GABA Therapeutics, Inc. – December 2024

Next-Generation Anxiety Treatment

gaba THERAPEUTICS

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The forward-looking statements and projections contained in this presentation are expressly qualified by this cautionary statement. Except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, after the date on which the statements are made or to reflect the occurrence of unanticipated events. Readers are cautioned not to place undue reliance on forward-looking statements or projections. Prospective investors should not construe the contents of this presentation as legal, tax, investment or other advice. All prospective investors should make their own inquiries and consult their own advisors as to legal, tax, investment, and related matters concerning an investment in the securities of the Company

Investment Highlights

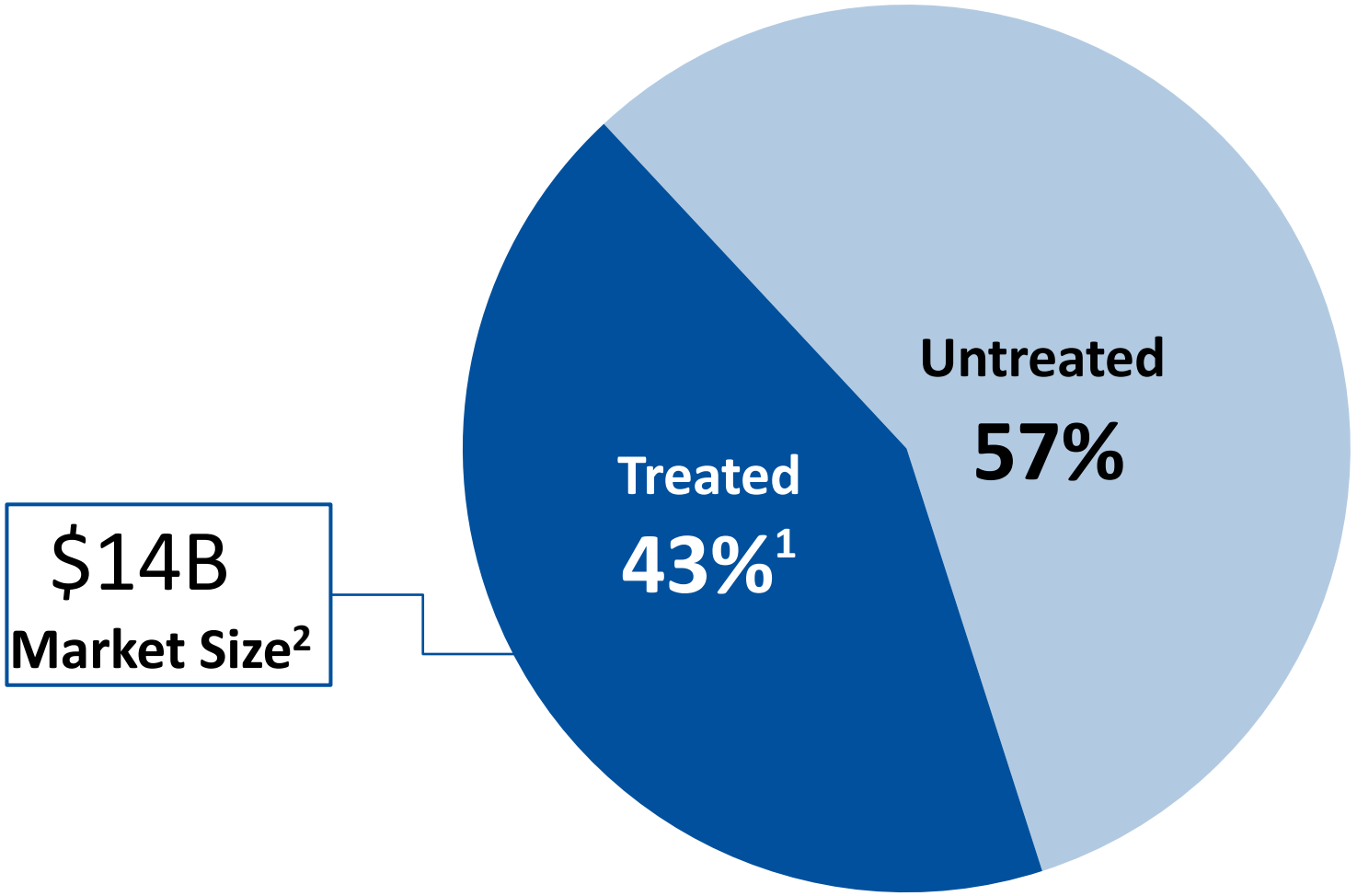
- GRX-917 is a deuterated analog of an anxiety drug shown to be safe and effective
- GRX-917 is a potentially superior treatment for anxiety:
  - Rapid onset and potential gold-standard efficacy
  - Without sedation, ataxia, cognitive impairment
  - No addiction liability
- Phase 2/3 ready – approval for GAD projected by 2028
- Additional indications include depression, epilepsy, pain and obesity
- U.S. patent exclusivity through at least 2042

GRX-917: Pipeline-in-a-Drug

Ready to start clinical trials in multiple indications

[1]Supported by MOA and preclinical data

Most GAD Patients Don’t Receive Treatment



[1]Anxiety and Depression Association of America (2024)
[2]Global Anxiety Market: IMS, per Foster Rosenblatt Market Research

GRX-917 vs. Current Available Treatments

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

GRX-917 Is Deuterated Etifoxine

Stresam®
Etifoxine

TID

- A safe, fast and effective anxiety medication
- Approved in France (1979)
- Substantial patient exposures[1]
- 100+ published studies

Improved PK via deuteration

GRX-917
Deuterated etifoxine

QD

- Identical MOA
- Comparable safety & efficacy
- Potentially improved compliance
- New chemical entity

[1]Based on management's extrapolation of 2000 - 2012 scripts in France (Source: IQVIA)

Deuterium Switch Strategy Has a Strong Track Record of Success

Successful Outcomes from Deuterated Products

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

~$1.6B[1]
2024 est.

Bristol Myers Squibb™
SOTYKTU™ (deucravacitinib) 6 mg tablets

$240M[2]
2024 est.

VERTEX

Vanza Triple
(Vanzacaftor/Tezacaftor/Deutivacaftor)
Next-Gen Therapy for Cystic Fibrosis

In Registration

teva
AUSPEX PHARMACEUTICALS

$3.2B
2015

Otsuka
AVANIR pharmaceuticals

$3.5B
2014

GSK
CoNCERT Pharmaceuticals Inc.®
D-atazanavir

$1B+
2009

Deuteration can:

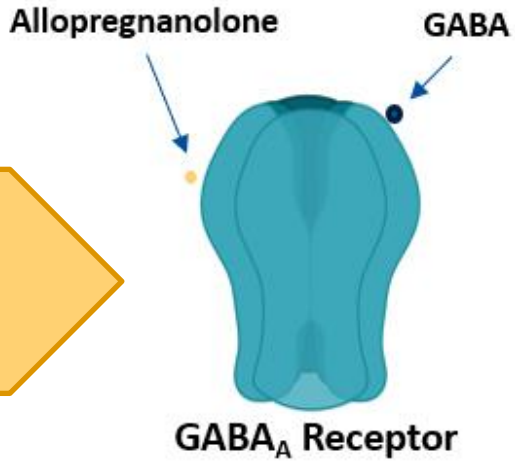
- ✓ Improve drugs
- ✓ Minimize risk in product development

[1]Per Teva FY 2024 Guidance
[2]Per broker consensus projections (Source: FactSet)

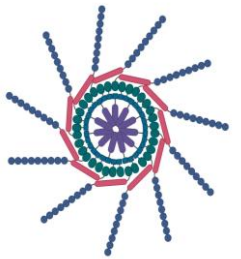
Novel Mechanism of Action

GRX-917/etifoxine increase neurosteroid synthesis[1]

Neurosteroids modulate receptors[2]
(anxiety, depression, epilepsy)



Neurosteroids inhibit NLRP3 inflammation[3]
(epilepsy, MS, pain, obesity)



[1]do Rego JL et al (2015) PLoS ONE 10(3): E0120473 ; internal data
[2]Lambert et al (2003) Prog Neurobiol 71(1); 67-80.
[3]Osmond et al (2023)

