



GABA Therapeutics, Inc. – October 2026

GRX-917 – Safe, Fast & Effective Anxiolytic for Chronic Use



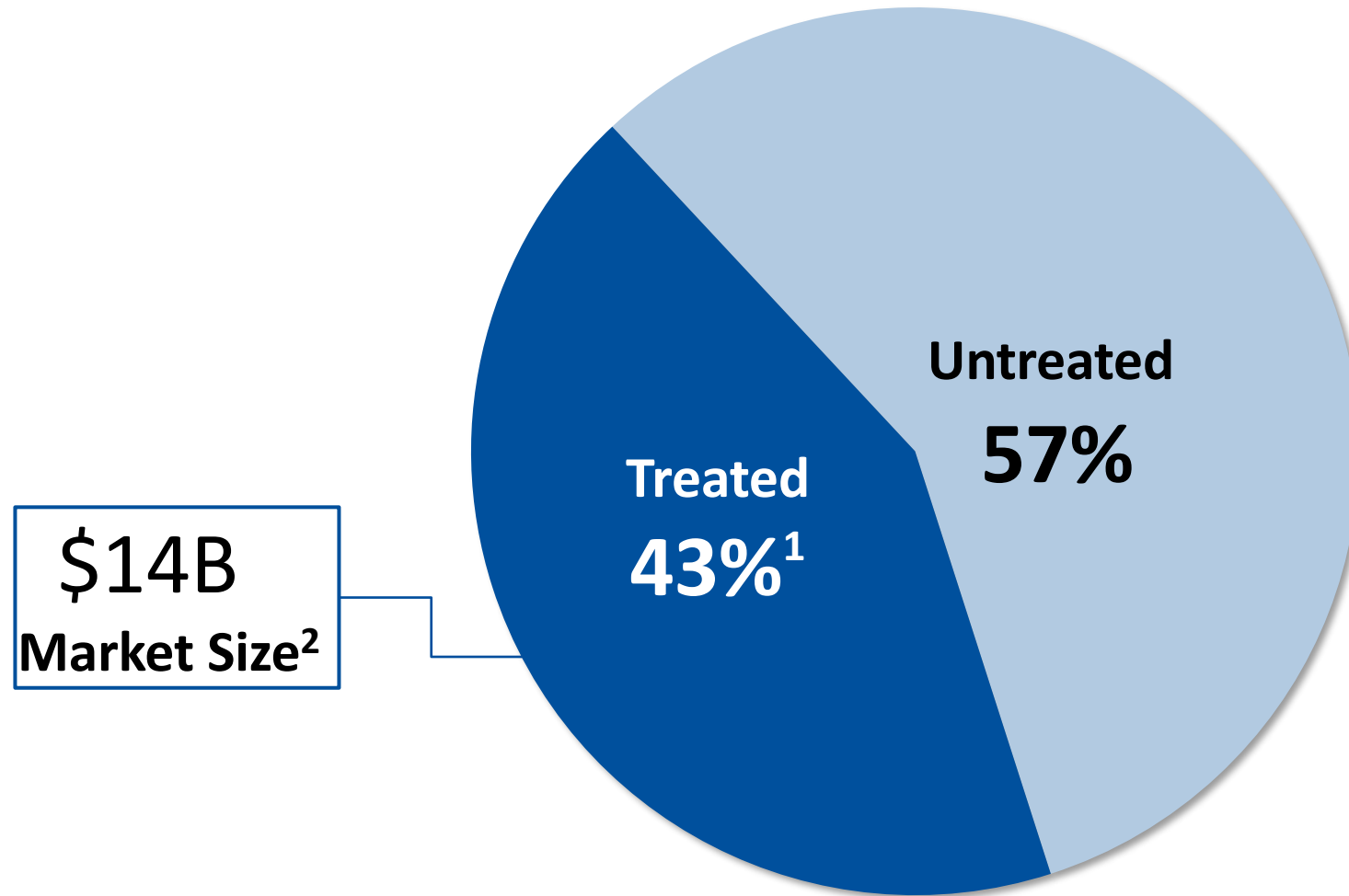
- GRX-917 is deuterated etifoxine – same pharmacology, efficacy, and safety/tolerability
- GRX-917 is derisked based on 40+ years of etifoxine clinical use and data
- Phase 2 ready in GAD, \$2.5B peak revs (US)
- Additional blockbuster indications in PPD, pain, epilepsy, obesity
- Strong IP with composition of matter patents through 2042 (US) and potentially 2046.



De-Risked Program

✓	Target Engagement
✓	Pharmacokinetics (PK)
✓	Safety
✓	Efficacy
✓	Commercial Differentiation

Most GAD Patients Do Not Use Available Anxiolytics



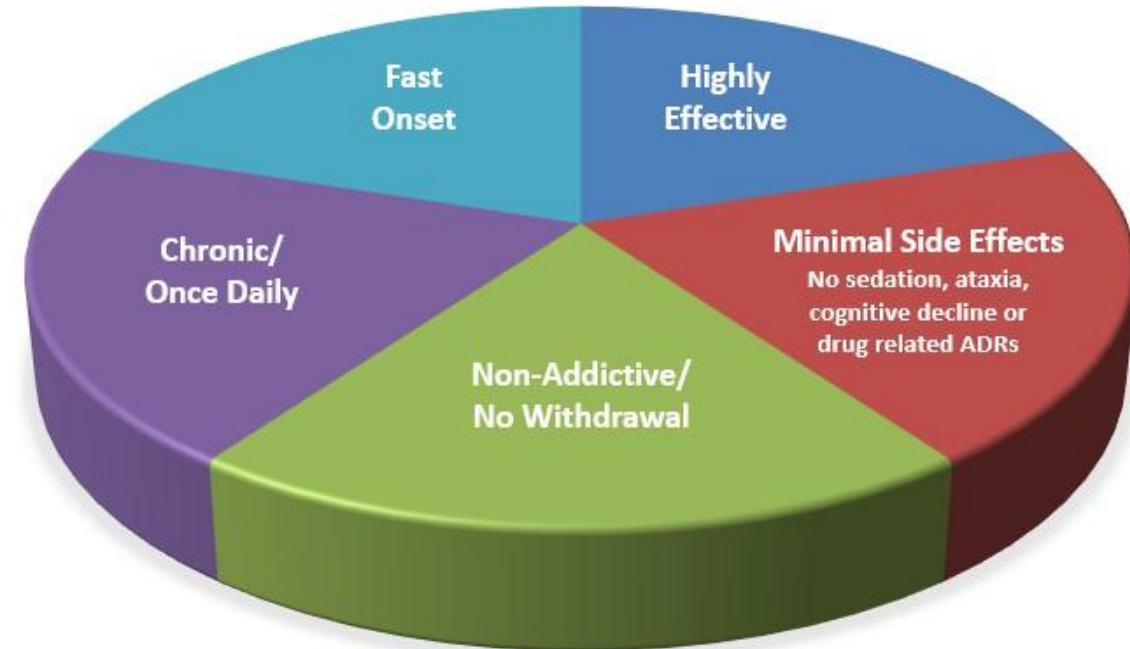
¹Anxiety and Depression Association of America (2024)

²Global Anxiety Market: IMS, per Foster Rosenblatt Market Research

GRX-917 Target Product Profile in Anxiety

- **Optimal Efficacy**
 - Rapid-onset and efficacy superior/comparable to Xanax[®], Ativan[®], Klonopin[®]
- **No Addiction Liability**
- **Minimal Adverse Events**
up to 10x predicted therapeutic dose
 - No sedation
 - No cognitive impairment
 - No ataxia
- **Once Daily, Chronic Dosing**

***“A Fast and Effective
Anxiolytic for Chronic Use”***



GRX-917 vs. Available Anxiolytics

Key Attributes	GRX-917	Benzodiazepines	SSRIs/SNRIs
Rapid Onset	✓	✓	4-8-week delay
Efficacy	✓	✓	Inferior
Side Effects	✓	Sedation, ataxia, impaired cognition	GI, sexual dysfunction, insomnia, weight gain
Addiction Liability	✓	X	✓
Chronic Usage	✓	X	✓

