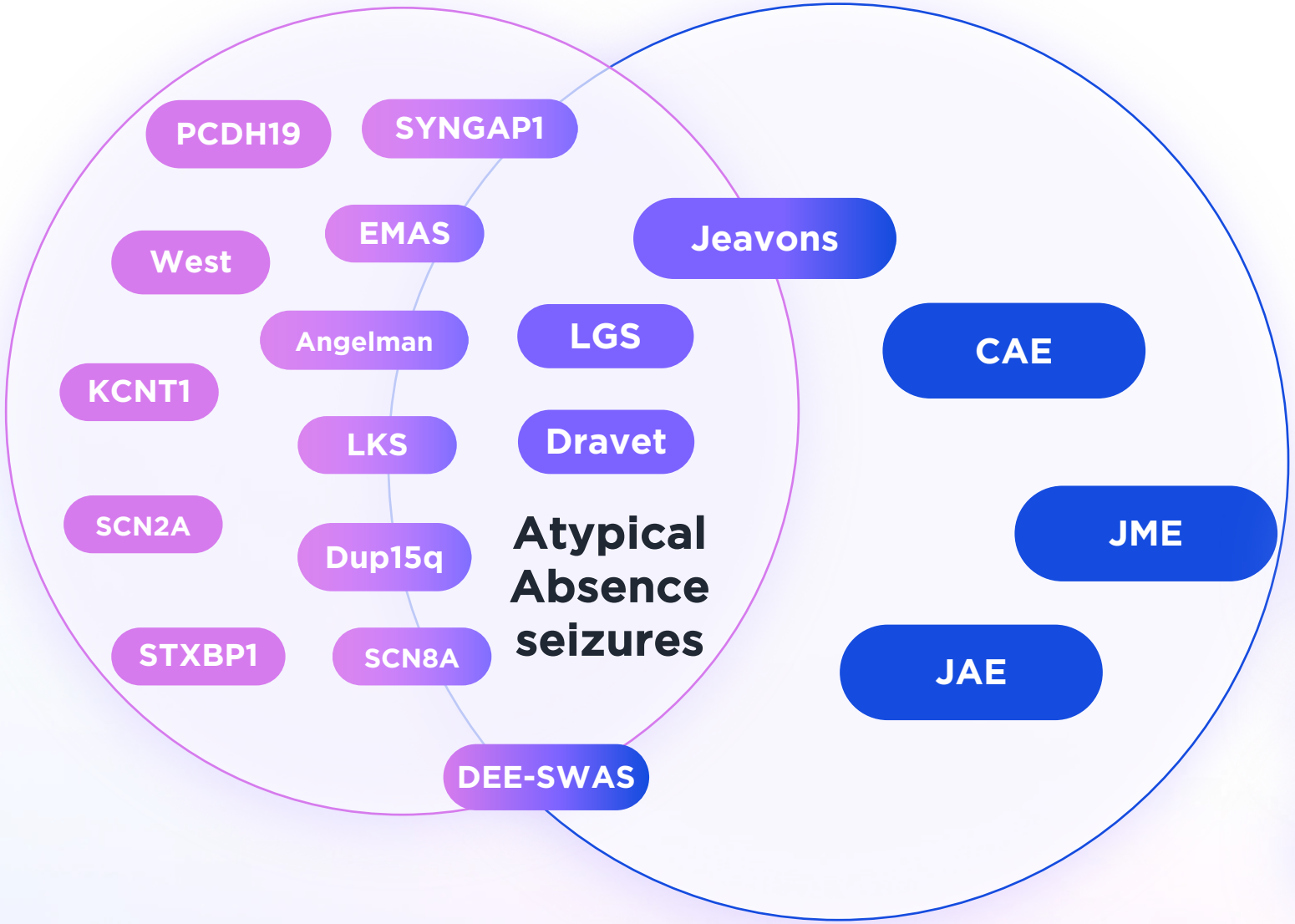
Indication	Prevalent Patients	% with Absence Seizures	Prevalent with Absence
Juvenile Absence Epilepsy (JAE)	74,000	100%	74,000
Childhood Absence Epilepsy (CAE)	53,500	100%	53,500
Juvenile Myoclonic Epilepsy (JME)	150,000	20%	30,000
Jeavons Syndrome (EEM)	64,000	80%	51,000
Lennox-Gastaut Syndrome (LGS)	49,000	60%	29,500
Dravet Syndrome (DS)	13,000	55%	7,200
Other DEEs*	--	--	33,500
Total	--	--	**278,700**