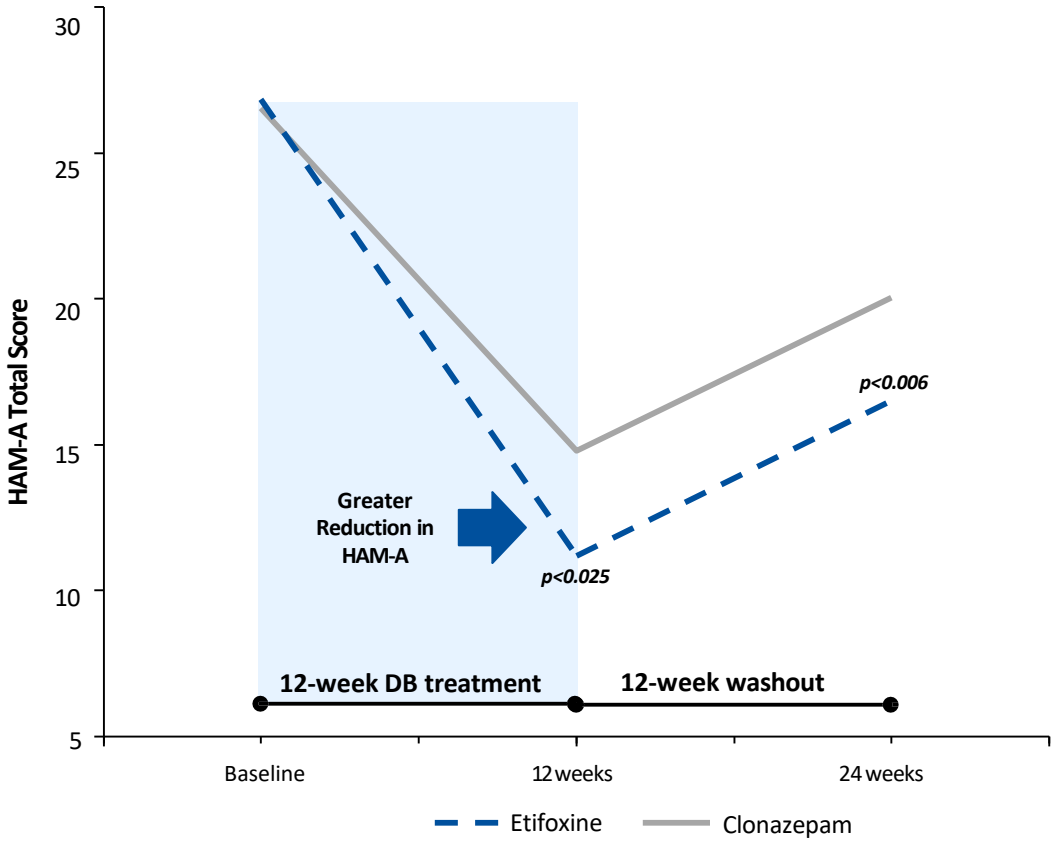
Etifoxine's Anxiolytic Efficacy is Well-Established

	Date	Clinical Study	Reference	N	Duration	Cohort	HAM-A	CGI scale	Result
1	1978	ETX vs Clobazam	S.132/GB	26	Not Available	Anxiety[1]	ETX = > Clobazam[2]		Marketing Authorization (France)
2	1978	ETX vs Clobazam	S.134/GB	20	Not Available	Anxiety[1]	ETX = > Clobazam[2]		Marketing Authorization (France)
3	1978	ETX vs Sulpiride vs Placebo	S.135/GB	23	Not Available	Anxiety[1]	ETX = > Sulpiride & Placebo[2]		Marketing Authorization (France)
4	1978	ETX vs Clobazam	S.137/GB	69	Not Available	Anxiety[1]	ETX = > Clobazam[2]		Marketing Authorization (France)
5	1978	ETX vs Placebo	S.139/GB	24	Not Available	Anxiety[1]	ETX = > Placebo[2]		Marketing Authorization (France)
6	1998	Etifoxine vs Buspirone	STRETI S.226/GB	170	31 days	ADWA	ETX > Buspirone	ETX > Buspirone	Superior efficacy to Buspirone
7	2006	Etifoxine vs Lorazepam (Ativan®)	ETILOR S.392/EN	191	28 days	ADWA	ETX = LZP (Ativan®)	ETX > LZP (Ativan®)	Comparable onset and efficacy to Lorazepam
8	2010	Etifoxine vs Phenazepam	Aleksandrovsky[3]	90	6 weeks	Adaption Disorder	ETX > Phenazepam	ETX > Phenazepam	Superior efficacy to Phenazepam
9	2015	Etifoxine vs Alprazolam (Xanax®)	ETIZAL S.650/EN	202	28 days	ADWA	ETX = ALP (Xanax®)	-	Comparable onset and efficacy to Alprazolam
10	2020	Etifoxine vs Clonazepam (Klonopin®)	Vicente[4]	179	24 weeks	GAD, PD, Phobias[5]	ETX = Clonazepam (Klonopin®)	ETX = Clonazepam (Klonopin®)	Superior efficacy to Clonazepam
11	2020	Etifoxine vs Lorazepam & Placebo	AMETIS ETI178	623	4 weeks	ADWA	Total HAM-A score reduction similar between ETX, lorazepam, placebo. EMA conclusion: "The decrease in HAM-A score in the etifoxine group was marked and clinically significant (52.6% reduction)."		
12	2022	EMA CHMP Etifoxine Assessment Report	EMA/CHMP 148255/2022	N/A	N/A	All available ETX data	"… the Committee considers that the benefit-risk balance of etifoxine remains favourable…" ETX was re-authorized for anxiety in France in Jan 2022 (29-1 vote).		

1. Various types of anxiety associated with psychological and somatic disturbances in diverse patient populations
2. "Results generally showed that etifoxine has similar or superior efficacy to active comparators or placebo for treating anxiety" per EMA/148255/2022 CHMP ETX Assessment

3. Aleksandrovsky et al., "Russian Psychiatric Journal"; Therapy of the mentally ill; No. 1; 2010; 74-78 Vicente et al.,
4. Psychopharmacology 237, 3357–3367 (2020)
5. Phobias categorized as agoraphobia, social phobia and specific phobias

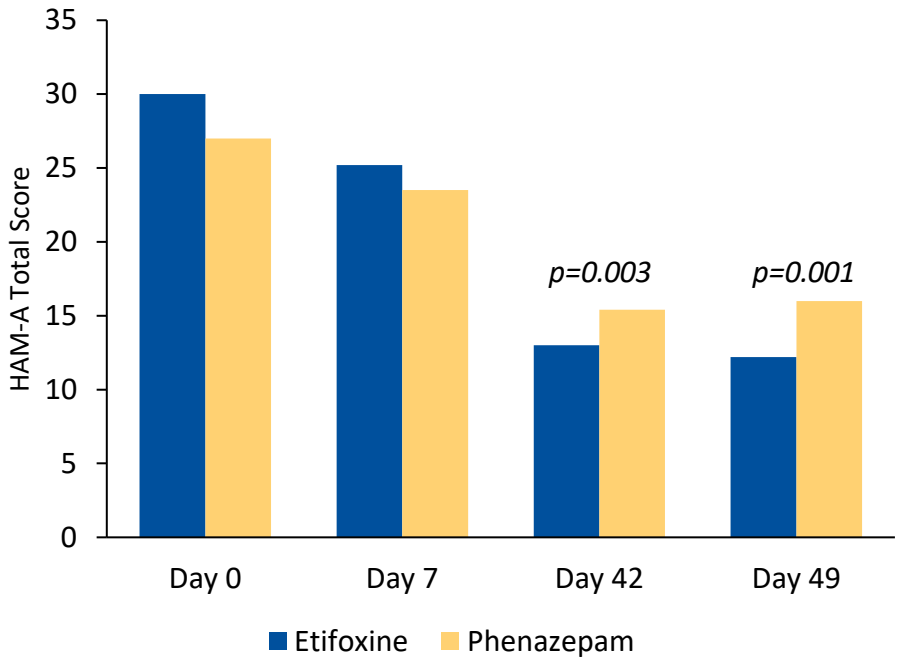
Etifoxine: Superior Efficacy vs. Clonazepam



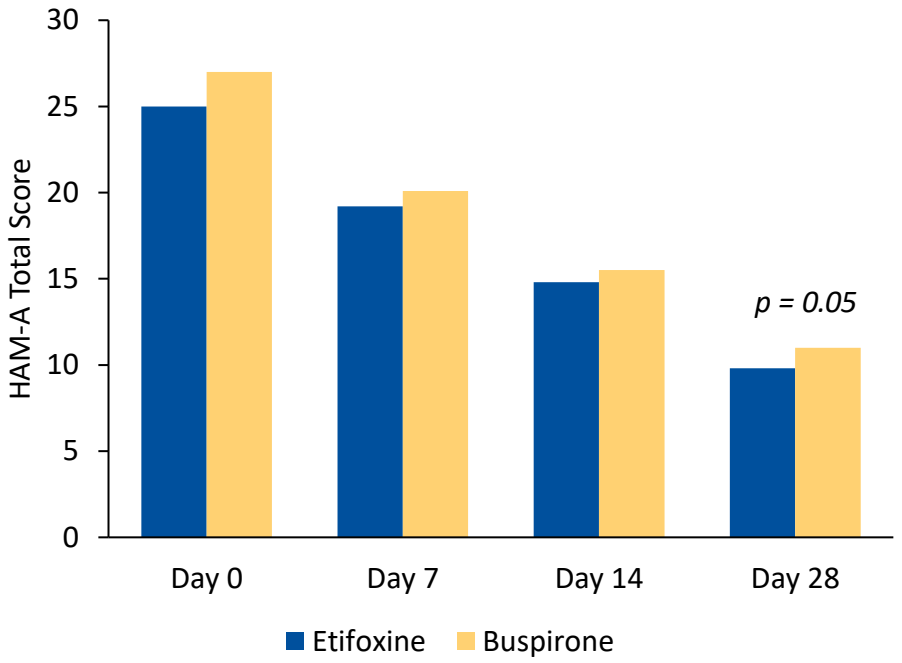
- Etifoxine demonstrated superior HAM-A reduction vs. clonazepam after 12-week treatment ($p<0.025$)
- Superior efficacy maintained following 12-week washout ($p<0.006$)