GRX-917 - Superior to Other GAD Treatments in Development

Company	GABA Therapeutics	GAD Development Candidates							
		AbbVie (Cerevel)	Engrail Therapeutics	Sumitomo/ Otsuka	MindMed	Seaport Therapeutics	Intra-Cellular Therapies	Cybin IRL Limited	AbbVie
Drug	GRX-917/ETX	Darigabat ^(1,2)	ENX-102 ⁽³⁾	SEP-363856 (ulataront)	MM-120 (LSD)	SPT-300 (glyph-ALLO)	ITI-1284 (deulumateperone)	CYB-004 (deu-DMT)	ABBV-932
MOA	Induces Neurosteroid Synthesis	GABA PAM	GABA PAM	TAAR1 agonist	5HT-1a/2a agonist	GABA PAM	Atypical antipsychotic	5HT2a agonist	D2/3 modulator
Mode of Administration	Oral QD/TID	Oral BID	Oral QD	Oral QD	Oral 1x dose	Oral TID-QID	QD sublingual	IM	oral
Onset of Action	Rapid	No Efficacy	N/A	N/A	Rapid	N/A	N/A	N/A	N/A
Efficacy (HAM-A Reduction)	60%	No Efficacy	No beta power after day one	?	75%	N/A	N/A	10-point change from baseline?	N/A
AEs	Minimal	High	High	Moderate	High	High	High	High	N/A
Somnolence	0% (Phase 1)	25%-33%	Somnolence 90%; Fatigue 87%	8%	<10%	74%	24%	N/A	N/A
Other	None	Impaired cognition; Impaired Epworth; Sleepiness scale	Sustained reduced arousal; Alpha power decrease	GI AEs	Psychedelic AEs Suicidality	Balance Disorder Euphoria Dizziness Cognitive Disorder	Risk of death in elderly; suicidal ideation	Hallucinations Depersonalization Nausea/vomiting Hypertension	N/A
Addiction Liability	None	Schedule IV probable	Schedule IV probable	N/A	Schedule I currently	Schedule IV probable	None	Schedule I currently	N/A
Treatment Duration	Chronic	Unknown but likely short term	Unknown but likely short term	N/A	Restricted	Likely short term	Chronic	Restricted	N/A

1) [Dandurand, 2023](#)

2) [Simen et al, Journal of Clinical Psychopharmacology 39\(1\):p 20-27, 2019](#)

3) [Vanover et al., 2023](#)

Deuteration – Multi \$Billion Pharma Strategy




(deutetrabenazine)
6 mg, 9 mg, and 12 mg tablets

~\$2.6B
2026 projected revs

 Bristol Myers
Squibb™


(deucravacitinib) 6 mg tablets

\$4B
BMS peak sales guidance




(Vanzacaftor/Tezacaftor/Deutivacaftor)

>\$2B
2026 estimate




PHARMACEUTICALS

\$3.5B
2015




pharmaceuticals

\$3.5B
2014


SUN
PHARMA


(deuruxolitinib) tablets 8mg

\$1B Peak Revs
2033 estimate

Deuteration:

- ✓ Improves PK
- ✓ Minimizes product development risk

Etifoxine: Comparable Efficacy to Benzodiazepines

Maurizio Fava, MD, Psychiatrist-In-Chief at MGH/Harvard, estimates an **80% probability of success** for GRX-917 in GAD

Etifoxine Study Result	Etifoxine Clinical Study	N	Reference	Date
Comparable onset and efficacy to Alprazolam (Xanax®)	(P3) ETX vs Alprazolam (Xanax®) Marketing Authorization in India 2024	260	Prabhakar et al (2024) ¹	2024
Superior efficacy to Clonazepam (Klonopin®)	(P4) ETX vs Clonazepam (Klonopin®)	179	Vicente ²	2020
Comparable onset and efficacy to Alprazolam (Xanax®)	(P4) ETX vs Alprazolam (Xanax®)	202	ETIZAL S.650/EN	2015
Superior efficacy to Phenazepam	(P4) ETX vs Phenazepam	90	Aleksandrovsky ³	2010
Comparable onset and efficacy to Lorazepam (Ativan®)	(P4) ETX vs Lorazepam (Ativan®)	191	ETILOR S.392/EN	2006
Superior efficacy to Buspirone	(P4) ETX vs Buspirone	170	STRETI S.226/GB	1998

Etifoxine is prescribed to 50% of new anxiety patients by high prescribers in France (GABA Market Research).

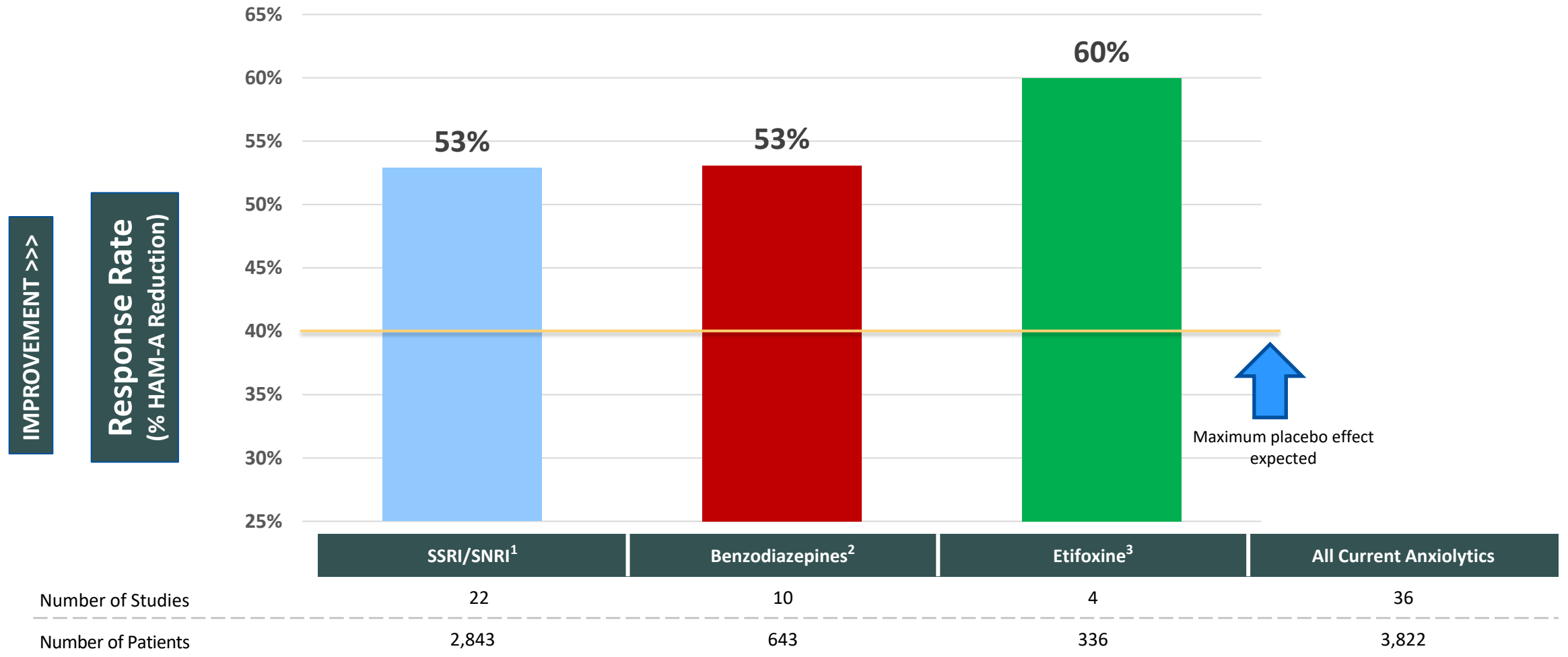
1. Prabhakar et al. Role of Etifoxine in Generalized Anxiety Disorder: a phase III randomized, double-blind, double-dummy, active-controlled study in India. *Neuroscience Applied*, Vol 3, Supplement 2, 104122 (2024).

2. Vicente et al., *Psychopharmacology* 237, 3357–3367 (2020)

3. Aleksandrovsky et al., *Russian Psychiatric Journal; Therapy of the mentally ill*; No. 1; 74-78 (2010)

Etifoxine is Highly Effective for Treatment of Anxiety

Anxiolytic clinical trials meta-analysis



1. Koponen et al 2007, *Prim Care Companion J Clin Psychiatry*; Rynn et al 2008, *Int Clin Psychopharmacol*; Hartford et al 2007, *Int Clin Psychopharmacol*; Alaka et al 2014, *Int J Geriatr Psychiatry*; Strawn et al 2015, *J Am Acad Child Adolesc Psychiatry*; Katz et al 2002, *J Am Geriatr Soc*; Baldwin et al 2006, *British Journal of Psychiatry*; Davidson et al 2004, *Depress Anxiety*; Bandelow et al 2010, *Int J Neuropsychopharmacology*
2. Rickels et al 2005, *Arch Gen Psychiatry*; Moller et al 2001, *J Clin Psychopharmacol*; Stein et al 2015, *Adv Ther*; Lydiard et al 1997, *J Clin Psychiatry*; Michelson et al 2013, *Int J Neuropsychopharmacology*; Nguyen et al 2006, *Hum Psychopharmacol*; Pande et al 2003, *Am J Psychiatry*; Woelk et al 2010, *Phytomedicine*; Vicente et al 2020, *Psychopharmacology (Berl)*; Strand et al 1990, *J Clin Psychiatry*
3. Stein et al 2015, *Adv Ther*; Vicente et al 2020, *Psychopharmacology (Berl)*; Aleksandrovsky et al 2010, *Russian Psychiatric Journal*; Nguyen et al 2006, *Hum Psychopharmacol*.

