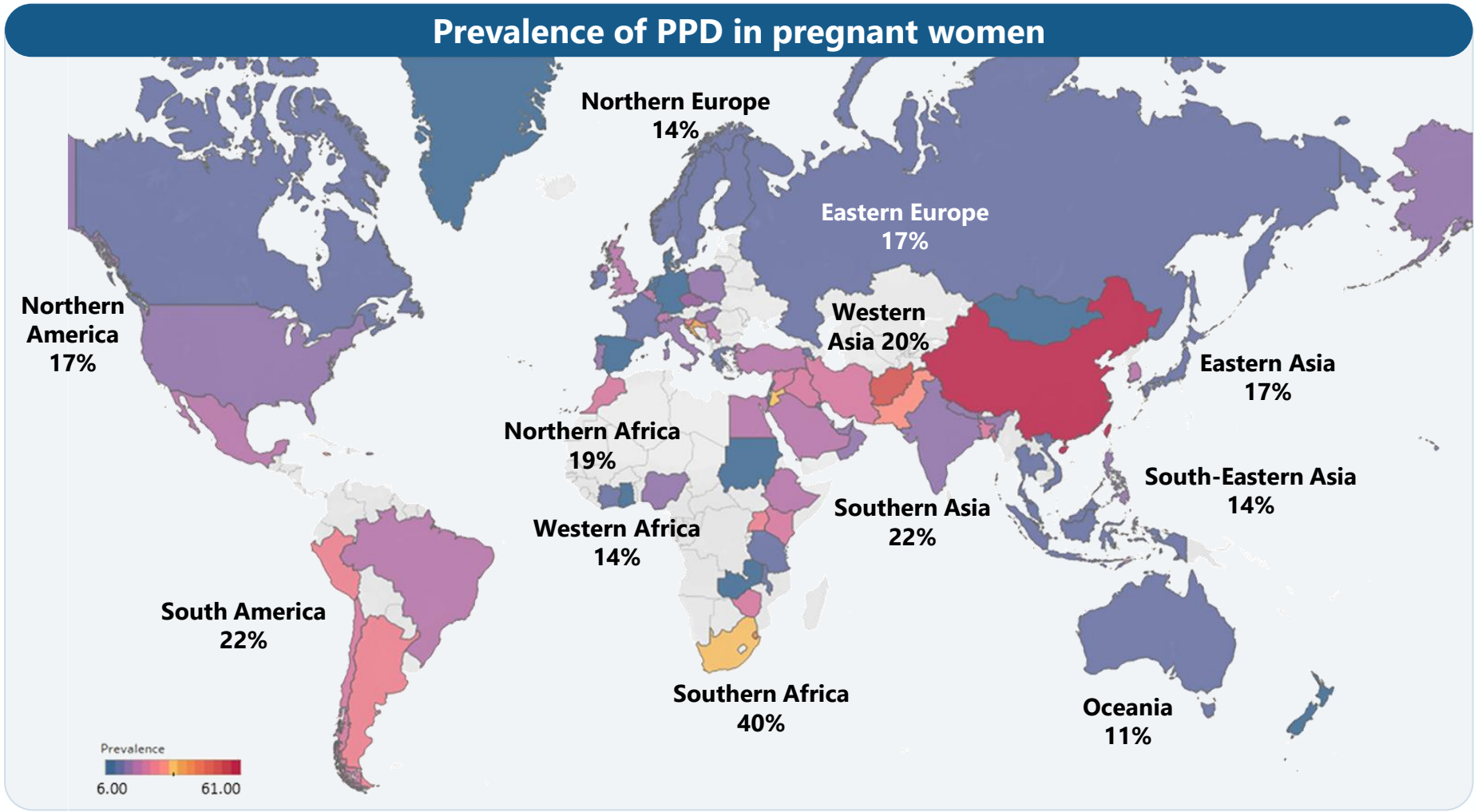
LPCN 1154 (BRLIZIO™)

Oral Brexanolone for Postpartum Depression (PPD)

Brlizio™ is a brand name conditionally approved by FDA

PPD - A Significant Global Health Issue Affecting Families Worldwide

Estimated ~ 24 million new cases of PPD annually worldwide[1]