- Vicente et al. (2020) Psychopharmacology
- Double-blind, parallel, randomized, active controlled study; multiple anxiety disorders; N=179
- Etifoxine 50 mg TID v clonazepam 1 mg QD; 12-week treatment; 12-week washout

Etifoxine: Superior Efficacy vs. Phenazepam and Buspirone

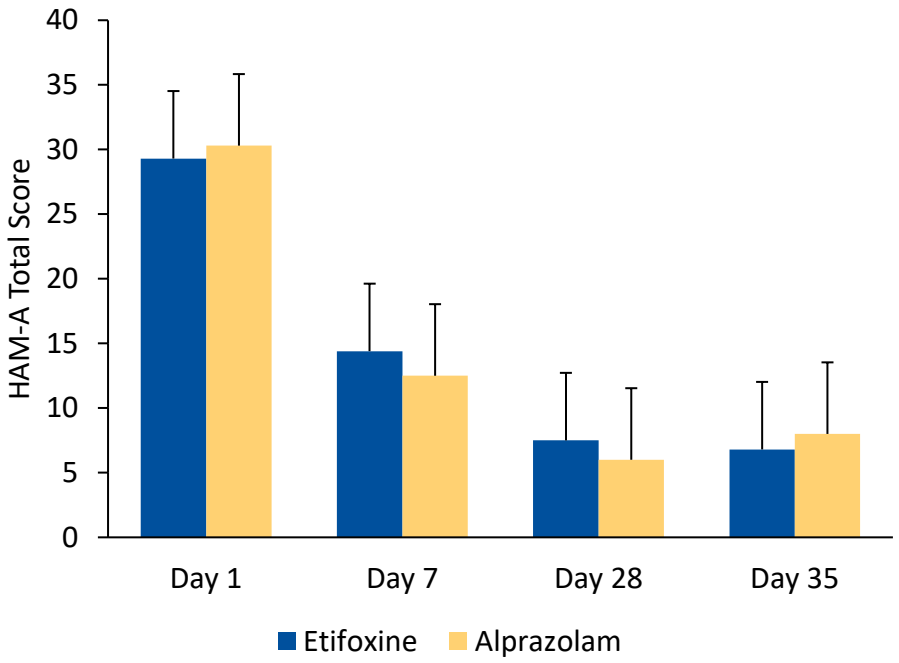


- Aleksandrovsky et al. (2010) Rus Psych J (1); 74-78.
- Randomized, parallel, open label, active controlled study; N=90;
- Adjustment Disorders
- Etifoxine (50 mg +100 mg) v phenazepam (0.5 mg BID); 6-week treatment

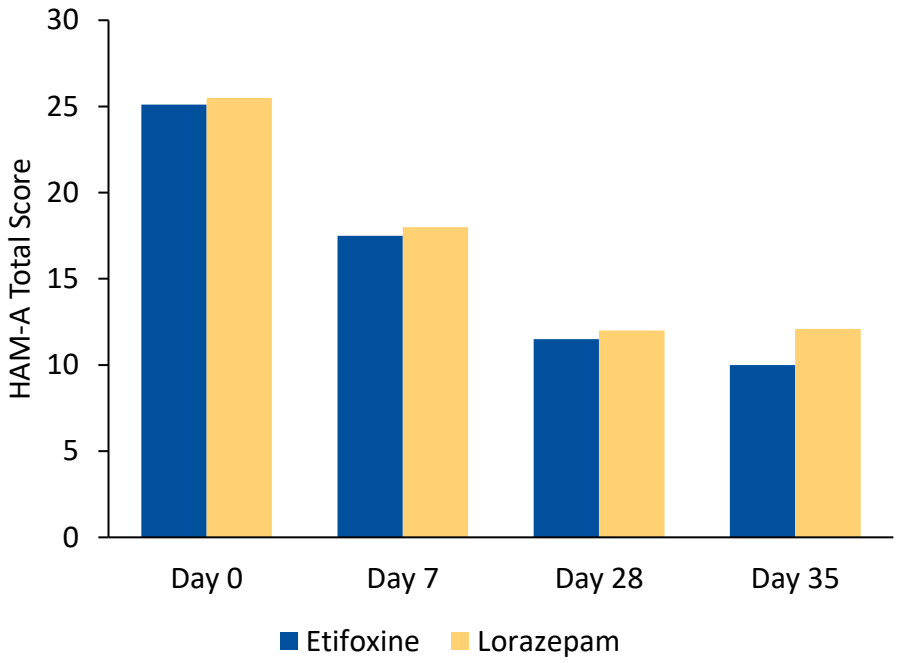


- Servant et al. (1998) Encephale 24(6):569-74.
- Double-blind, parallel, randomized, active controlled; N=170;
- Adjustment Disorder with Anxiety (ADWA)
- Etifoxine (150-200 mg/day) v buspirone (15-20 mg/day); 4-week treatment

Etifoxine: Comparable Efficacy to Leading Benzodiazepines



- Stein et al. (2015); N=202; ADWA
- Double-blind, randomized, parallel, active controlled 4-week treatment
- Etifoxine (150 mg/day) v. alprazolam (1.5 mg/day)



- Nguyen et al. (2006); N=191; ADWA
- Double-blind, randomized; parallel, active controlled 4-week treatment
- Etifoxine (50 mg TID) v lorazepam (2 mg/day)

Etifoxine's Safety Profile is Well-Established

Adverse Event	Comment	Source
Non-Addictive	"No cases of abuse, misuse or pharmacodependence."	Cottin et al[1]
No Sedation	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]
Serious Adverse Drug Reactions (ADRs)	Very rare ADRs not consistent with causation (1-2 per 15.7M Rx)	PV Analysis of Etifoxine Serious ADRs in EudraVigilance Database[4]

1. Cottin et al., Fundamental & Clinical Pharmacology 30 (2016) 147–152
2. Micallef et al., 2001 Blackwell Science Fundamental & Clinical Pharmacology 15 (2001) 209-216
3. Deplanque et al., European Neuropsychopharmacology (2018) 28, 925-932
4. Kinexum-Pharmacovigilance Analysis of Etifoxine 2023-03-13

Phase 1 Program: GRX-917 vs. Etifoxine

- GRX-917 demonstrated improved PK and once-daily dosing
- Safe, well-tolerated, with minimal adverse events

	Etifoxine	GRX-917
Half-life	4 hours	>12 hours
Daily dose	200 mg	60 mg
Dosing regimen	**TID**	**QD**

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%

Etifoxine Phase 1: (Study GRX-ETI-001) - A Two Stage, Double-Blind, Placebo-Controlled Single and Multiple Dose Study To Evaluate The Pharmacokinetics, Pharmacodynamics, and Safety of Oral Etifoxine in Normal Healthy Volunteers

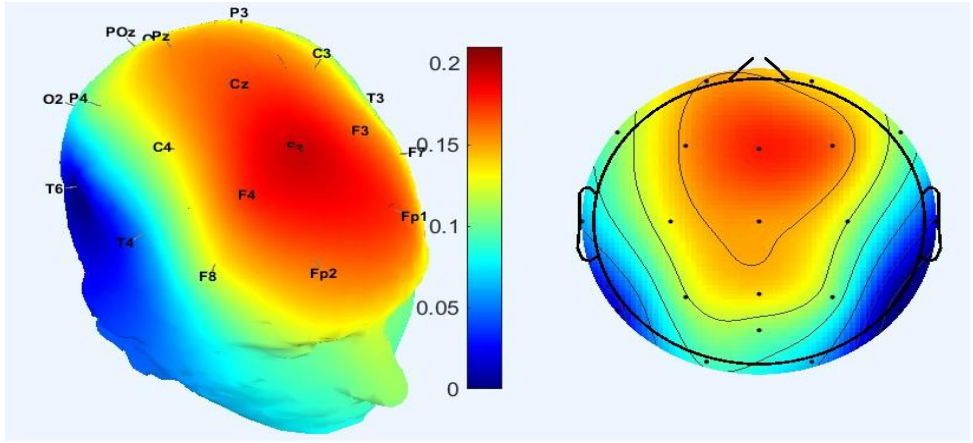
GRX-917 Phase 1: (Study GRX-917-01) - A Phase 1, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single and Multiple Ascending Doses of GRX-917 in Healthy Adult Subjects