Etifoxine's Safety/Tolerability is Well-Established

Superior profile vs. benzodiazepines and SSRIs

Safety	Comment	Source
Non-Addictive	"No cases of abuse, misuse or pharmacodependence."	Cottin et al ¹ (based on +15M Rx)
No Sedation or Amnesia	No effects on vigilance or psychomotor performance	Micallef et al ²
No Impaired Cognition	No effect on alertness or other cognitive parameters in elderly	Deplanque et al ³
Minimal Adverse Events	- Minimal adverse events - Minimal SAEs in clinical trials (N=4 over 40+) - Absence of drug-related SAEs in controlled clinical trials - Low rate (< 1 per 15 million) serious ADRs in EudraVigilance	Nuss et al (2019) ⁶ Etifoxine Assessment ⁵ Cottin et al (2016) ¹ Kinexum Assessment ⁴

1. Cottin et al (2016) Fundamental Clin Pharmacol 30:147–152.

2. Micallef et al (2001) Fundamental Clin Pharmacol 15:209-216.

3. Deplanque et al (2018) Eur Neuropsychopharmacol 28:925-932.

4. Kinexum (2023) Etifoxine Pharmacovigilance Assessment –report on file

5. Etifoxine Assessment CHMP/EMA/148255; 27JAN2022

6. Nuss et al (2019) Neuropsych Disease and Treatment 15:1781–1795.

Etifoxine: Non-Addictive

“No cases of abuse, misuse or pharmacodependence.”¹

15.7 million prescriptions of etifoxine (Stresam®) were reviewed and analyzed by the French National Agency for the Safety of Medicines and Health Products, between 2000 and 2012 (“**ANSM Report**”), for marketing reauthorization.

¹) Cottin et al., Fundamental & Clinical Pharmacology 30 (2016) 147–152.

GRX-917 Phase 1: Placebo Like Side Effects

Phase 1 – GRX-917

Placebo like side effects
up to 10x therapeutic doses

Nervous System Disorders	GRX-917 (n=75)	Placebo (n=25)
Dizziness	4%	4%
Headache	17%	12%
Paresthesia	1%	4%
Somnolence	0%	8%
Ataxia	0%	0%
Lethargy	3%	0%
Cognitive Deficit	0%	0%

GRX-917 Phase 1: A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single and Multiple Ascending Doses of GRX-917 in Healthy Adult Subjects

EMA Etifoxine SAE Assessment

Across All Controlled Clinical Trials +40 Years

System Organ Class (SOC) MedDRA PT	Etifoxine hydrochloride	Blinded	Active comparator	Placebo
Ear and labyrinth disorders	0	0	1	0
Vertigo	0	0	1	0
Eye disorders	0	0	1	0
Retinal artery thrombosis	0	0	1	0
Hepatobiliary disorders	1	0	0	0
Jaundice	1	0	0	0
Injury, poisoning and procedural complications	1	4	1	1
Contusion	0	1	0	0
Ligament injury	1	0	0	0
Ligament sprain	0	1	0	0
Overdose	0	0	1	0
Road traffic accident	0	1	0	0
Wound	0	1	0	0
Injury	0	0	0	1
Musculoskeletal and connective tissue disorders	0	0	1	0
Back pain	0	0	1	0
Neoplasms, benign malignant and unspecified (incl cyst)	1	0	0	0
Fibroma	1	0	0	0
Nervous system disorders	0	0	1	0
Somnolence	0	0	1	0
Psychiatric disorders	0	0	1	0
Suicidal ideation	0	0	1	0
Surgical and medical procedures	1	0	0	0
Cervical conisation	1	0	0	0
TOTAL	4	4	6	1

Source: EMA/CHMP Etifoxine Assessment Report, Jan 2022

Phase 1 PK Modeling and Dose Selection

Etifoxine 100 mg BID = GRX-917 60 mg QD

- GRX-917 demonstrated improved PK and once-daily dosing vs. etifoxine.
- Certara will conduct GRX-917 PK/PD modeling for dose selection

	Etifoxine	GRX-917
Half-life	4 hours	>12 hours
Daily dose	150 mg - 200 mg	60 mg
Dosing regimen	BID - TID	QD
	Etifoxine (Stresam®) Summary of Product Characteristics	Etifoxine and GRX-917 PK modeling

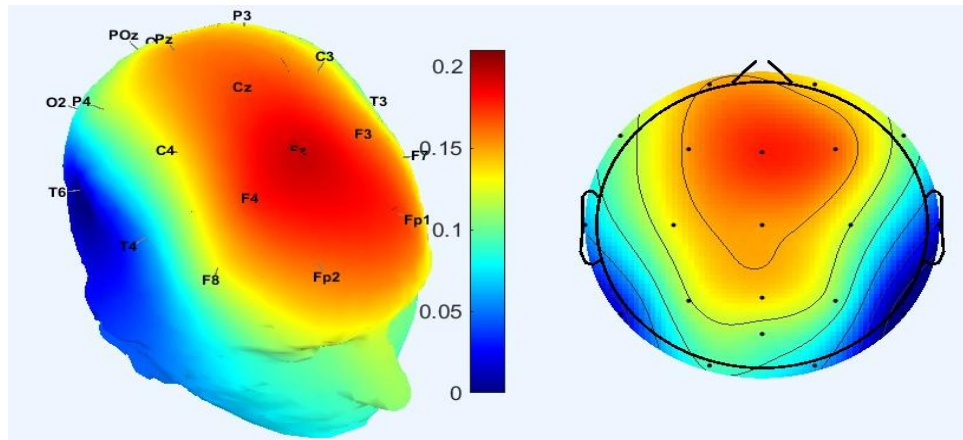
GRX-917 qEEG Beta Power Increase Supports Anxiolytic Efficacy

Phase 1 Study

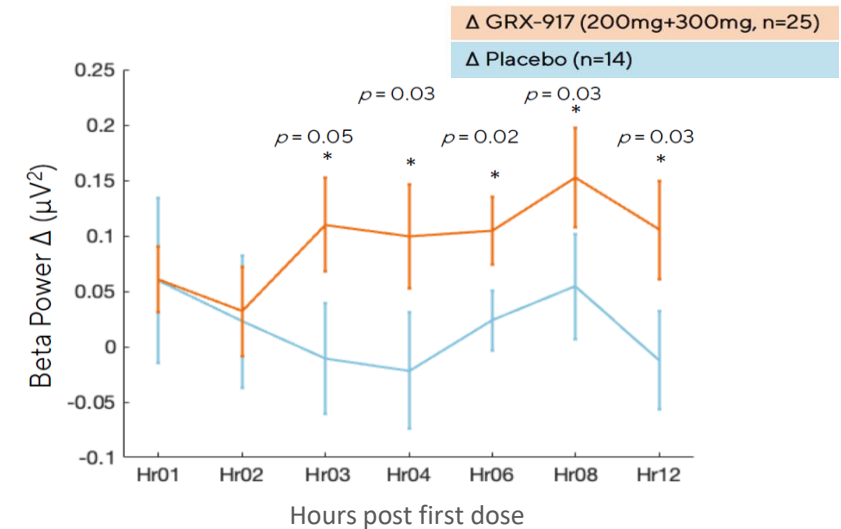
Increased Beta Power:

- Confirms GABA_A target engagement
- Dose- and time-dependent for 12 hours ($p < 0.05$)
- Demonstrates GRX-917 exposure response ($p < 0.0001$)
- Rapid onset, sustained, significant

GRX-917 Exposure Response Heat Map ($p < 0.0001$)



GRX-917 Increases qEEG Beta Power



GRX-917 Phase 1: (Study GRX-917-01) - A Phase 1, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single and Multiple Ascending Doses of GRX-917 in Healthy Adult Subjects