Switzerland	22%
Korea	22%
UK	21%
Brazil	21%
China	18%
Italy	17%
France	15%
Canada	14%
Japan	13%
Germany	10%

Figure is modified based on data and map from reference Wang et al (2021)

1. Wang et al. Translational Psychiatry (2021) 11:543

PPD is a Life-Threatening Condition with Few Existing Treatment Options

Rapid relief, short treatment duration, and superior tolerability advantages

Maternal depression and suicide can have far-reaching consequences for child development, family function, and the nation's economy[1-3]

Rapid Relief Benefits

- Faster management of depression
- Reduces the risk of suicidal thoughts and behaviors
- Leads to fewer hospitalizations
- Positive outcomes in terms of mother and family relationships
- Reduces financial burden

Short Treatment Duration Benefits

- Better compliance
- Scheduling flexibility (e.g. weekend) with minimal family disruption
- More amenable to discreet treatment
- Quicker return to normal daily activities

Superior Tolerability Benefits

- Low infant sedation risk
- Better treatment adherence
- Increase treatment success
- Reduced risk of complications and hospitalization
- More quality time with family
- Less dependence on caregivers

Prompt Access Benefits

- Convenient oral route allows independent use
- Increased treatment reach
- Reduced stigma-lower visibility of treatment
- Reduced risk of crisis or suicide
- Rapid treatment initiation in time sensitive indication
- Higher treatment engagement
- Reduced health inequities

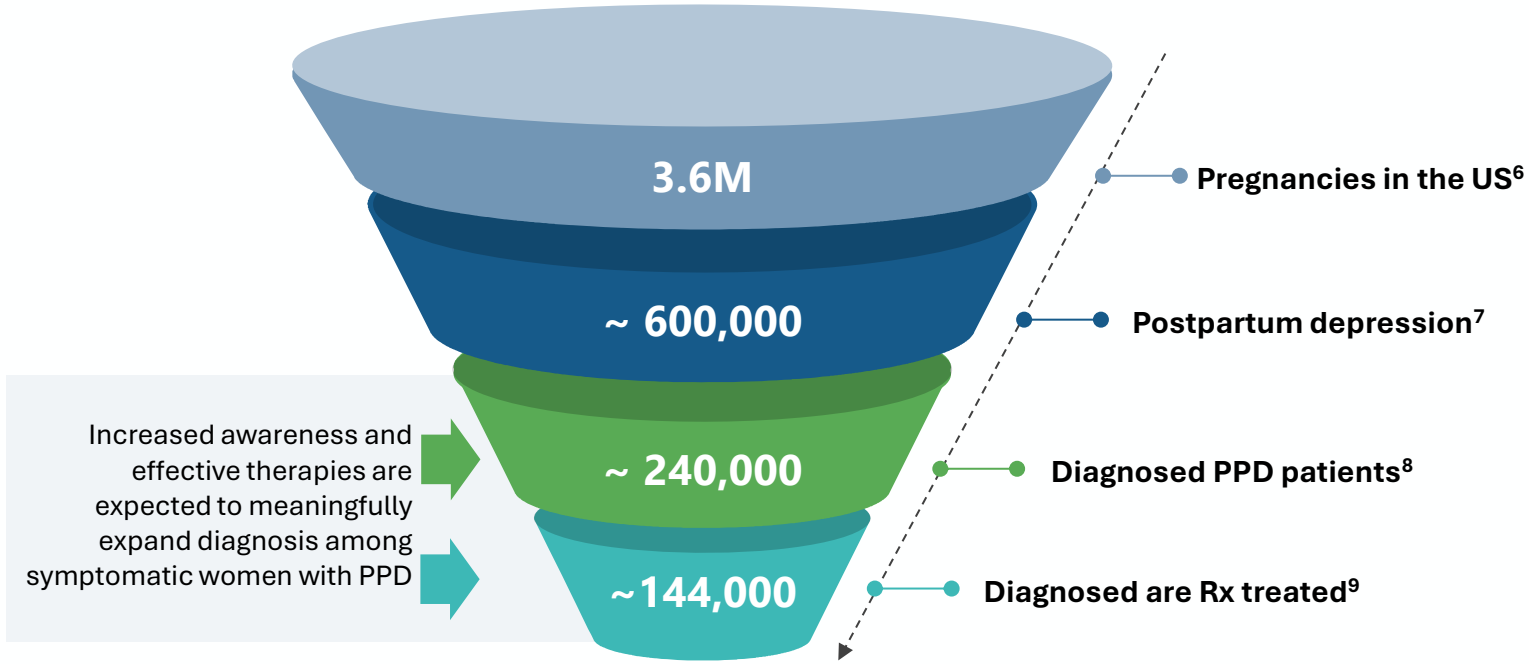
1. Mauri et al. Arch Womens Ment Health. 2012; 15(1): 39-47
2. Chin et al. Curr Psychiatry Rep, 2022; 24(4):239-275
3. www.nytimes.com/2025/07/22/health/post-partum-depression-treatment-pill.html