* Other DEEs included in this estimate are Dup15q, EMAS, Angelman Syndrome, SNYGAP1, DEE-SWAS, and SCN8A; ASM: Anti-seizure medication; EEM: Epilepsy with Eyelid Myoclonia

* Prevalence estimates are presented as median values, source: research from Trinity Life Sciences

Opportunity for BMB-101

DEEs



Efficacy of branded DEE drugs in Absence seizures is limited or unknown

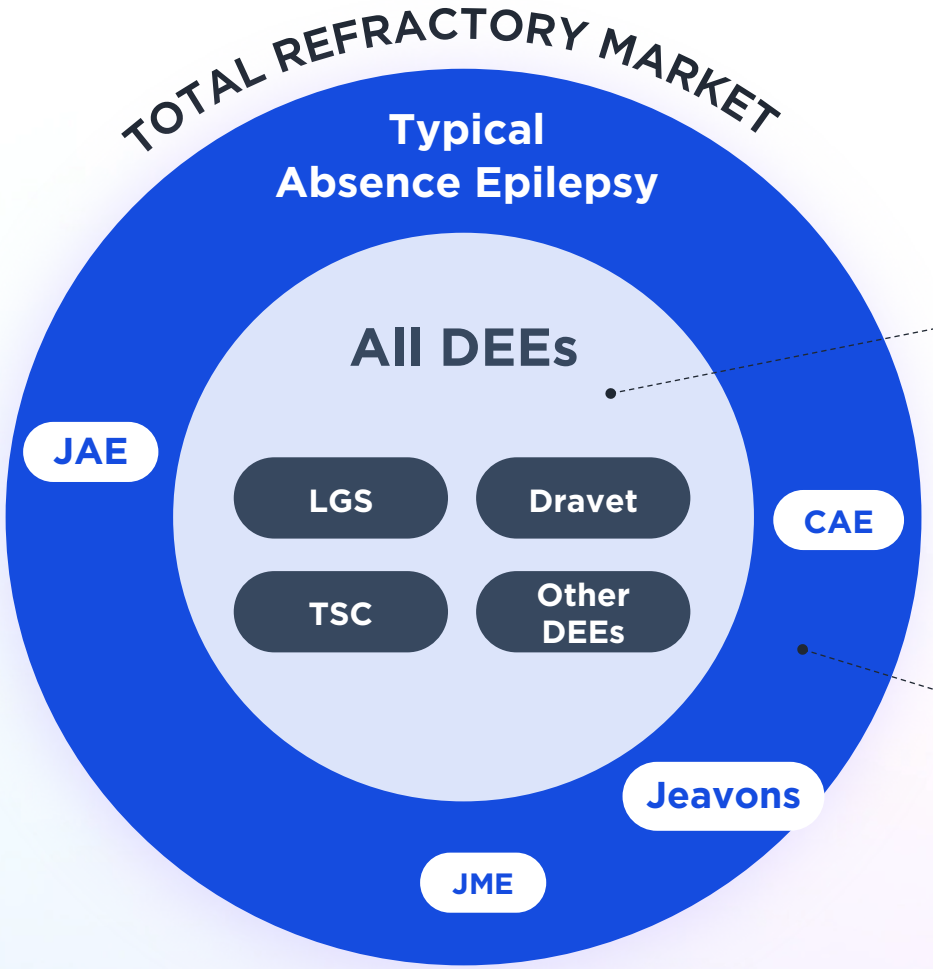
GABA modulation may worsen absence seizures

Epidiolex was reported to worsen seizures in Jeavons syndrome*

ABBREVIATIONS:
CAE: Childhood Absence Epilepsy; DEE: Developmental and Epileptic Encephalopathy; JAE: Juvenile Absence Epilepsy; JME: Juvenile Myoclonic Epilepsy; LGS: Lennox-Gastaut Syndrome; TSC: Tuberous Sclerosis Complex