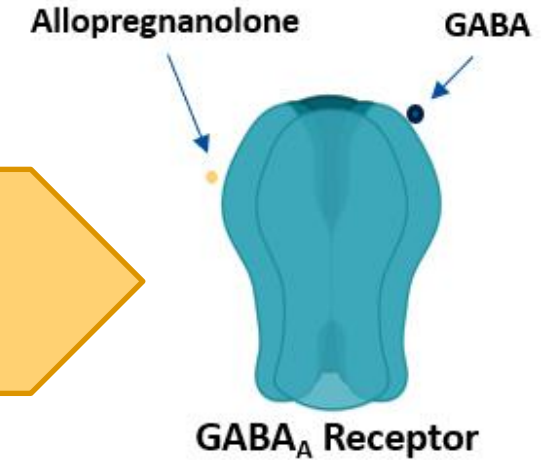
GRX-917 – Induction of Endogenous Neurosteroids

Potent neuromodulatory and anti-inflammatory activity

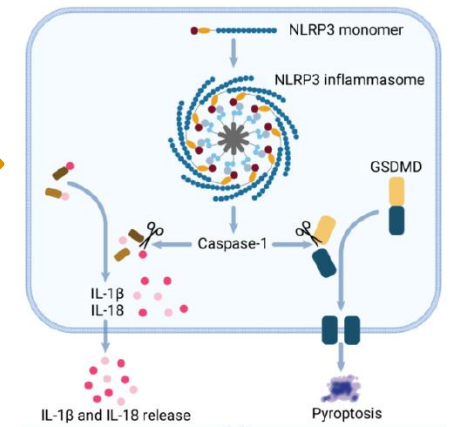
**GRX-917/etifoxine increase
neurosteroid synthesis¹**



**Neurosteroids modulate
receptors²**
(anxiety, depression, epilepsy)



**Neurosteroids inhibit NLRP3
inflammation³**
(epilepsy, MS, pain, obesity)



NLRP3/IL-1beta Pathway

¹do Rego JL et al (2015) PLoS ONE 10(3): E0120473 ; internal data

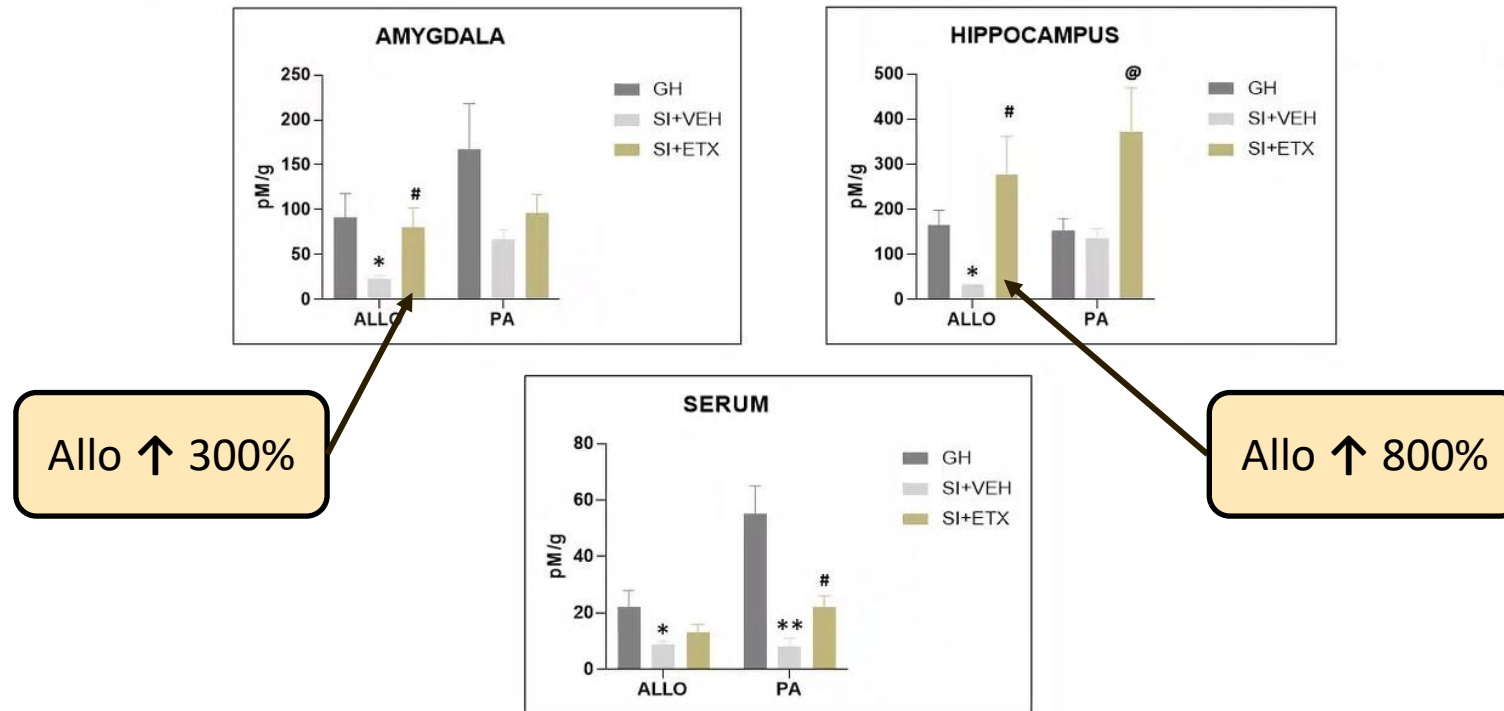
²Lambert et al (2003) Prog Neurobiol 71(1); 67-80.

³Osmond et al (2023)

Etifoxine – Rapid, significant increases in brain neurosteroid levels

Highly selective regional distribution 60 minutes following etifoxine administration.

Allopregnanolone (ALLO) and pregnanolone (PA) levels in brain and serum of socially isolated mice treated with etifoxine



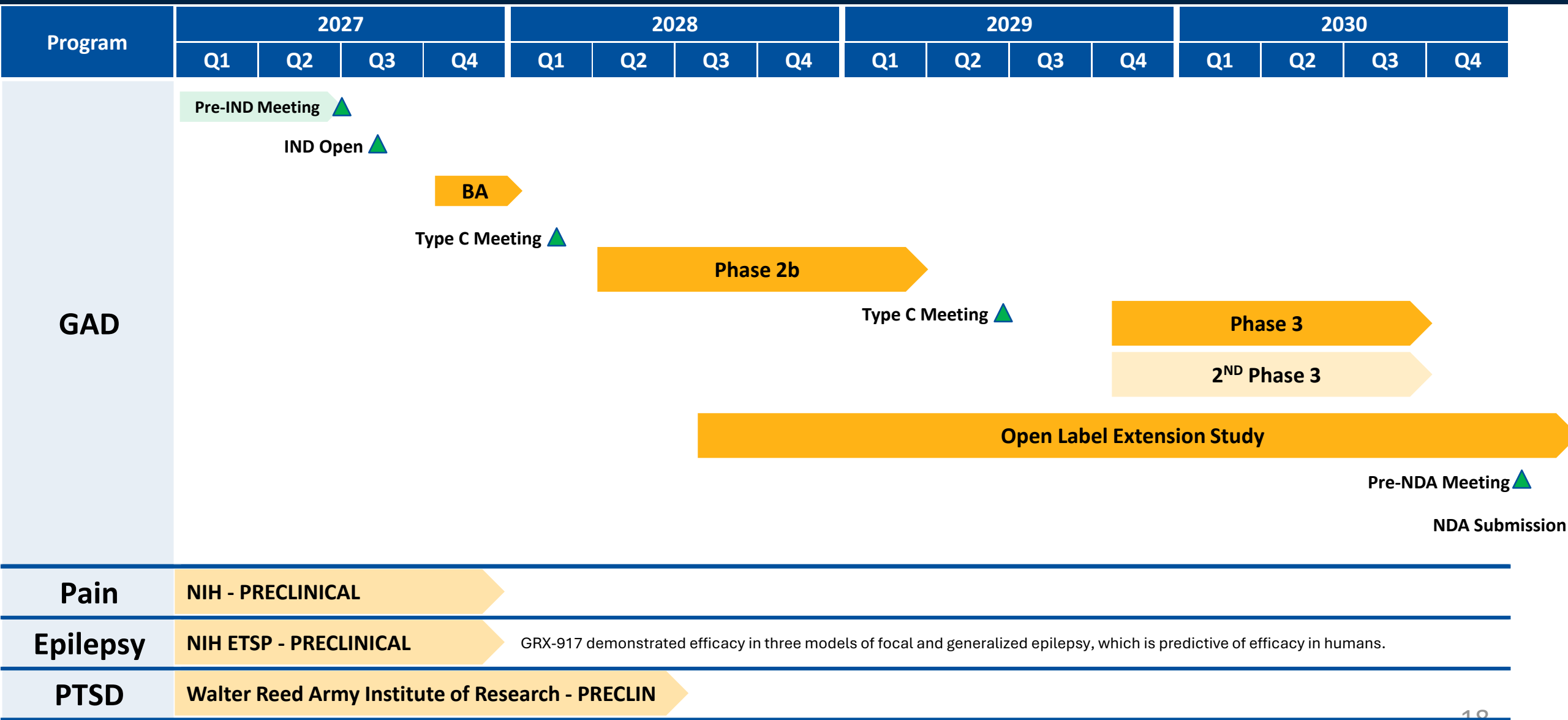
Etifoxine was administered at the dose of 50mg/kg IP and mice were killed 60 min after drug injections. Results are Mean $\pm$ SEM of 5-10 mice. * $P < 0.05$ and ** $P < 0.001$ compared with group-housed (GH) mice; # $P < 0.05$ compared with socially isolated (SI) mice plus vehicle (VEH); @ $P = 0.06$ compare with SI + VEH