PPD – An Expanding Market Opportunity

Awareness drives diagnosis - empowering women with PPD through effective therapies

- High clinical and economic burden with consequences beyond the mother
- Treatment goal is rapid harm reduction for both mother and infant
- Meaningful negative impact on family stability, child development, and society
- PPD commonly presents with psychiatric comorbidity; 64% report anxiety symptoms[1]
- Suicide is a leading cause of maternal death in the first year postpartum[2]
  - Up to 30% of women with PPD report suicidal ideation[3]
- Compelling pharmacoeconomic rationale for early, effective intervention[4]

Estimated patients in the U.S. with PPD[5]



ZURZUVAE® Rx price: $16,377

ZURZUVAE revenue $66M Q4-25[10]

Projected peak ZURZUVAE® sales of ~$1B[11]

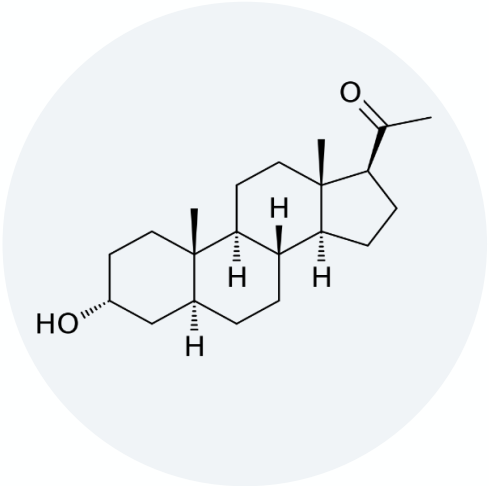
ZURZUVAE® is an FDA-approved oral treatment for adults with PPD

1. Farr et al. J Womens Health (Larchmt). 2013 Oct 26;23(2):120–128
2. Chin et al. Curr Psychiatry Rep, 2022; 24(4):239-275
3. Mauri et al. Arch Womens Ment Health. 2012; 15(1): 39-47
4. Leerink Center for Pharmacoeconomics, 2025 MEDACorp LLC
5. Foster Rosenblatt market research 2023 (Lipocine internal data)
6. National Vital Statistics Report vol 72, num 1, 2023; Vital Statistics Rapid Release, report 26, 2023
7. Van Niel et al. Cleveland Clinic J of Medicine. 2020;87(5):273-277
8. Cox et al. J Clin Psychiatry. 2016;77:9, Beck. AJN. 2006;106:5
9. Sage/Biogen HEOR Claims Analysis
10. Biogen 4th Quarter 2025 Financial Results
11. Sage May 2025 Management Projection

LPCN 1154 - Oral Bioidentical Neuroactive Steroid (NAS) for PPD

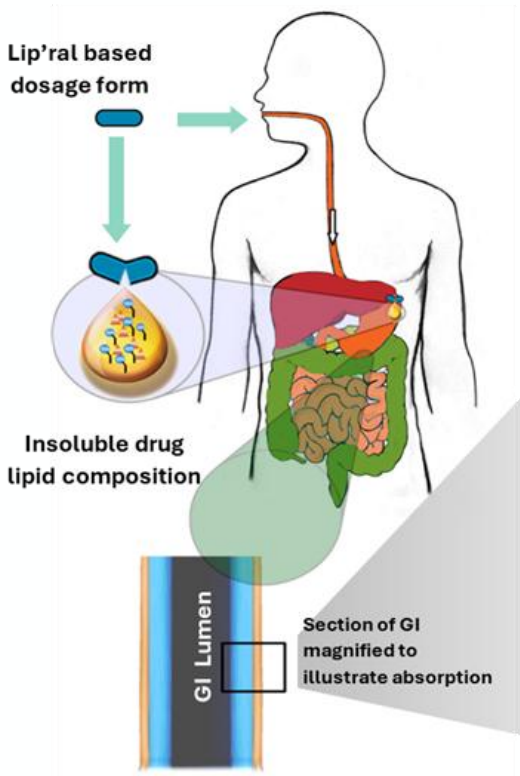
Overcoming brexanolone oral delivery challenges