*Sources: Perucca E, et al.. CNS Drugs. 2023, Zawar I, et al . Epileptic Disord. 2021

Potential for best-in-class drug in DEE and absence seizures



– Opportunity in All DEEs

– Opportunity with Absence

All DEE Refractory Market

~$16B

Absence Epilepsy Refractory Market

~$5.1B

~$21B
Total Refractory Market

Additional research needed to assign a product-specific peak sales estimate

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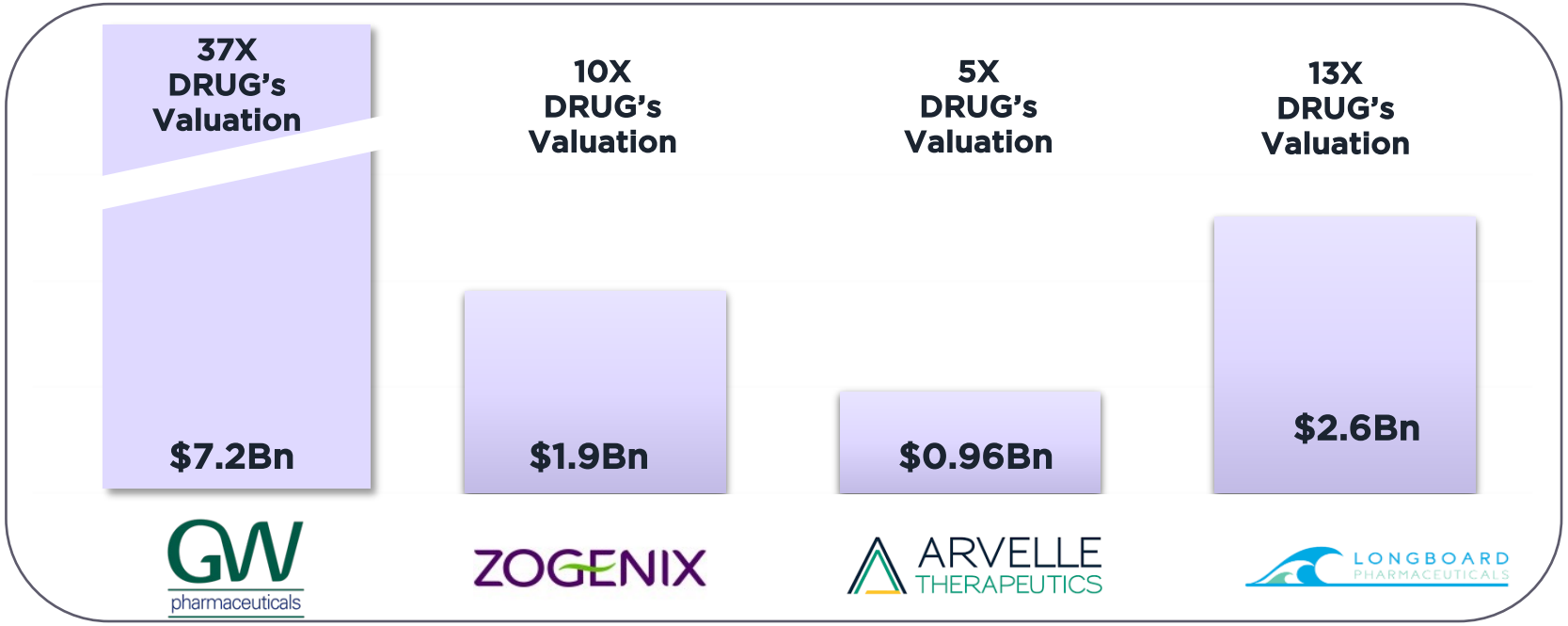
Undervalued relative to rare epilepsy peers