Source: Graziano Pinna PhD, Univ IL Chicago

Intellectual Property Overview: Global CoM IP Strategy through 2046

Patents	Non-Obvious/ Inventive Factors	Countries	Priority	Int'l Filing	Expiry
PCT/US16/23231 (WO 2016/154039) DEUTERATED ANALOGS OF ETIFOXINE, THEIR DERIVATIVES AND USES THEREOF - 10,080,755 claims compounds including GRX-917; methods of treatment - 10,736,901 claims GRX-917 compounds; methods including treating anxiety - 11,672,805 claims methods of treating anxiety with GRX-917 - 12,433,896 claims methods of treating convulsive disorder	Specific deuteration at a location differing from expected metabolic “hot spot” led to novel deuterated molecule (GRX-917) with optimal metabolic stability (see EU prosecution)	US, AU, BR, CA, CN, EP, IL, IN, JP, KR, MX	62/135,979 filed 2015 Mar 20	2016 Mar 18	2036 Mar 18 PTE TBD
PCT/US23/77643 (WO 2024/091943) METHODS OF TREATMENT ANXIETY AND OTHER DISORDERS USING DEUTERATED ANALOGS OF ETIFOXINE - 18/493,488 - US 20240189316 A1 - PTA current est. 2 months	Claims directed to specific dosing regimen with GRX-917 that unexpectedly avoids autoinduction	US, AU, BR, CA, CN, EP, IN, JP, KR, MX, NZ	63/380,737 filed 2022 Oct 24	2023 Oct 24	2043 Oct 24
100016_00055 - US - 63/793,999 - Stable Oral Solid Formulation of Deuterated Etifoxine HCl, THEIR DERIVATIVES, AND USES THEREOF	Oral composition for GRX-917 that provides significant and unexpected stability and bioavailability	US & PCT	63/793,999 filed 2025 Mar 24	2026 Mar 24	2046 Mar 24

GRX-917 Clinical Development Program



Capital Requirements and Use of Funds

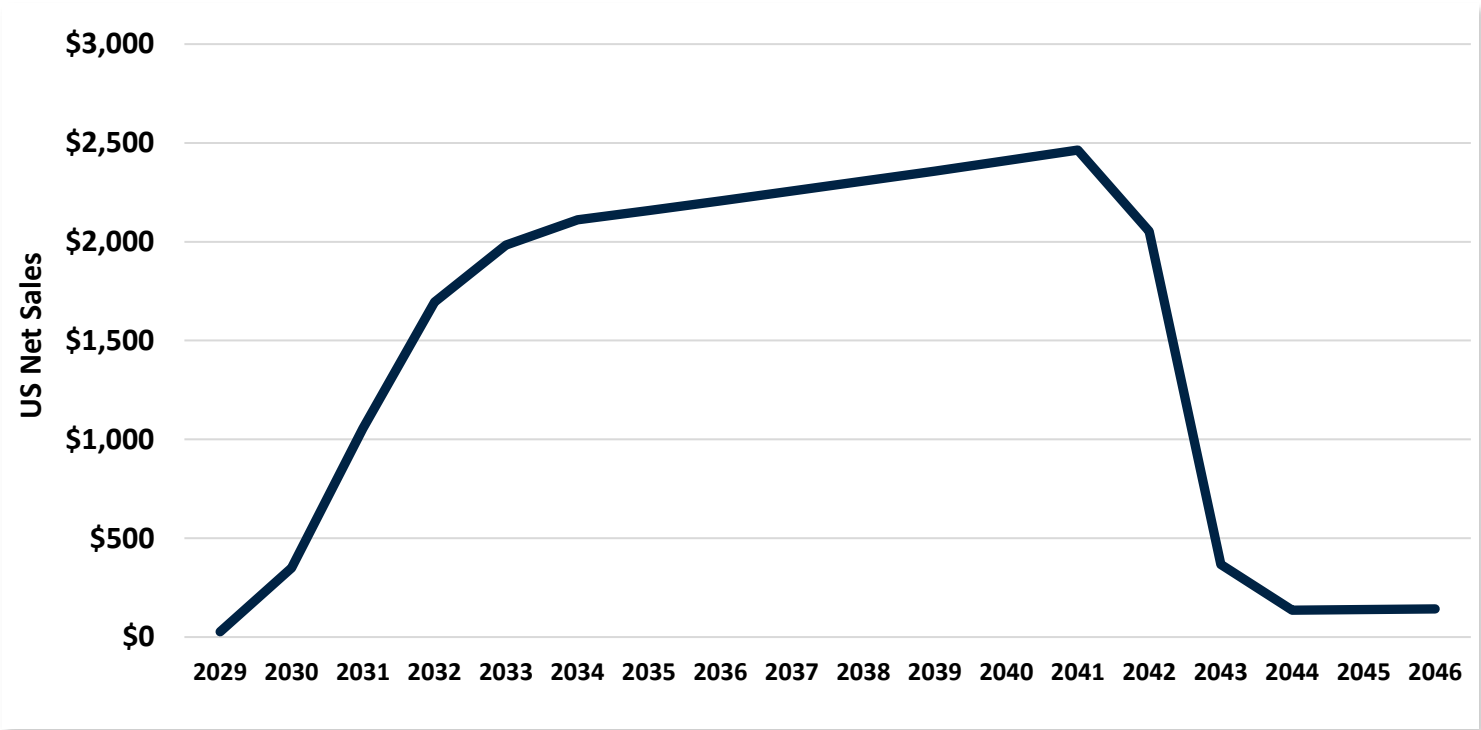
\$ in millions

Use of Funds	GAD Phase 2B
IND Opening Studies	\$4.5
Clinical Trials (assuming 2x Phase 3)	\$78.0
Tox & Research	\$10.6
CMC	\$18.2
Regulatory	\$2.5
G&A	\$34.0
Total	\$147.80

All costs supported by vendor quotes. Some quotes are being updated.

GRX-917 US GAD Sales Forecast: \$2.5B Peak Revs (\$3.5B Global)

GRX-917 US GAD Sales



Key Forecast Assumptions

- US GAD prevalence (2029): 10.8m
- US GAD treated patients (2029): 4.9m
- GRX-917 peak penetration:
 - First line treatment: 10%
 - Uncontrolled patients: 20%
- GRX-917 peak patients on drug: 653k
- Average Rx per year: 4.7
- GRX-917 gross price per Rx: \$623 at launch increasing 1.5% per year
- Gross to net discount: 30%
- US peak revenue: \$2.5B
- Gross margin: 90%

Source: Rosenblatt Life Science

Key Advisors

Decades of successful leadership in pharma development, psychiatry, regulatory and deuteration



Robert Berman, M.D.

Scientific Advisory Board Chairman
Co-Founder, Biohaven



Maurizio Fava, M.D.

Clinical & Regulatory Advisor
Psychiatrist-in-Chief
Mass General/ Harvard Med



Thomas Laughren, M.D.