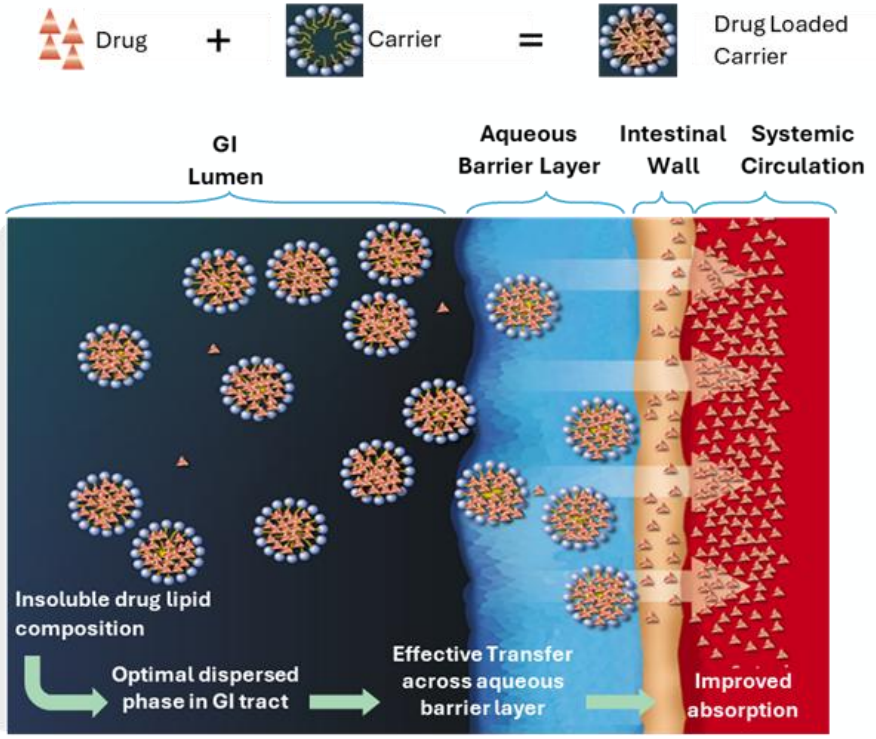
Brexanolone



Molecular Weight:	318.5 g/mol
Lipophilic:	Log P ≈ 5.0
Poor aqueous solubility:	Saq <1.0 µg/mL