Phase 1: GRX-917 Activates an Established Anxiolytic Biomarker

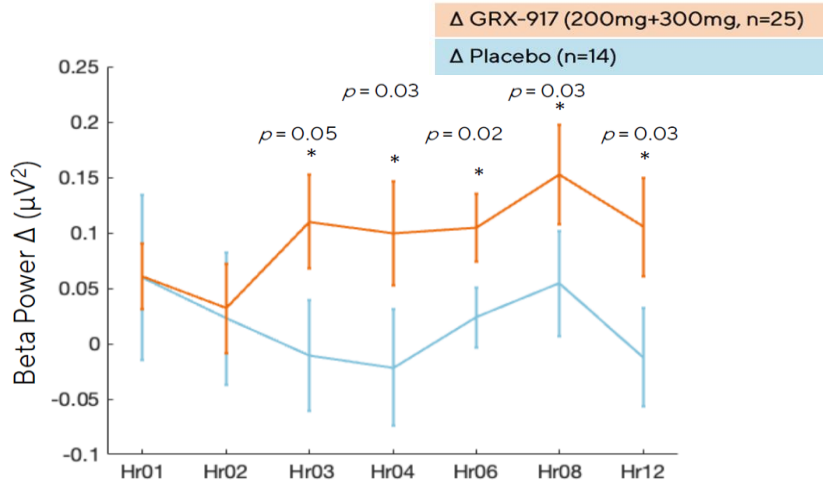
- GRX-917 increases qEEG Beta Power:
  - Exposure-dependent
  - Dose- and time-dependent
  - Rapid and sustained

- qEEG Beta Power increased signal suggests:
  - $GABA_A$ receptor target engagement
  - Anxiolytic efficacy

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



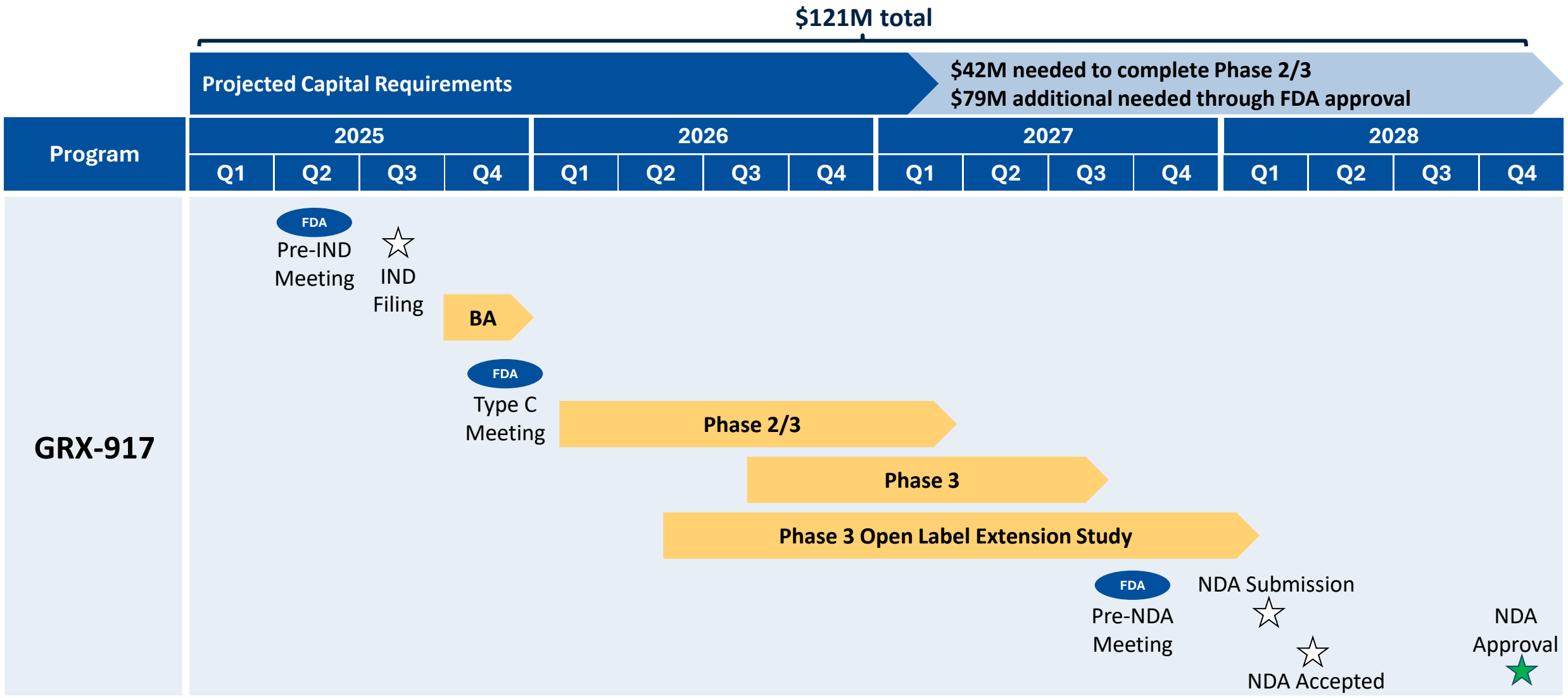
GRX-917 vs. Placebo (p<0.05)



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

GAD Clinical Program

NDA Projected by 2028



Capital Requirements and Use of Funds

$ in millions

Use of Funds	Phase 2/3 GAD	Total to NDA (est. 2028)
IND Opening Studies	$4.5	$4.5
Clinical Trials	$19.0	$58.0
Tox & Research	$4.3	$10.6
CMC	$0.6	$18.2
Regulatory	$0.5	$2.5
G&A	$13.5	$27.7
Total	**$42.0**	**$121.0**

Notes:

1) Phase 2/3 pivotal study, ending Q1’27.
2) All costs supported by vendor quotes.

Key Milestones

Accomplished to Date

Phase 1 Etifoxine (Non-deuterated Analog)

- Safety and tolerability
- qEEG biomarker demonstrating anxiolytic efficacy
- PK/dosing benchmarking for GRX-917

Phase 1 GRX-917

- Safety and tolerability
- qEEG biomarker demonstrating anxiolytic efficacy

GRX-917 Oral Formulation

- Phase 2/3 ready

2025

Q2'2025:

- Corporate updates
- Publications & presentations
- Pre-IND meeting

Q3'2025:

- IND filing

Q4'2025:

- Start bioavailability study
- BA data readout

2026 - 2028

Q1'2026:

- Start Phase 2/3 pivotal trial

Q3'2026:

- Start Phase 3 pivotal trial

Q2'2027:

- Phase 2/3 data readout

Q3'2027:

- Phase 3 data readout

Q1'2028:

- NDA Submission

Intellectual Property Overview

- **Robust IP portfolio with composition patent protection through at least 2036**
- **Potential Hatch-Waxman extensions through 2042**

Composition of matter patent protection in US, Australia, Canada, Brazil, China, EU, UK, Israel, Japan, South Korea, Mexico, with patent pending in India.

Name / Description	Patent	Status	Expiry
Deuterated Analogs of Etifoxine and Methods of Administration Without Autoinduction of Metabolism	U.S. Application No. 18/493,488	Published	10/24/2043
Deuterated analogs of etifoxine, their derivatives and uses thereof	US Patent No. 11,672,805	Issued	3/18/2036
Deuterated analogs of etifoxine, their derivatives and uses thereof	U.S. Patent No. 10,080,755	Issued	3/18/2036
Deuterated analogs of etifoxine, their derivatives and uses thereof	U.S. Patent No. 10,736,901	Issued	3/18/2036
Enantiomerically pure S-etifoxine, pharmaceutical compositions thereof and methods of their use	U.S. Patent No. 8,110,569	Issued	10/1/2027

Key Executives

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

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

Pfizer
Abbott
Shire
Johns Hopkins School of Medicine

Richard Farrell
Chief Financial Officer,
Director, & Co-Founder

EY
Deloitte.