Clinical & Regulatory Advisor
Former Director, Div. Psych
Products, FDA/CDER



Roger Tung, PhD

Strategic Advisor - Deuteration KOL
Venture Partner, Longwood Fund
Founder/CEO, Concert Pharmaceuticals



Yale SCHOOL OF MEDICINE



LONGWOOD FUND

CoNCERT

Pharmaceuticals Inc.*

Deuterated >100 molecules



Key Executives

Decades of successful leadership, clinical development, and commercialization in pharma and biotech



Mario Saltarelli, M.D., Ph.D.
Chief Executive Officer,
Director



Richard Farrell
Chief Financial Officer,
Director, & Founder



Kathryn King, Ph.D.
Clinical Development
Advisor



Mary Szela
Commercial Consultant



David Putnam, Ph.D.
Inventor



Olivier Dasse, Ph.D.
Inventor

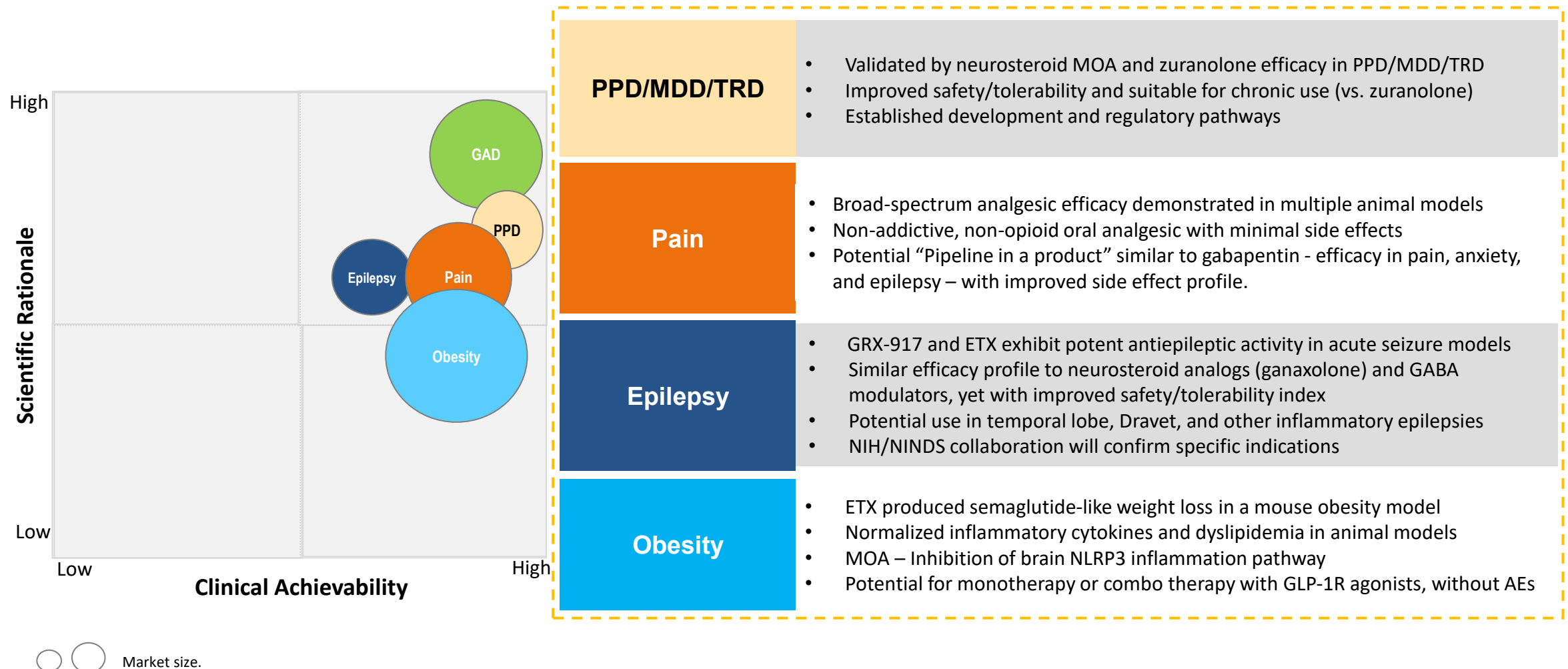


Appendix

- Additional Indications
- ETX and GRX have Identical Pharmacology / Metabolite Profile

GRX-917 Additional Indications Strategy

Phase 2 ready for multiple blockbuster indications beyond GAD



GRX-917 Effects in Acute & Chronic Seizure Models

Broad-spectrum anti-epileptic efficacy confirmed at tolerated doses

ETSP GRX-917 Data
March/April 2026

	Maximal Electroshock (acute generalized seizure model)	6 Hz Test (acute focal seizure model)	Corneal Kindled Mouse (chronic focal seizure model)
Antiseizure Activity	75, 100, 150 mg/kg	85, 100, 200 mg/kg	25, 50, 100, 150 mg/kg
ED₅₀	86.6 mg/kg	104 mg/kg	81.5 mg/kg
TD₅₀ (Rotarod)	183.9 mg/kg	138.3 mg/kg	Not reported
Protective Index	2.1	1.3	Not reported

GRX-917 Rationale in PPD & MDD

Zuranolone Approved in PPD (14-days only)

GRX-917 Rationale in PPD & MDD

- Mechanism of action – allopregnanolone GABA_A PAM activity
- Efficacy and approval of both brexanolone and zuranolone for PPD
- Efficacy of zuranolone in MDD (see next slide)

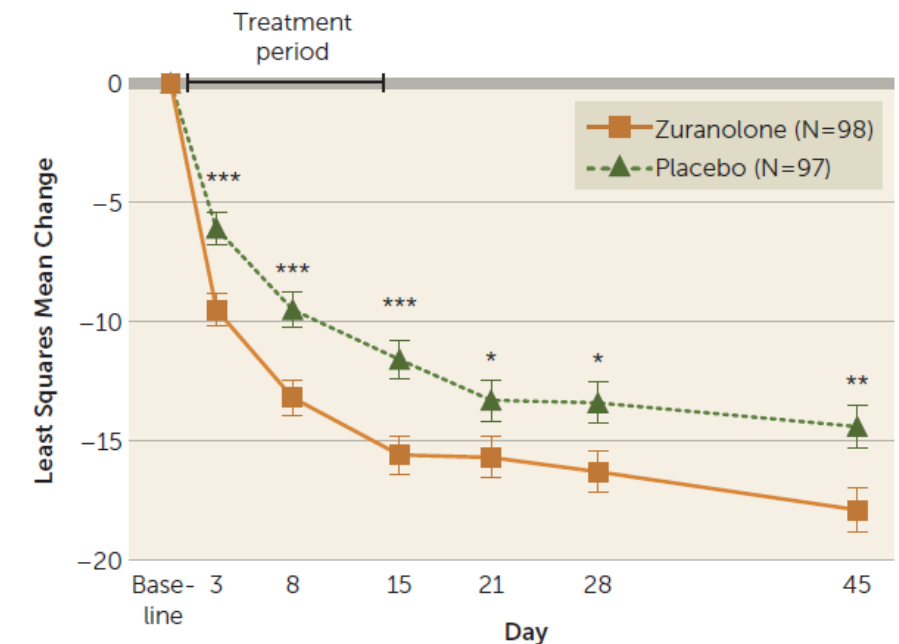
Depression Rationale	Zuranolone (ZURZUVAE®)	GRX-917/ETX
Administration	Exogenous Allo analog	Endogenously produced Allo
Regional Selectivity	None (all brain regions)	Regionally specific (hippocampus, amygdala, cortex)
Max Dose	50mg due to safety concerns	No MTD (Phase 1)
Duration	14 days due to safety concerns	Chronic

GRX-917 Superior Profile in PPD & MDD

- No dose limitations due to wide therapeutic index
- Ability to dose chronically vs. 14-days
- Minimal adverse events vs. blackbox
- Lack of abuse potential and scheduling
- Potential for enhanced efficacy due to above

Zuranolone for the Treatment of Postpartum Depression (Phase 3)

FIGURE 2. Change from baseline in HAM-D score in a placebo-controlled trial of zuranolone 50 mg/day for postpartum depression (full analysis set)^a



^aThe primary endpoint was change from baseline in score on the 17-item Hamilton Depression Rating Scale (HAM-D) at day 15, and the key secondary endpoints included change from baseline in HAM-D score at days 3, 28, and 45. Multiplicity was accounted for when analyzing primary and key secondary endpoints. All other secondary endpoints were not adjusted for multiplicity and are to be interpreted with nominal p values. Error bars indicate standard error. *p<0.05. **p<0.01. ***p<0.001.