BRIGHT MINDS

Transaction Value	$7.2Bn	$1.9Bn	$0.96Bn	$2.6Bn	$195M M CAP
% Premium (30-day volume)	50%	72%	N/A (Private)	77%	N/A
Indication	Epidiolex (Dravet, LGS, TSC)	Fintepla (Dravet syndrome)	Cenobamate (Focal seizures) - EU Rights	Bexicaserin Dravet Syndrome and DEE basket	**BMB-101** Absence/DEE basket
Date of Transaction	May, 2021	March, 2022	January, 2021	October 2024	Public - NASDAQ:DRUG
Stage of Development	Marketed	Marketed	Marketed	Phase 3	Phase 2
Acquirer Name	JAZZ Pharmaceuticals	UCB	Angelini Pharma	Lundbeck	

*as of May 30, 2025

BMB-101 – Opportunity for Best-In-Class 5-HT_{2C} agonist

Well-Tolerated Safety & Flexible Dosing

- BID dosing; potential for QD
- Well-tolerated in Ph1 SAD/MAD (most AE only seen at the high dose)
- No daily dose limitations allowing for flexible dosing in both adult and pediatric patients

Favorable PK Profile

- Reduced on-target adverse events attributed to lower C_{max} compared to bexicaserin
- No significant food effects observed in Ph1 SAD/MAD
- PK linear and dose-proportional over the therapeutic range

Optimal 5-HT_{2C} Pharmacology

- Biased G-protein agonism of 5-HT_{2c} with sustained receptor activation
- Lack of β-arrestin pathway recruitment ensuring lack of receptor desensitization
- Decades-long safety profile of parent molecule

Ideal Properties for Commercial Supply

- API stable at room temperature and 40℃; no cold chain is required for commercial supply
- API stability: no degradation for at least 3 years in the ongoing studies
- Liquid formulation: at least 2 years

Appendix

Absence Epilepsy & Seizures

Absence seizures impact on patients' lives

- **Absence seizures are defined as profound impairments of consciousness**
    - Typical Absence Seizures last 10-30 seconds
    - Atypical Absence Seizures last up to 90 seconds
- **Consequences of the absence seizures ("Silent killers")**
    - Impaired attention - difficulties with learning and social interactions.
    - Reduced safety of mobility - risk of falls, no driving, no swimming, etc
    - Disrupted frontal connectivity.
        - Functional impairment
        - Memory and cognition deficits
        - Impaired learning

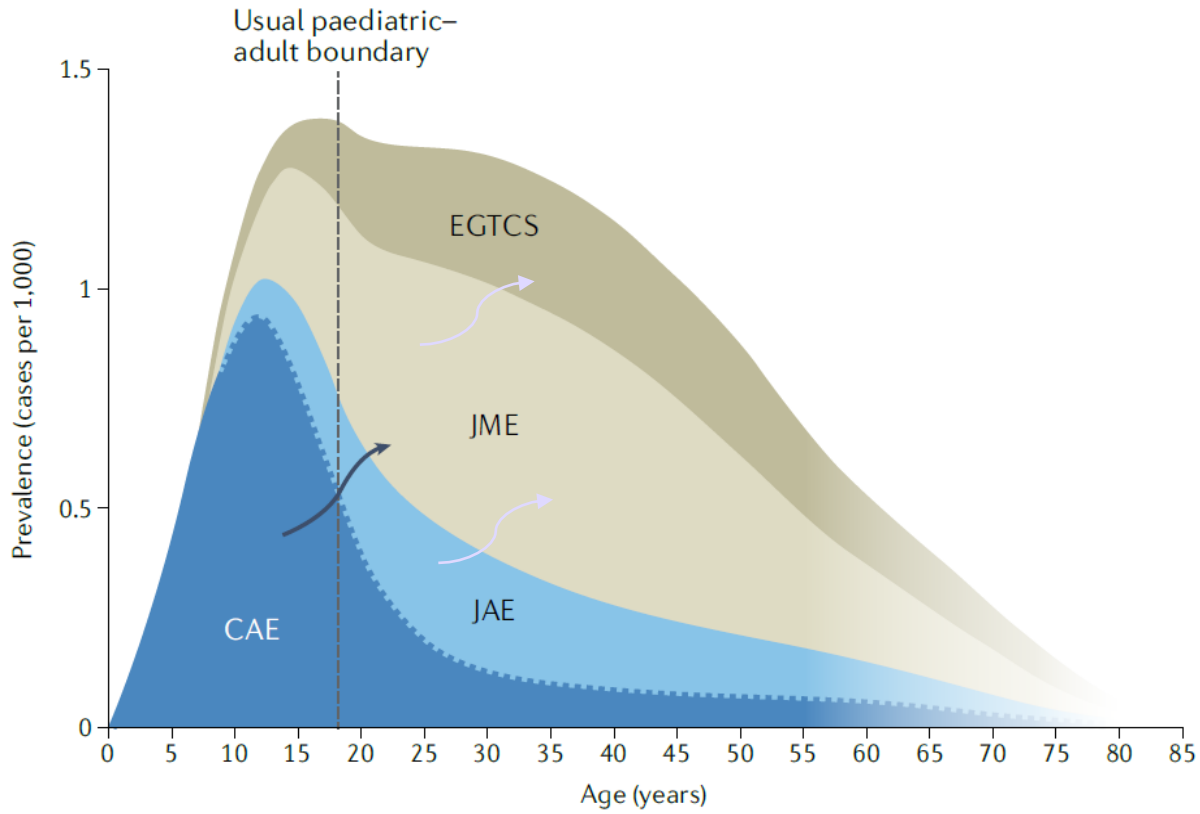
Fonseca Wald ELA, Hendriksen JGM, Drenthen GS, Kuijk SMJV, Aldenkamp AP, Vles JSH, Vermeulen RJ, Debeij-van Hall MHJA, Klinkenberg S. Towards a Better Understanding of Cognitive Deficits in Absence Epilepsy: a Systematic Review and Meta-Analysis. Neuropsychol Rev. 2019 Dec;29(4):421-449.
Sun J, Li Y, Zhang K, Sun Y, Wang Y, Miao A, Xiang J, Wang X. Frequency-Dependent Dynamics of Functional Connectivity Networks During Seizure Termination in Childhood Absence Epilepsy: A Magnetoencephalography Study. Front Neurol. 2021 Oct 25;12:744749.