Kathryn King, Ph.D.
Chief Operating Officer

Abbott
abbvie
Takeda
APTINYX

David Putnam, Ph.D.
Chief Scientific Officer,
Co-Founder

Roche
ucb

Olivier Dasse, Ph.D.
Senior VP of Chemistry,
Co-Founder

ucb

Key Advisors

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

Robert Berman, M.D.
Scientific Advisory Board Chairman
Co-Founder, Biohaven

biohaven pharmaceuticals

Bristol Myers Squibb

Pfizer

Yale SCHOOL OF MEDICINE

Maurizio Fava, M.D.
Clinical & Regulatory Advisor
Psychiatrist-in-Chief
Mass General/ Harvard Med

MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY

Thomas Laughren, M.D.
Clinical & Regulatory Advisor
Former Director, Div. Psych Products, FDA/CDER

FDA

MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY

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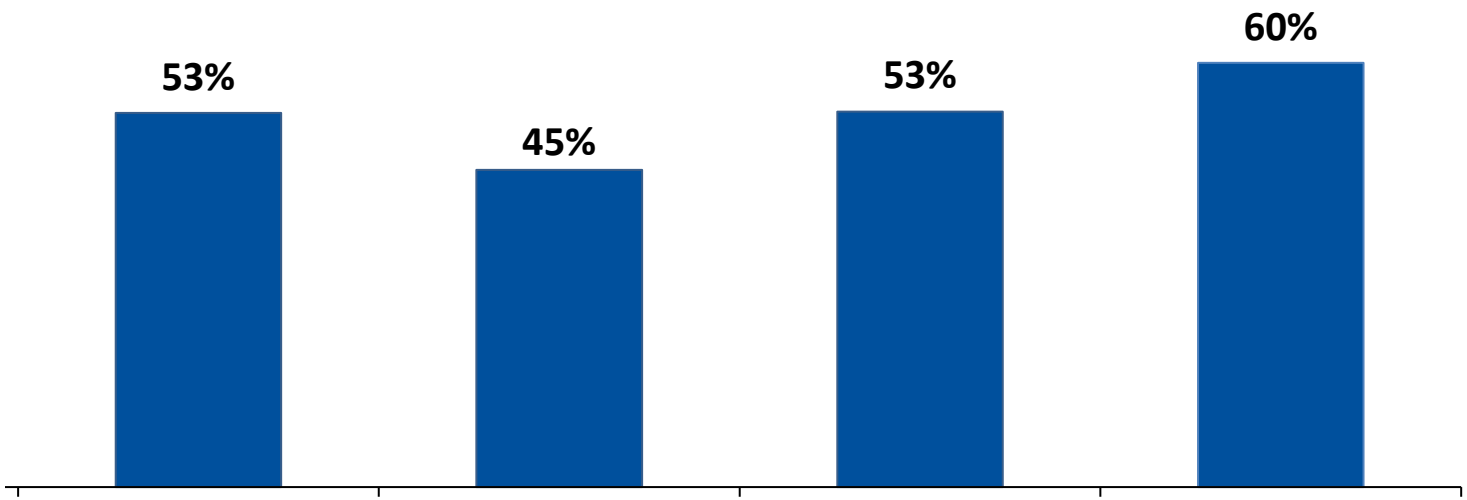
Appendix

Etifoxine Trials Show Comparable Efficacy to Other Anxiolytic Classes

HAM-A Reduction from Baseline



	SSRI/SNRI[1]	Pregabalin[2]	Benzodiazepines[3]	Etifoxine[4]
Number of Studies	22	5	10	4
Number of Patients	2,843	409	643	336

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;* Pande et al 2003, *Am J Psychiatry*
3. Rickels et al 2005, *Arch Gen Psychiatry;* Moller et al 2001, *J Clin Pyschopharmacol;* Stein et al 2015, *Adv Ther.*; Lydiard et al 1997, *J Clin Psychiatry*; Michelson et all 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*
4. 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.*

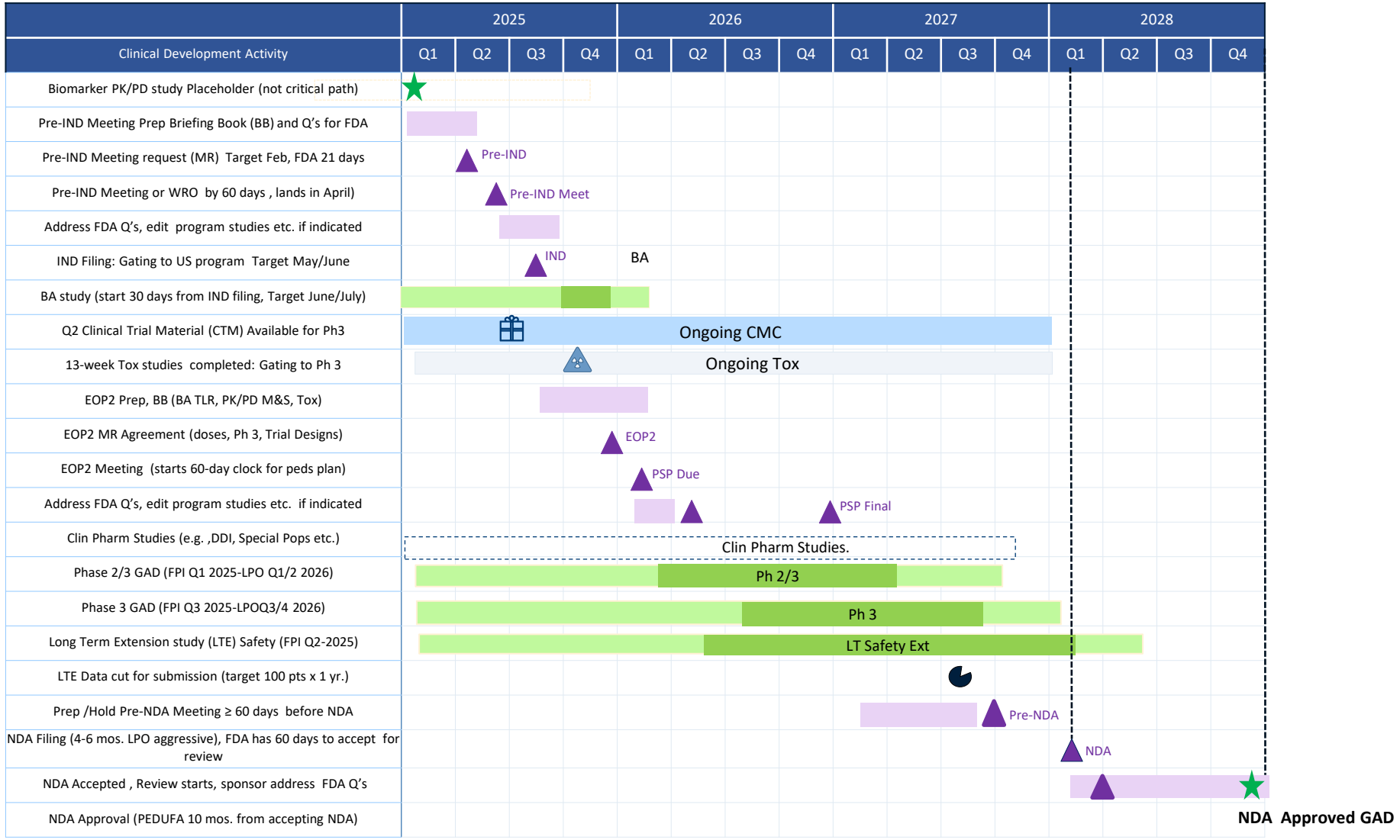
Favorable Profile vs. Other Anxiety Therapies

		Approved Drugs			Drug Candidates			
Drug	**GRX-917 / Etifoxine**	**SSRIs/SNRIs**	**Benzodiazepines**	**Allopregnanolone analogs[1]**	**Darigabat[2][3]**	**ENX-102[4]**	**SEP-363856 (ulataront)**	**LSD (MM-120)**
MOA	Neurosteroid Inducer	SERT/NE transporter inhibitor	GABA PAM	GABA PAM	GABA PAM	GABA PAM	TAAR1 AGONIST	5HT-1a/2a agonist
Mode of Administration	Oral QD	Oral QD	Oral (variable)	IV/oral	Oral BID	Oral QD	Oral QD	Oral x1
Onset of Action	Rapid	4–8 Week Delay	Rapid	Rapid	No Efficacy	Rapid	?	Rapid
Efficacy (HAM-A Reduction)	60%	52%	52%	60% (zuranolone)	No Efficacy	No beta power increase was reported	?	75%
AEs	Minimal	Moderate	High	High	High	High	Moderate	High
Somnolence	0% (Phase 1)	11% (Zoloft USPI)	41% (Xanax USPI)	20-50%	25%-33%	Somnolence 90%; Fatigue 87%	8%	<10%
Other	None	Emotional detachment; Sexual dysfunction	Impaired cognition; Ataxia	Blackbox warning for excessive sedation	Impaired cognition; Impaired Epworth; Sleepiness scale	Sustained reduced arousal; Alpha power decrease	GI AEs	Psychedelic AEs; suicidality
Addiction Liability	None	None	Schedule IV	Schedule IV	Schedule IV probable based on drug class	Schedule IV probable based on drug class	Unknown	Schedule I currently
Treatment Duration	Chronic	Chronic	Short Term	Restricted	Unknown but likely short term	Unknown but likely short term	Chronic	Restricted Administration

1) Brexanolone, zuranolone, ganaxolone,SPT-300
2) Vanover et al., 2023
3) Gurrell et al 2023
4) Simen et al, Journal of Clinical Psychopharmacology 39(1):p 20-27, 1/2 2019

GXR-917 GAD Expedited Phase 2/3 Registration Program

First NDA by 2028



The timings are estimates based on current knowledge and may/will be slightly shorter or longer (-/+ ~1-3 mos.), pending confirmative data, agency interactions, site factors etc.