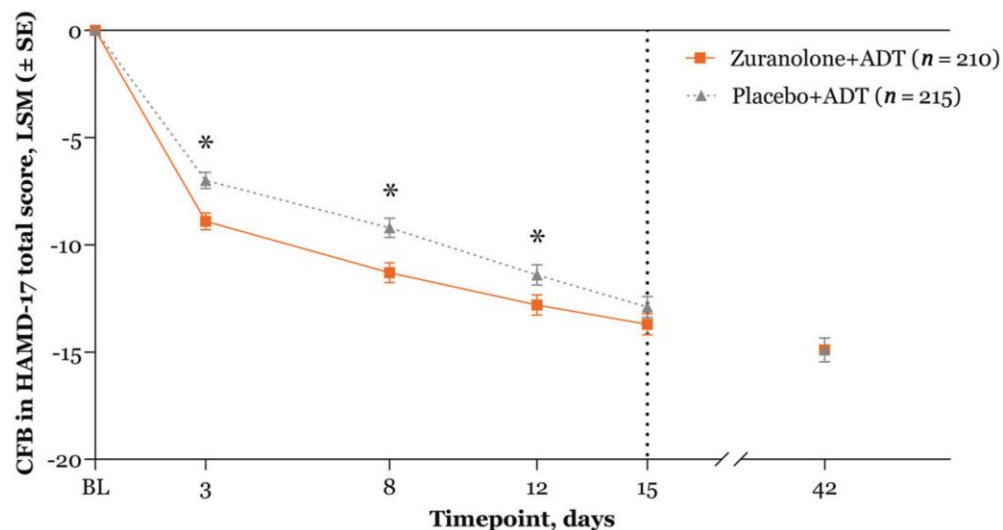
GRX-917 MDD/TRD Rationale

Zuranolone demonstrates efficacy in MDD

Phase 3 CORAL Zuranolone MDD¹

Outcome

Rapid, statistically significant reductions in HAM-D-17 observed by day 3
Efficacy not sustained following cessation of dosing on Day 14

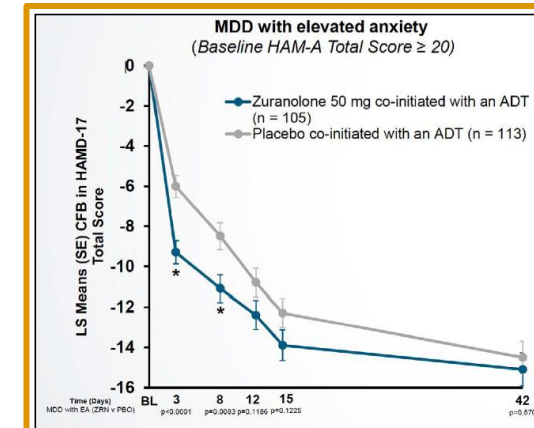
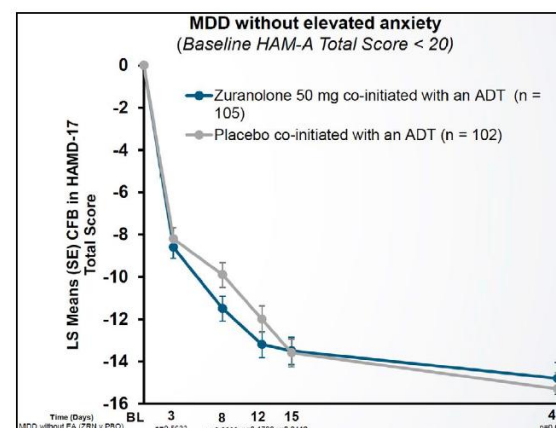


Phase 3 CORAL Study Design

- Ph3, randomized, double-blind, parallel-group, placebo-controlled
- Baseline HAM-D-17 Total Score ≥ 24 (potentially TRD)
- Zuranolone 50 mg vs. placebo (plus open label ADT) x 14 days

CORAL Post-hoc Analysis

Presence of comorbid anxiety symptoms (HAM-A total score ≥ 20) confers rapid (3 days), enhanced treatment response



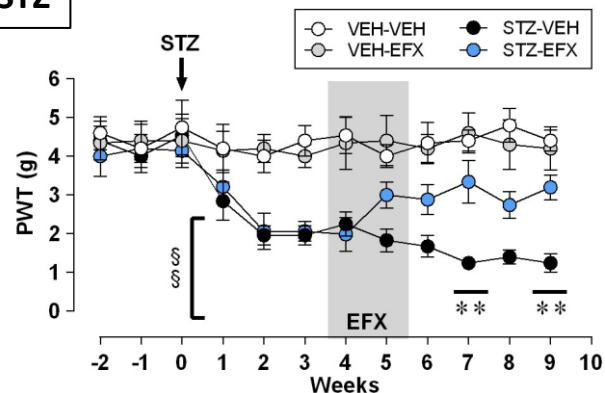
Opportunities for GRX-917 in MDD/TRD

- Treatment of co-morbid anxiety and depression
- Dose escalation
- Chronic dosing
- Monotherapy

Etifoxine Demonstrates Broad Spectrum Efficacy in Rodent Pain Models

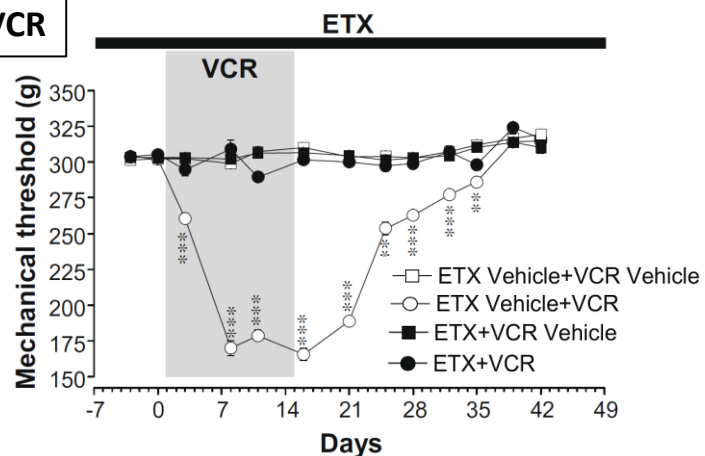
Supports human efficacy in neuropathic, diabetic, and inflammatory pain

STZ



The non-benzodiazepine anxiolytic etifoxine limits mechanical allodynia and anxiety-like symptoms in a mouse model of streptozotocin-induced diabetic neuropathy
Gazzo et al., PLOS ONE 2021
<https://doi.org/10.1371/journal.pone.0248092>

VCR



Reduction and prevention of vincristine-induced neuropathic pain symptoms by the non-benzodiazepine anxiolytic etifoxine are mediated by 3 α -reduced neurosteroids
Aouad et al., Pain 2009
DOI: 10.1016/j.pain.2009.08.001

Profound analgesic efficacy across all pain models

- Rapid onset, complete in sciatic cuff
- Sustained following dosing cessation
- Pretreatment blocks development of pain (VCR)

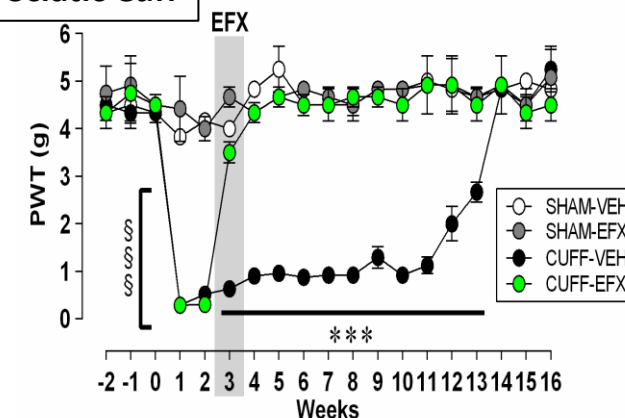
Etifoxine reduces mechanical allodynia in rodent pain models

- mononeuropathy model (Sciatic Cuff)
- inflammatory pain model (CFA)
- streptozotocin diabetic neuropathy (STZ)
- vincristine toxic neuropathy (VCR)

Etifoxine's analgesic efficacy is associated with

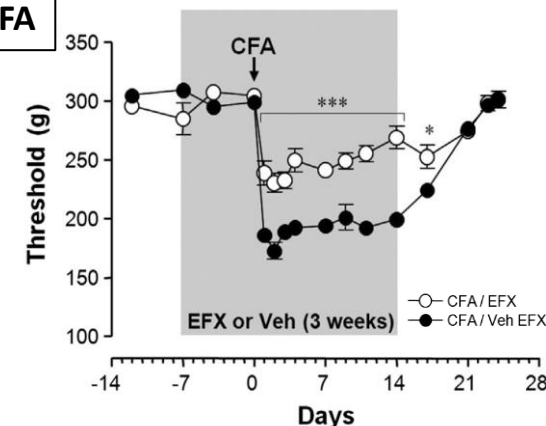
- Increased spinal cord ALLO levels
- Reversal by neurosteroid synthesis inhibitors (e.g. finasteride)
- Marked reductions in NLRP3 inflammatory cytokines, including IL-1 β
- Reduced anxiety in animals

Sciatic Cuff



Long-lasting analgesic and neuroprotective action of the non-benzodiazepine anxiolytic etifoxine in a mouse model of neuropathic pain
Kamoun et al. Neuropharmacology 2021.
<https://www.sciencedirect.com/science/article/abs/pii/S0028390820304755>