Idiopathic Generalized Epilepsies (IGE) overlap in age and presentation

Prevalence across age

IGE syndromes transition from one to another

Absence seizures remain common even in adulthood (~20-40% of JME)



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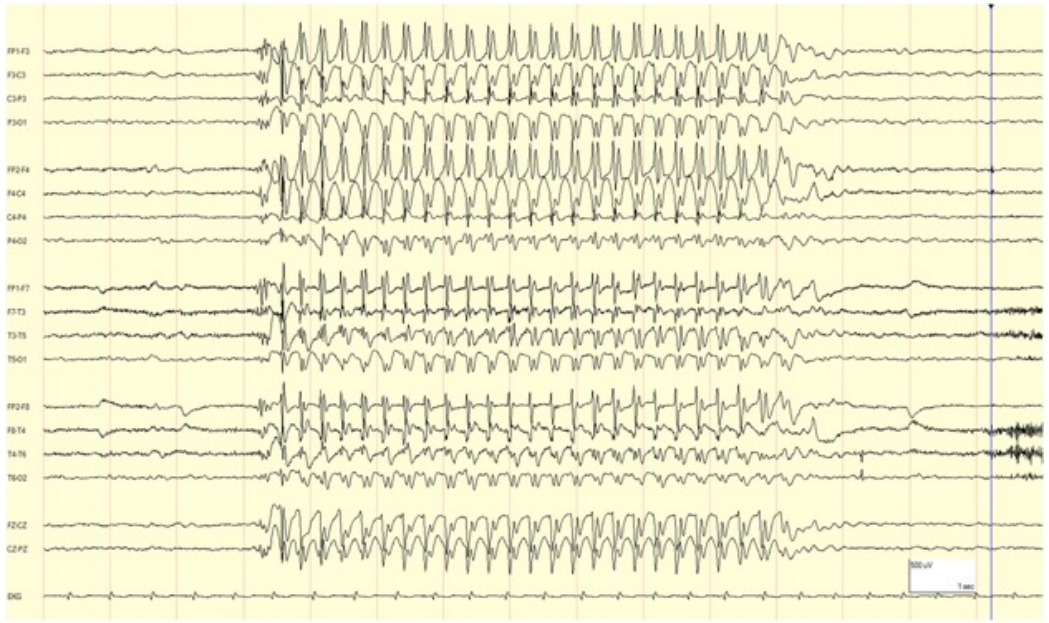
CAE: Childhood Absence Epilepsy; DEE: Developmental and Epileptic Encephalopathy; JAE: Juvenile Absence Epilepsy; JME: Juvenile Myoclonic Epilepsy; EGTCS: Epilepsy with generalized tonic-clonic seizures

Vorderwülbecke et al., Nature Reviews 2022

What is an absence seizure?