KEY FDA Prep, Docs, Q's | FDA milestone | Toxicology | Data Cut | Clinical Trial Material (CTM) | NDA Approval

Planning/Start-up activity | FPI | study conduct | LPO | Reports

GAD Clinical Studies Can Be Conducted with Highly POS

Lyrica® (pregabalin) Latest Drug Approved in GAD

- 6 of 7 GAD studies were positive and statistically superior to placebo
- 16 of 17 arms successfully separated from placebo
- Pregabalin reduces HAM-A score by 45%
- Etifoxine reduces HAM-A by 60%

Source: Anxiolytics Meta-analysis

Baldwin and Ajel

Table 2 Randomized controlled trials of pregabalin in acute treatment of GAD

Study	Treatments		N	Change in HAMA (LOCF, ITT)	Response[a] (%) (LOCF, ITT)
Pande et al 2003	Placebo		69	–6.82	28
	Pregabalin 150 mg/day	✓	69	–9.24*	Not stated. (NS)
	Pregabalin 600 mg/day	✓	70	–10.25**	47*
	Lorazepam 6 mg/day	✓	68	–11.96***	57*
Pande et al 2000 "Failed" trial	Placebo			No significant difference in efficacy for any treatment versus placebo	
	Pregabalin 150 mg/day				
	Pregabalin 600 mg/day				
	Lorazepam 6 mg/day				
Feltner et al 2003	Placebo		67	–9.27	42.4
	Pregabalin 150 mg/day	Low dose	70	–10.89	47.8
	Pregabalin 600 mg/day	✓	66	–13.17**	49.2
	Lorazepam 6 mg/day	✓	68	–11.62*	56.3
Rickels et al 2005	Placebo		91	–8.4	31
	Pregabalin 300 mg/day	✓	91	–12.2***	61***
	Pregabalin 450 mg/day	✓	90	–11.0*	44
	Pregabalin 600 mg/day	✓	89	–11.8**	51**
	Alprazolam 1.5 mg/day	✓	93	–10.9*	45*
Montgomery et al 2006	Placebo		101	–11.6	42
	Pregabalin 400 mg/day	✓	97	–14.7**	56*
	Pregabalin 600 mg/day	✓	110	–14.1*	59*
	Venlafaxine 75 mg/day	✓	113	–14.1*	61**
Pohl et al 2005	Placebo		86	–9.3	34
	Pregabalin 200 mg/day	✓	78	–12.4**	56**
	Pregabalin 400 mg/day	✓	89	–12.9***	55**
	Pregabalin 450 mg/day	✓	88	–12.4**	59**
Khan et al 2006 (elderly patients)	Placebo		96	–10.7	Not reported
	Pregabalin 150–600 mg/day (mean maximal 270 mg/day)	✓	177	–12.8 *	

[a]Response defined as Clinical Global Impression of Improvement score of 1 ("very much improved") or 2 ("much improved").
*p<0.05, **p<0.01, ***p<0.001, all vs placebo. NS not significant.
Abbreviations: HAMA, Hamilton Rating Scale for Anxiety; ITT-LOCF Intention-to-treat, last-observation-carried forward.

Neuropsychiatric Disease and Treatment 2007:3(2) 185–191

Etifoxine Rare, Serious ADRs: No Causality

A French Pharmacovigilance Study of 15.7M Rx of etifoxine identified rare serious ADRs (left column), per Cottin et all column. An independent PV consulting firm (Kinexum) replicated and analyzed the data using the EudraVigilance database. They discovered errors in the Cottin et al analysis, and many confounds that limit the significance of these events. Actual numbers of serious ADRs (right column) attributable to etifoxine were much lower - 0-2/15.7M.

Figure 1. Serious ADRs Reported for Etifoxine in France (2000-2012)

Serious Adverse Drug Reaction (ADR)	No. of Serious ADRs	No. of Serious ADRs	ICSRs Associated with Drugs Known to Cause the ADR	ICSRs Reporting Etifoxine Monotherapy	Serious ADR Event Rate
	Cottin, et al (2)	EudraVigilance (3)	EudraVigilance (3)	EudraVigilance (3)	(10)
DRESS	5	2	1	**1**	1/15.7M
Stevens-Johnson	5	4	3	**1**	1/15.7M
Erythema multiforme	10	2	2	**0**	0
Hepatic cytolysis	25	5	3	**2**	2/15.7M
Microscopic colitis	3	1	1	**0**	0

- The French Pharmacovigilance Study (2) analyzed 15.7 million prescriptions of etifoxine from 2000-2012

GRX-917 vs. Zuranolone

Safety Explained by Diverse MOAs

	GRX-917/ETX	Zuranolone (ZURZUVAE)
Drug Class	Benzoxazine	Allopregnanolone analogue
Source of Neuroactive Steroids	Endogenous induction	Exogenous
Neurosteroid Distribution	Regionally specific (hippocampus, amygdala, cortex)	All brain regions (no selectivity)
Brain ALLO Increases at Therapeutic Doses	Up to 8 X increase (in mice)	+100 X (estimated)
Dosing	Chronic	14-day max
Observed Abuse Liability	No observed abuse liability/Not scheduled	Schedule IV
Adverse Events	Minimal No AEs above placebo in Phase 1	Blackbox warning Somnolence, dizziness, confusion, diarrhea, suicidal thoughts

GRX-917 – Safe, Effective & Vetted Anxiolytic

KOL viewpoints

1. Maurizio Fava, MD, Psychiatrist-In-Chief at MGH/Harvard Med is familiar with GRX-917/etifoxine and estimates an **80% probability of success** for GRX-917 in GAD, based on three published studies demonstrating etifoxine statistical superiority to benzodiazepines and buspirone. Maurizio has agreed to advise GABA regarding trial design and how to ensure success via mitigation of placebo response. He will attend our pre-IND meeting to ensure regulatory and operational success.

2. Tom Laughren, MD, former Division Director for Psychiatry Products at FDA, believes GRX-917/etifoxine safety and efficacy is well-established, and that it would be reasonable to apply for **Breakthrough Therapy Designation** given its superior safety profile. Tom has agreed to advise on development and regulatory matters.

3. Philippe Nuss MD, PhD, Psychiatrist at Pitié-Salpêtrière/ St-Antoine Hospital and researcher at the Sorbonne (Paris) is an etifoxine prescriber and researcher. Prof Nuss confirms etifoxine's safety and efficacy and uses it regularly to treat severe anxiety patients who have failed SSRIs/SNRIs and/or benzos (**treatment-resistant anxiety**). He uses etifoxine for treatment of GAD, social anxiety disorder and mixed anxiety-depression.

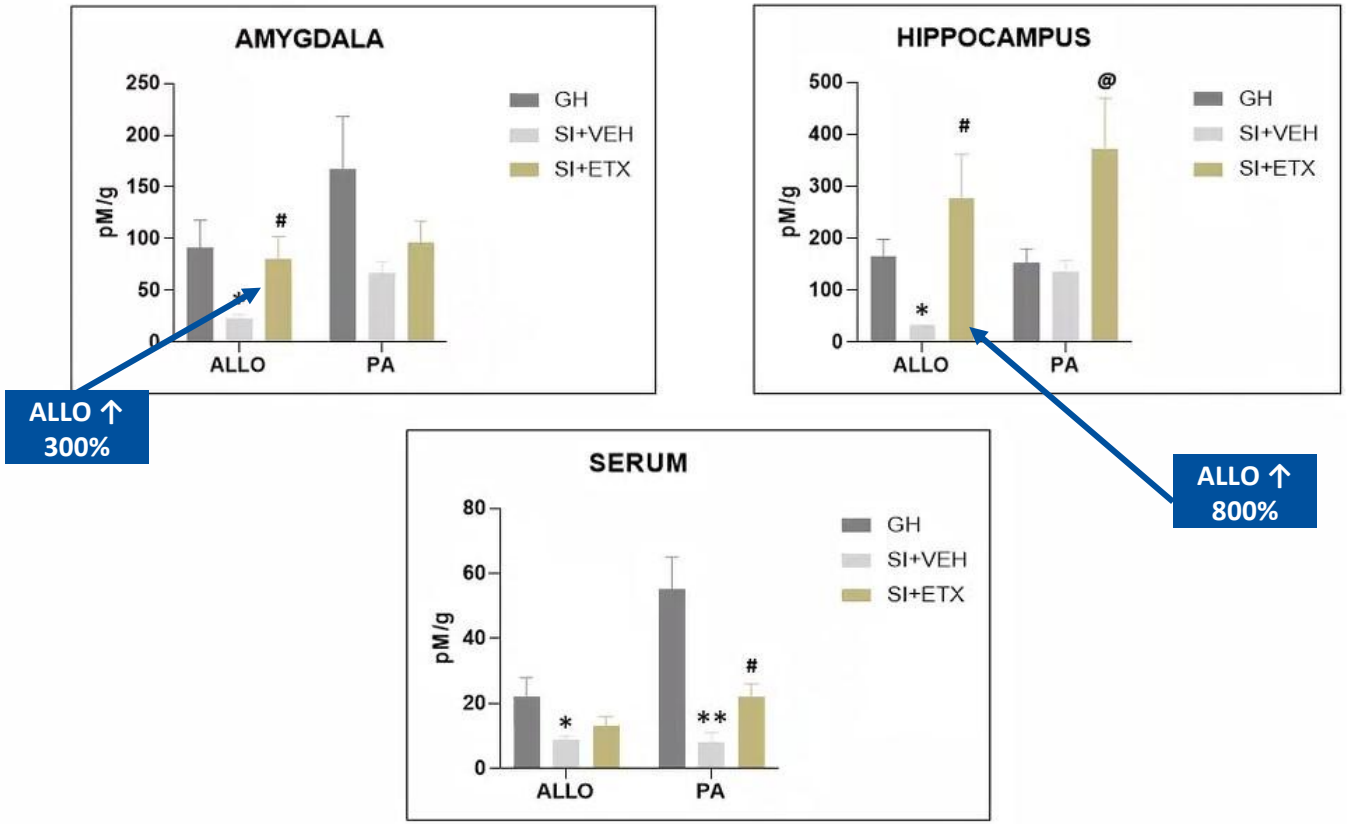
All recognize the importance of getting GRX-917 safe and effective drug to market and have agreed to join GABA's SAB. They are also available to speak with investors. Please let us know if you would like us to arrange a call.