Oral enablement



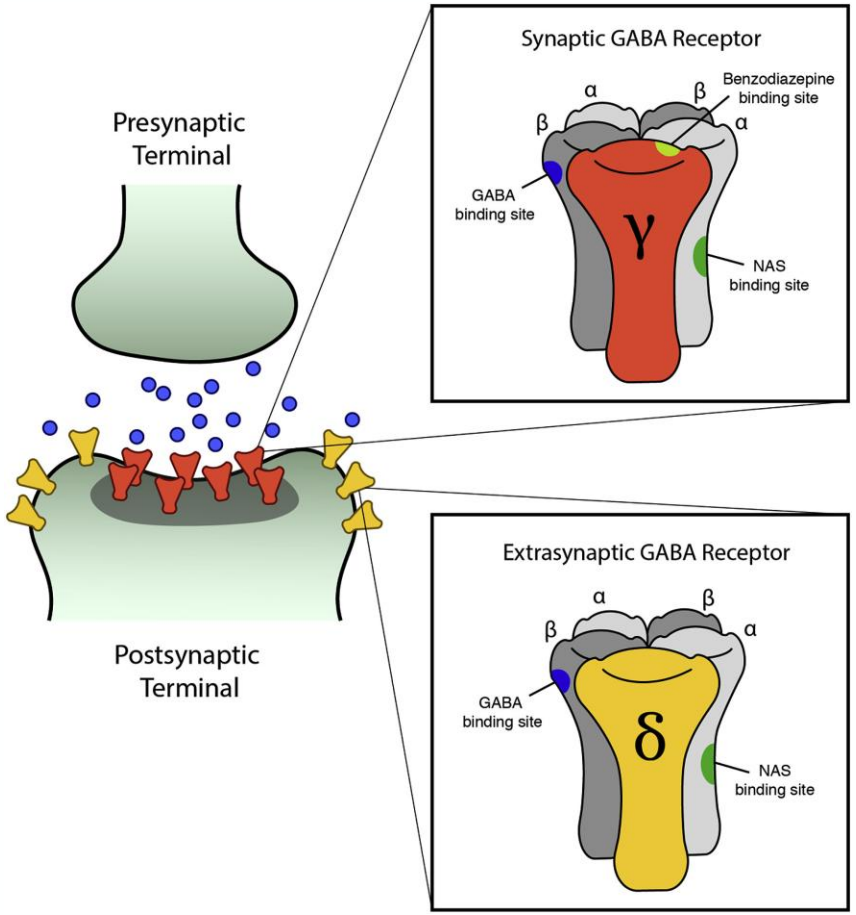


Source: Giliyar et al. Drug Delivery Technology, Jan 2006, Vol 6 No.1

LPCN 1154 - Distinctive Pharmacological Pathway

Validated through approved IV Brexanolone

Positive allosteric modulator of the $GABA_A$ receptor[1] and TLR signaling modulator[2]



Modulation of GABAergic Inhibition[1]

- **Synaptic** $GABA_A$ receptors especially those containing the γ subunit which mediate phasic inhibition, short bursts of inhibitory signaling)
- **Extrasynaptic** $GABA_A$ receptors, especially those containing the δ subunit, which mediate tonic inhibition, sustained inhibitory tone

Modulating TLR Signaling Pathways[2]

- **Reduce pro-inflammatory** cytokines (e.g., IL-1β, TNF-α) and increase anti-inflammatory cytokines (e.g., IL-10)
- **Modulate inflammatory processes** associated with neuropsychiatric disorders

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1 Meltzer-Brody and Kanes, Neurobiology of stress, 2020
2. Balan et al. Life 2024, 14, 582

LPCN 1154 – Poised to Lead the Market and Set the Standard of Care

Therapy overview – LPCN 1154 vs. existing options

LPCN 1154 (Brlizio) is expected to provide more rapid relief of PPD than approved treatments, with only a short (48-hour) treatment requirement.

Zuranolone (ZURZUVAE®) treatment is associated with frequent CNS depressant effects such as somnolence, dizziness, and sedation.

SSRIs / SNRIs have slow onset, longer treatment duration, and lower response rates. Additionally side effects such as sexual dysfunction, changes in sleep pattern and weight gain are common.

	Oral Brexanolone *(LPCN 1154)*	**Zuranolone** *(ZURZUVAE®)*	***SSRIs/SNRIs*** *Off-Label Use*
Description	**Bioidentical NAS**	Synthetic NAS Derivative	Synthetic SSRI/SNRI
Median Time to Response Onset	**2.6 days***	9 Days[1]	Weeks
CNS depressant AEs	**Low**[3]	High[2]	Moderate[4]
Onset of Action	**Hours**	Days	Weeks
Treatment Duration	**48 Hours**	14 Days	Months

No head-to-head clinical trials have been conducted. Data are derived from published reports of different clinical trials at different points in time, with differences in trial design, size, and patient populations.

1. Deligiannidis et al., Am J Psychiatry 180:9, September 2023
2. Zurzuvae label; Somnolence (36%), dizziness (13%), dose Reduction (14%), and discontinuation (2%),
3. Defined as less than 5% with no drug discontinuations, drug-related SAEs, loss of consciousness, or excessive sedation
4. https://www.uptodate.com/contents/image?imageKey=PSYCH%2F143603

*internal data, Psychiatric History Subset

Median time to response is defined as time to 50% of participants experiencing response (≥50% reduction in HAM-D)