Absence seizure is defined as:

- A distinct 3/s spike-and-wave discharge – an abnormal, and unique paroxysmal pattern of a high velocity spike followed by a slower dome shaped wave on the background of a normal EEG.
- The 3/s spike-and-wave on EEG is the clinically accepted proof of absence seizure, has extremely high specificity and sensitivity, and has been so defined for over 70 years



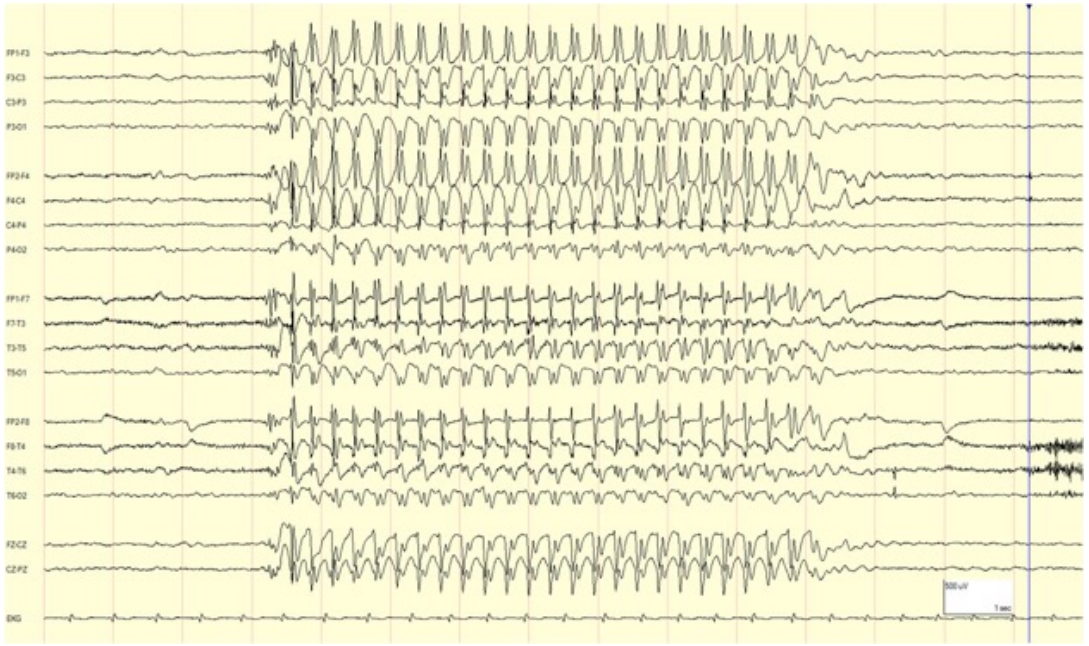
Source: ILAE https://www.epilepsydiagnosis.org/seizure/absence-typical-eeg.html

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.
Porter, R. J. (1993). The Absence Epilepsies. Epilepsia, 34, S42–S48

How are we documenting absence seizures?