MOA and Additional Indications

GRX-917 - Primary Mechanism of Action

Stimulation of Brain Neurosteroid Synthesis

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

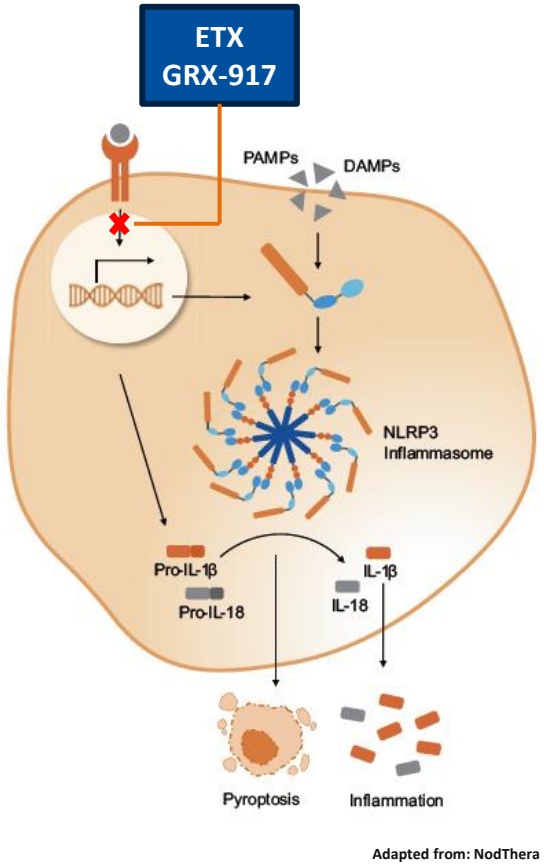


Etifoxine was administered at the dose of 50mg/kg IP and mice were killed 60 min after drug injections. Results are Mean ± SEM of 5-10 mice. *P<0.05 and **P<0.001 compared with group-housed (GH) mice; #P<0.05 compared with socially isolated (SI) mice plus vehicle (VEH); @P=0.06 compare with SI + VEH

Source: Graziano Pinna PhD, Univ IL Chicago

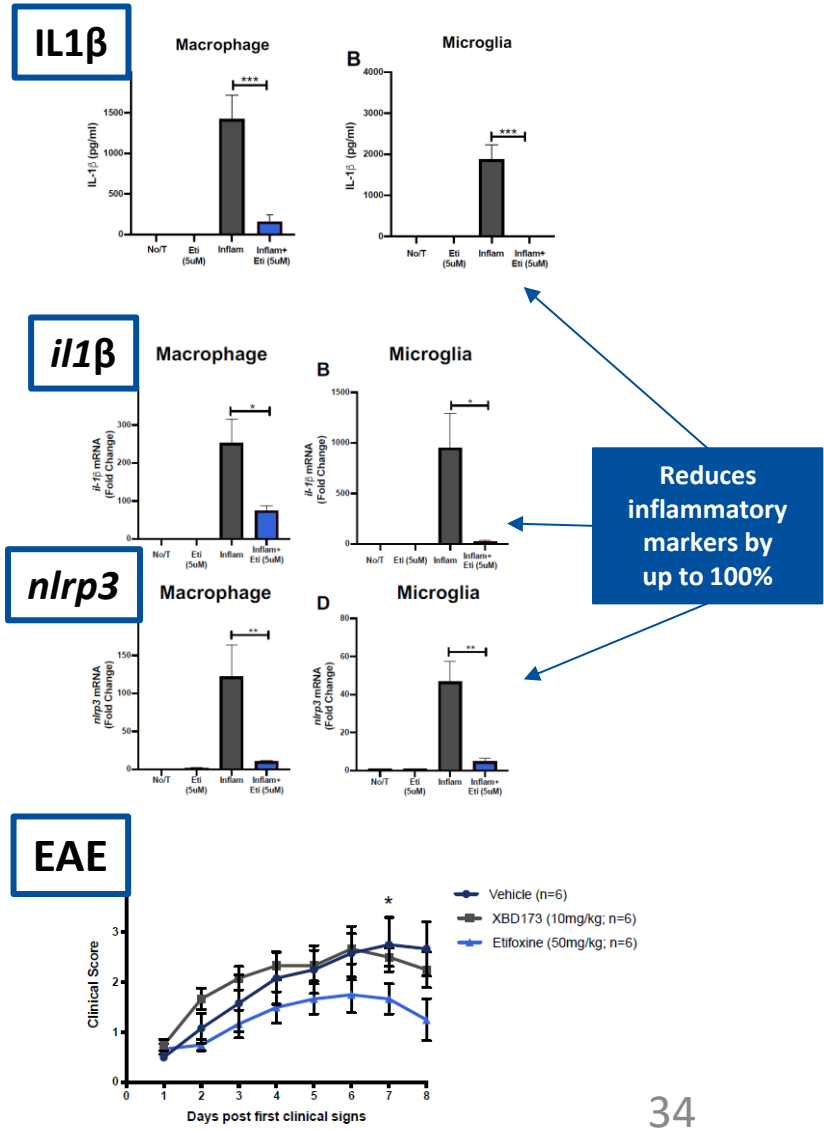
Etifoxine Inhibits NLRP3/ IL1B Pathway Inflammation

Etifoxine Inhibits NLRP3/ IL1B Pathway Inflammation



Adapted from: NodThera

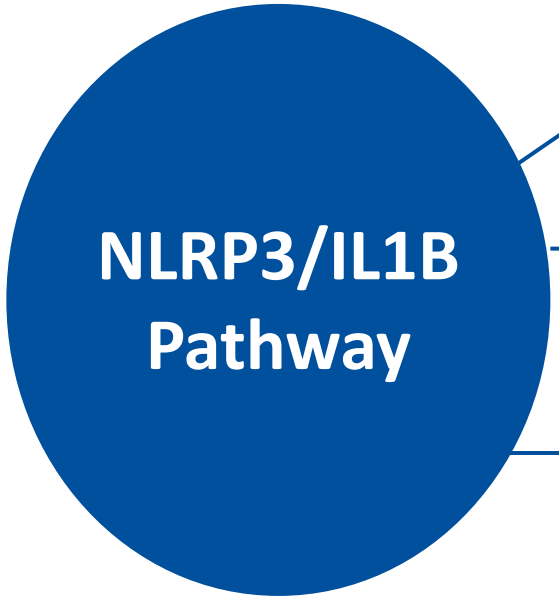
- **NLRP3 inflammasome activity contributes to:**
  - IL-1β, IL-18 and cytokine release
  - Cell death via pyroptosis
  - CNS and peripheral inflammation
- **Osmond et al (2023) showed that ETX:**
  - Blocks NLRP3 pathway activation
  - Reduces IL-1β, NLRP3, TNF
  - Improves clinical scores in EAE model
- **NLRP3 inhibition explains ETX efficacy in preclinical models:**
  - EAE (acute neuroinflammation)
  - AD, PD
  - Pain
  - Obesity
  - TBI, stroke



Etifoxine inhibits NLRP3 inflammasome activity in human and murine myeloid cells
Jordan M. Osmond, John B. Williams, Paul M. Matthews, David R. Owen, Craig S. Moore
https://doi.org/10.1101/2023.09.19.558428