CFA



Etifoxine analgesia in experimental monoarthritis: A combined action that protects spinal inhibition and limits central inflammatory processes Aouad et al 2014
<http://dx.doi.org/10.1016/j.pain.2013.11.003>

Etifoxine Weight Loss Comparable to Semaglutide

Phase 2 Ready in Obesity

Obese High Fat Diet Model

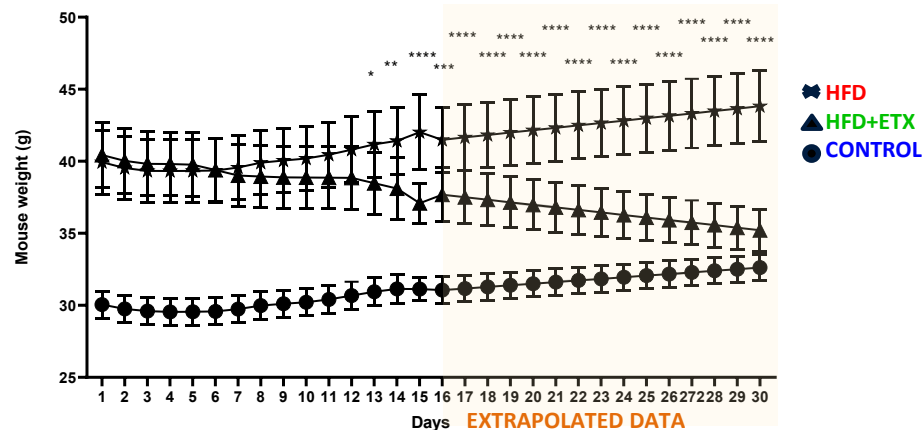
Mechanism of Action in Obesity:

- Obesity is an NLRP3-driven neuroinflammatory disease
- Etifoxine is a brain-penetrant inhibitor of TLR/NF-kB/NLRP3/IL-1 β pathway

1

Etifoxine induced 11% weight loss in 15 days, comparable to:

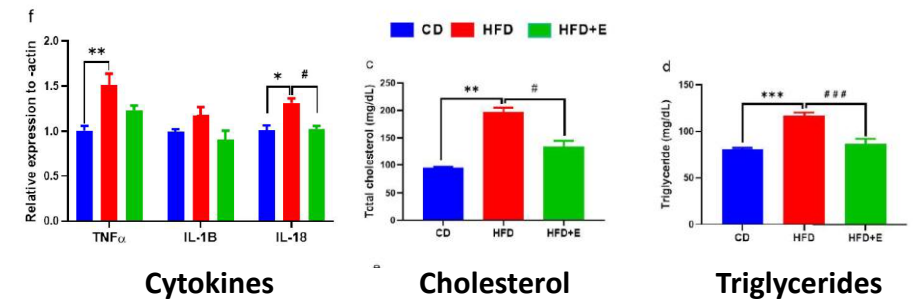
- Semaglutide
- Brain-penetrant NLRP3 inhibitors (e.g. NT-0796)



2

Etifoxine normalized:

- Proinflammatory markers (IL-18, IL-1 β , TNF α)
- Serum lipids (cholesterol, triglycerides)



1) Ibrahim, K. S., Craft, J. A., Biswas, L., Spencer, J., & Shu, X. (2020). Etifoxine reverses weight gain and alters the colonic bacterial community in a mouse model of obesity. *Biochemical Pharmacology*, 180, Article 114151. <https://doi.org/10.1016/j.bcp.2020.114151>

Potential Additional Therapeutic Indications

NLRP3/IL-1Beta Inflammatory Diseases

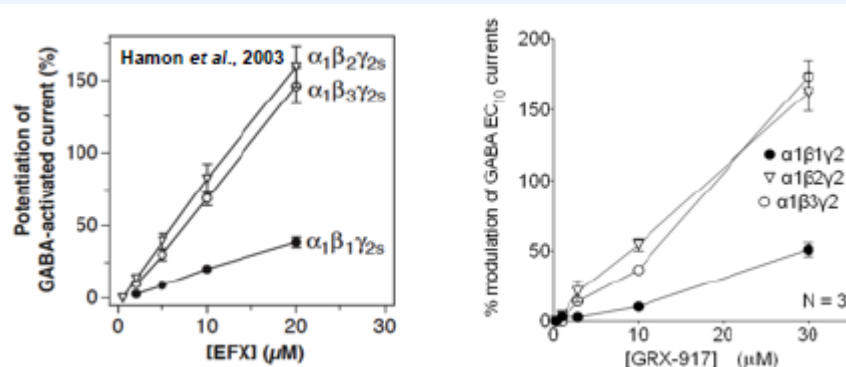
Neuroinflammatory Diseases	Systemic Inflammatory Diseases	Cardiometabolic Diseases
Anxiety	Rheumatoid arthritis	Obesity
Depression	IBD	MASH
Epilepsy Seizures	OA	NAFLD
Pain	Gout	Atherosclerosis
Neuropathy	Asthma	Diabetes
Multiple sclerosis	Systemic juvenile idiopathic arthritis	
Alzheimer’s disease	Still’s disease	
Parkinson’s disease	Psoriasis	
Traumatic brain injury	SLE	
ALS	Endometriosis	
	Cystic fibrosis	
	Hidradenitis suppurativa	
	Lupus nephritis	

Efficacy Supported by Etifoxine Preclinical Data

Deuterated Etifoxine (GRX-917) & Etifoxine Identical Anxiolytic Activity, MOA and Pharmacology

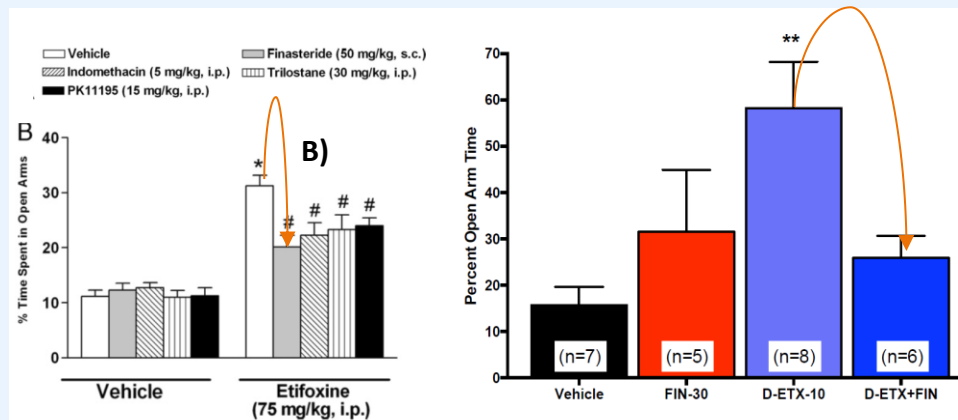
1) Identical GABA-A Channel Activity

ETX and GRX-917 show the same profile for $\beta 2/3$ -subunit-containing GABA_A receptors.



2) Identical Induction of Neurosteroid MOA

ETX and GRX both increase % time in open arm in EPM which is reversed by 5-alpha reductase inhibitor (finasteride)

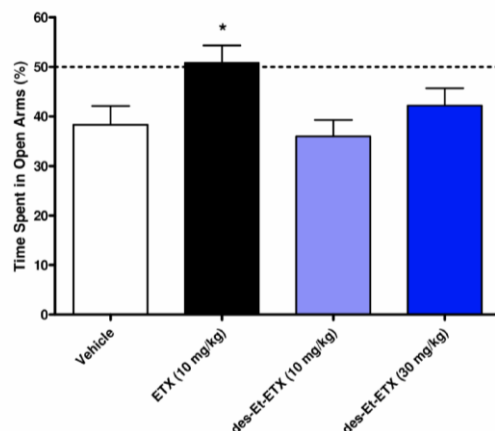


Ugale, R. et al. Brain research 1184 (2007), 193-201

Finasteride 30 mg/Kg i.p., GRX-917 10 mg/Kg i.p.

3) M4 Metabolite is Pharmacologically Inactive

at up to 10x etifoxine minimum effective dose



In Phase 1 GRX-917, M4 (N-desethyl analogue) did not show anxiolytic activity at doses up to 30 mg/kg IP, compared to 3 mg/kg IP of etifoxine, which was used as a positive control in the EPM mouse model, at its minimum effective dose.

Note: GABA management and its advisors have not found any published data confirming M4 has any activity either in animals or in humans, and we believe that casual references to its putative activity in the literature are incorrect.