Primary Method

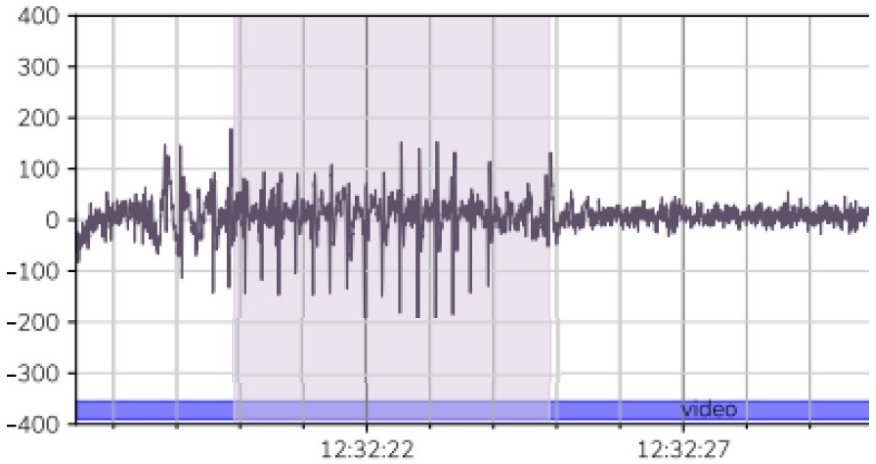
24h EEG Ambulatory



- ✓ Quantitative seizure detection
- ✓ Potential for sleep assessment

Exploratory Method

Wearable EEG device



- ✓ Designed and validated for absence seizure detection
- ✓ Convenient absence seizure monitoring

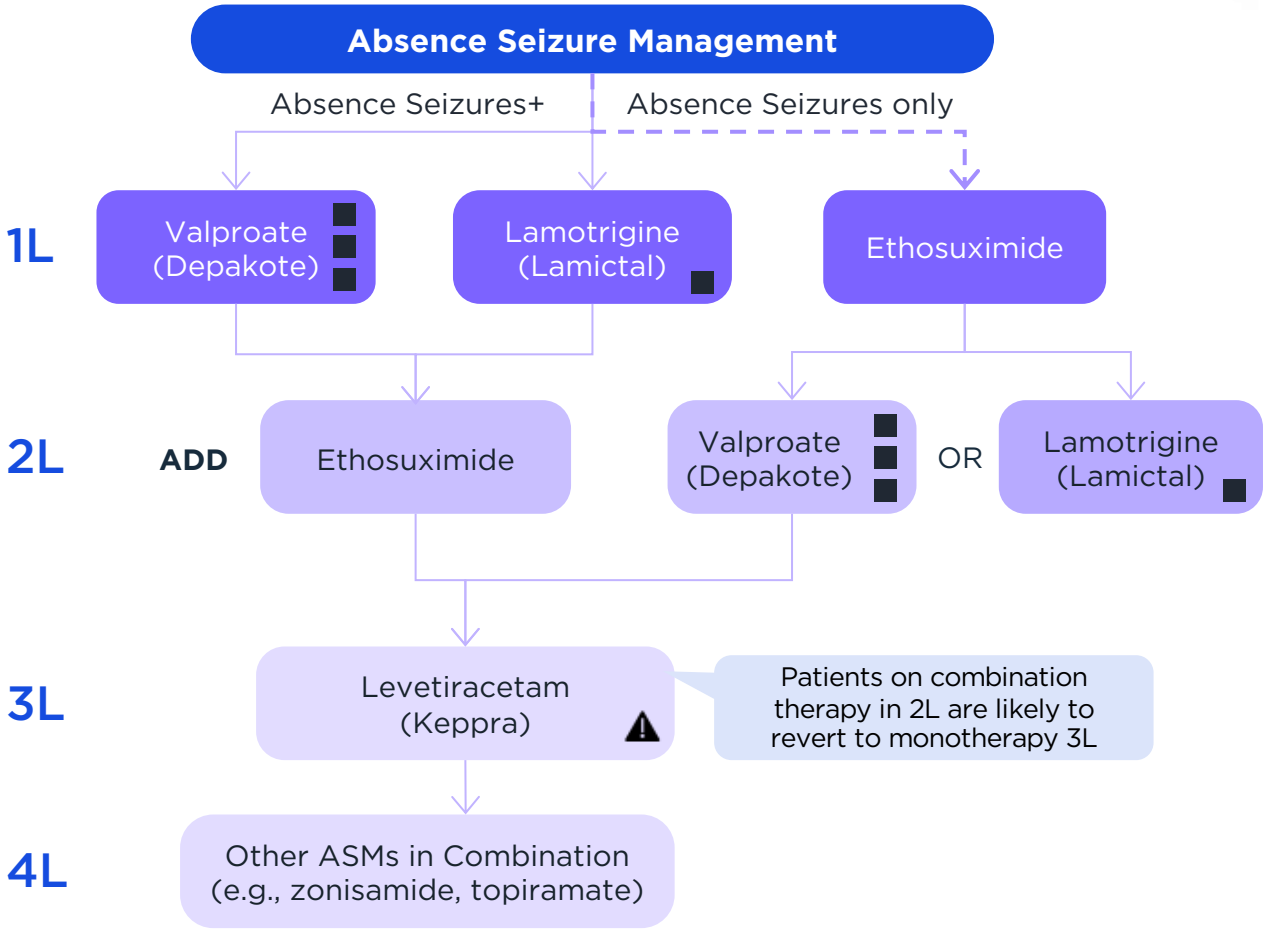
Source: ILAE https://www.epilepsydiagnosis.org/seizure/absence-typical-eeg.html