GRX-917/ETX-Class Drugs Inhibit NLRP3 Inflammation

Potential therapy for multiple CNS and systemic diseases



Systemic Inflammatory Diseases

Inflammatory bowel disease, osteoarthritis, gout, rheumatoid arthritis, asthma, psoriasis, SLE, endometriosis, cystic fibrosis, fibrotic disorders

Cardiometabolic Diseases

Obesity, MASH, NAFLD

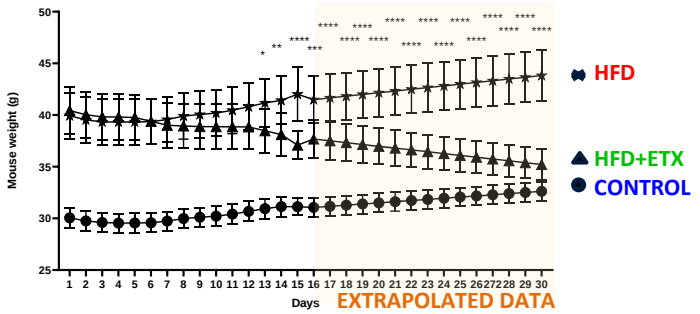
Neuroinflammatory Diseases

Multiple sclerosis, Alzheimer's disease, Parkinson's disease, ALS, anxiety, depression, PTSD, epilepsy, traumatic brain injury, neuropathy, pain

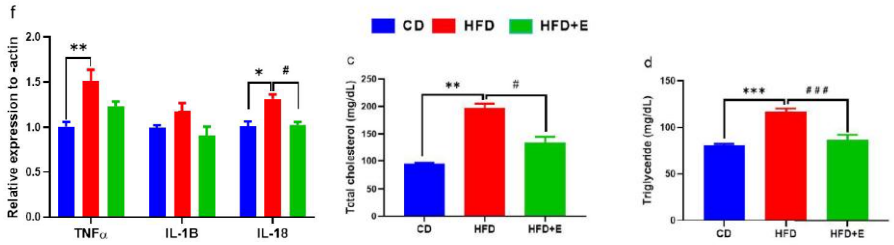
Reversal of High Fat Diet-Induced Obesity by Etifoxine

- Obesity is an NLRP3-driven neuroinflammatory disease
- Etifoxine is a potent inhibitor of NLRP3/IL-1beta pathway
- Obese HFD-fed mice lost 11% body weight following 15 days treatment with low dose ETX (50 mg/kg QD)
- ETX treatment normalized proinflammatory markers serum lipids
- ETX-induced weight loss is comparable to:
  - semaglutide
  - direct NLRP3 inhibitors (e.g. NodThera NT-0796)

Etifoxine Induces Weight Loss (11% in 15 days)



Normalization of inflammatory and lipid biomarkers



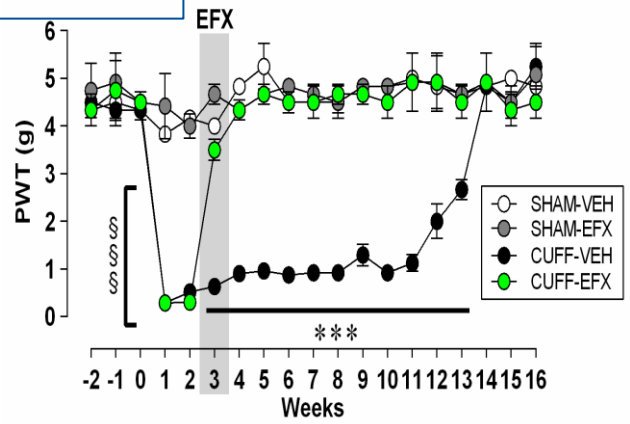
Cytokines **Cholesterol** **Triglycerides**

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

Etifoxine Reduces Pain and Inflammation in Rodent Models

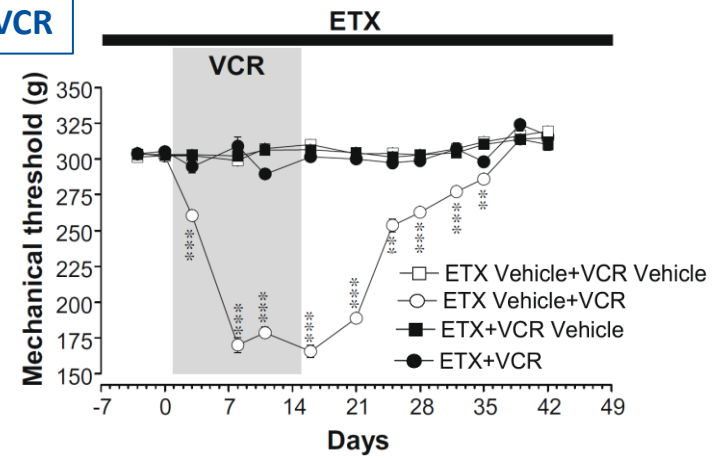
- **Etifoxine reduces mechanical allodynia in rodent pain models**
  - mononeuropathy model (sciatic cuff) Kamoun et al., 2021
  - inflammatory pain model (CFA) Aouad et al, 2014
  - streptozotocin diabetic neuropathy (STZ) Gazzo et al, 2021
  - vincristine toxic neuropathy (VCR) Aouad et al, 2009
- **Analgesic MOA is demonstrated by:**
  - Allopregnanolone synthesis in spinal cord
  - Reversal of efficacy by neurosteroid synthesis inhibitors
  - Normalization of inflammatory markers (e.g. IL-1B, TNF, IL-6, COX-2, PGE2)
  - Reduced anxio-depressive comorbidities
- **Data support GRX-917's analgesic profile**
  - Non-opioid analgesic for neuropathic, inflammatory, and nerve injury pain
  - Minimal side effects, without observed abuse liability
  - Disease modification
  - Improvement in anxiety and depressive symptoms

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

VCR

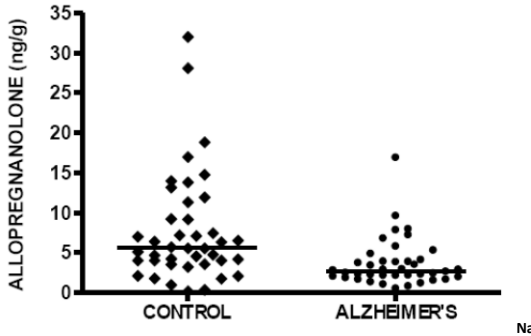


Reduction and prevention of vincristine-induced neuropathic pain symptoms by the non-benzodiazepine anxiolytic etifoxine are mediated by 3α-reduced neurosteroids
Aouad et al, Pain 2009
DOI: 10.1016/j.pain.2009.08.001

GRX-917 for Neurodegenerative Disorders

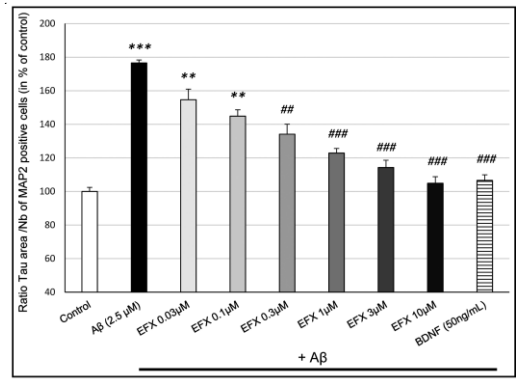
Neuroprotective, neuroregenerative, and anti-inflammatory effects

- ALLO is reduced in human post-mortem AD brain and serum (Naylor 2010;Marx 2006; Bernardi 2000)
- ETX reduces oxidative stress, apoptosis, tau hyperphosphorylation, synaptic loss, and behavioral impairments in beta amyloid toxicity models (Riban 2020)
- ETX reduces NLRP3 pathway proinflammatory cytokines including IL-1B, IL-19, TNF-a (Daugherty 2013; Aouad 2014; Ravikumar 2016; Osmond 2023)
- ALLO stimulates neurogenesis, promotes neuronal differentiation and improves behavior the in 3xTgAD mouse (Chen 2020)



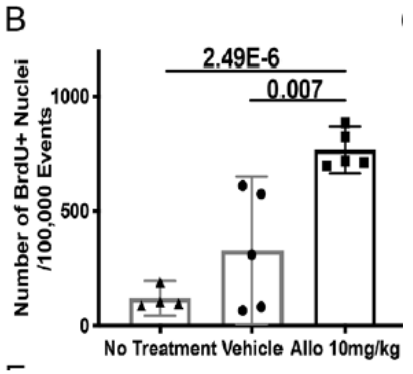
Naylor 2010

ALLO reduced in AD brain



Riban 2020

ETX blocks amyloid toxicity



Chen 2020

ALLO stimulates neurogenesis