Why are we developing novel drugs for absence seizures?

Absence epilepsies have high unmet need

- Current drugs don’t effectively treat all patients and have tolerability and potentially even severe safety issues
- The unmet need is in both people with typical absence and those with mixed seizure disorders, including DEE’s. All of these patients need an effective, wide-spectrum, safe and well-tolerated therapy.

Limited treatment options represent significant opportunity for new branded agent in the absence treatment paradigm



Ethosuximide

- Standard-of-care drug for CAE - only manages absence seizures (narrow-spectrum)
- Associated with GI disturbance

Valproate (three FDA black boxes) ■ ■ ■

- Not preferred for first-line in females due to its association with birth defects
- Also associated with hepatotoxicity, it requires liver monitoring which adds additional burden for patients

Lamotrigine (one FDA black box) ■

- more limited in effectiveness against absence seizures
- often selected in 2L, particularly in females due to lack of terratogenicity

Levetiracetam (FDA warning – DRESS) ⚠

- often used later-line and not preferred in patients with co-morbid behavioral issues

4L+ options are limited due few antiseizure medicines with proven efficacy against typical and atypical absence seizures

■ A “black box” warning, also known as a boxed warning, is the strictest and most serious warning issued by the FDA for prescription drugs. This warning is displayed alert healthcare providers and patients to serious or life-threatening risks associated with the medication

⚠ DRESS - Drug Reaction with Eosinophilia and Systemic Symptoms

Kessler SK, McGinnis E. A practical guide to treatment of childhood absence epilepsy. Paediatr Drugs Internet. 2019
Albuja A, Ighodaro E, Khan GQ. Absence Seizure Internet. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024

Opportunities for other BMB 5-HT2 agonists

Opportunities for 5-HT_{2C} agonists
In the treatment of feeding disorders and obesity

BMB-10X Feeding behaviour and Obesity	BMB-10X Genetic Obesity and Rare Metabolic Disorder
Description	
✓ To be used in conjunction with GLP1 agonists	✓ PWS is debilitating neuropsychiatric disorder
✓ Improved fat-mass weight-loss	✓ Will treat compulsive over-eating (hyperphagia)
✓ Designed improve feeding behaviour after GLP1 agonist treatment	✓ Will also treat neuropsychiatric symptoms of PWS: Compulsivity, Anxiety.
✓ Proprietary NCE	✓ Proprietary NCE
✓ ADMEPK profiling ongoing	✓ ADMEPK profiling ongoing
✓ Designed for chronic use	✓ Designed for chronic use

BMB-201 and 202 – potential for best-in-class 5-HT_{2A} agonists

BMB-201

Potent inducer of neuroplasticity

Description

- ✓ Designed to have minimal or absent psychoactive effects
- ✓ Efficacy in rodent models of depression, anxiety, pain, substance use disorder
- ✓ Proprietary NCE
- ✓ ADMEPK profiling completed

Treatment paradigm

Designed for chronic use and use at home

BMB-202

The most selective 5-HT_{2A} agonist in development*

Description

- ✓ Designed to have short psychoactive effects time
- ✓ Durable effects in rodent models of depression and anxiety
- ✓ Proprietary NCE
- ✓ ADMEPK profiling completed

Treatment paradigm

Designed for fast relief of depression and Infrequent use

*Based on publicly available information as of December 2024