LPCN 1154 – Phase 3 Safety and Efficacy Study Design

Utilizes same dose and regimen as the PK dose confirmation study

Study design

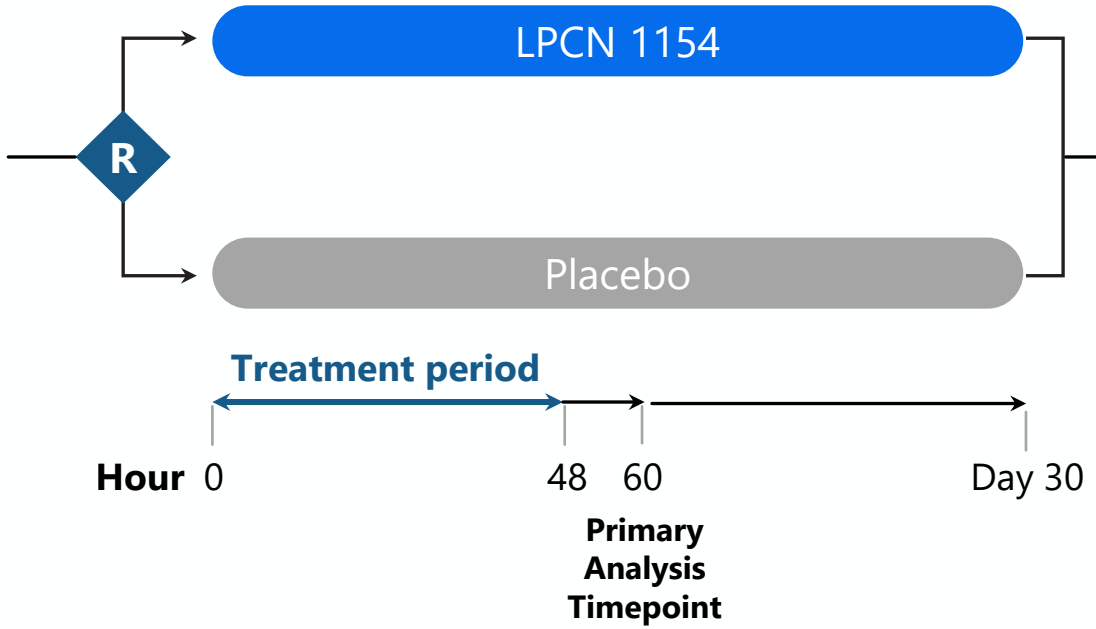
- Two arm, outpatient, randomized, blinded, placebo-controlled in women with postpartum depression at home administration with no medical monitoring

Inclusion criteria

Severe PPD (HAM-D ≥26)

Age ≥15 yrs

N= 90 women



Endpoints

Rating Scales:
Administered at baseline, 12h, 36h, 60h, 7 day and 30 day

Primary endpoint:
HAM-D change from baseline at hour 60

https://clinicaltrials.gov/study/NCT06979544

Overall population

Baseline Demographics

Characteristics	LPCN 1154	Placebo	Overall
N	45	45	90
Age (years) (Mean, SD)	30.7 (5.41)	30.8 (6.52)	30.8 (5.96)
BMI (kg/m2) (Mean, SD)	30.0 (5.96)	29.6 (6.06)	29.8 (5.98)
Ethnicity (HISP; %)	64.4	60.0	62.2
Race (White; %)	62.2	66.7	64.4
AD use at baseline (%)	8.9	8.9	8.9
HAM-D at baseline (Mean, SD)	28.3 (2.8)	28.2 (3.1)	28.3 (2.9)
History of psychiatric condition (based on MINI) (N, %)	24 (53.3)	30 (66.7)	54 (60.0)
History of depression	19 (42%)	19 (42%)	38 (42%)

- 15 sites randomized participants

MINI: Mini-International Neuropsychiatric Interview
AD: Antidepressant

Efficacy Results

Placebo-Adjusted HAM-D17 Score Change from Baseline

Timepoint	Overall Population N=90		History of Psychiatric Condition Subset* N=54	
	Placebo-adjusted Difference	Statistical Significance	Placebo-adjusted Difference	Statistical Significance
Hour 12	-3.9	P < 0.01	-7.2	P < 0.001
Hour 36	-1.7	NSS	-5.0	P < 0.05
Hour 60	-1.3	NSS	-6.1	P < 0.01
Day 7	-1.2	NSS	-4.2	NSS
Day 30	-2.3	NSS	-5.3	P < 0.05

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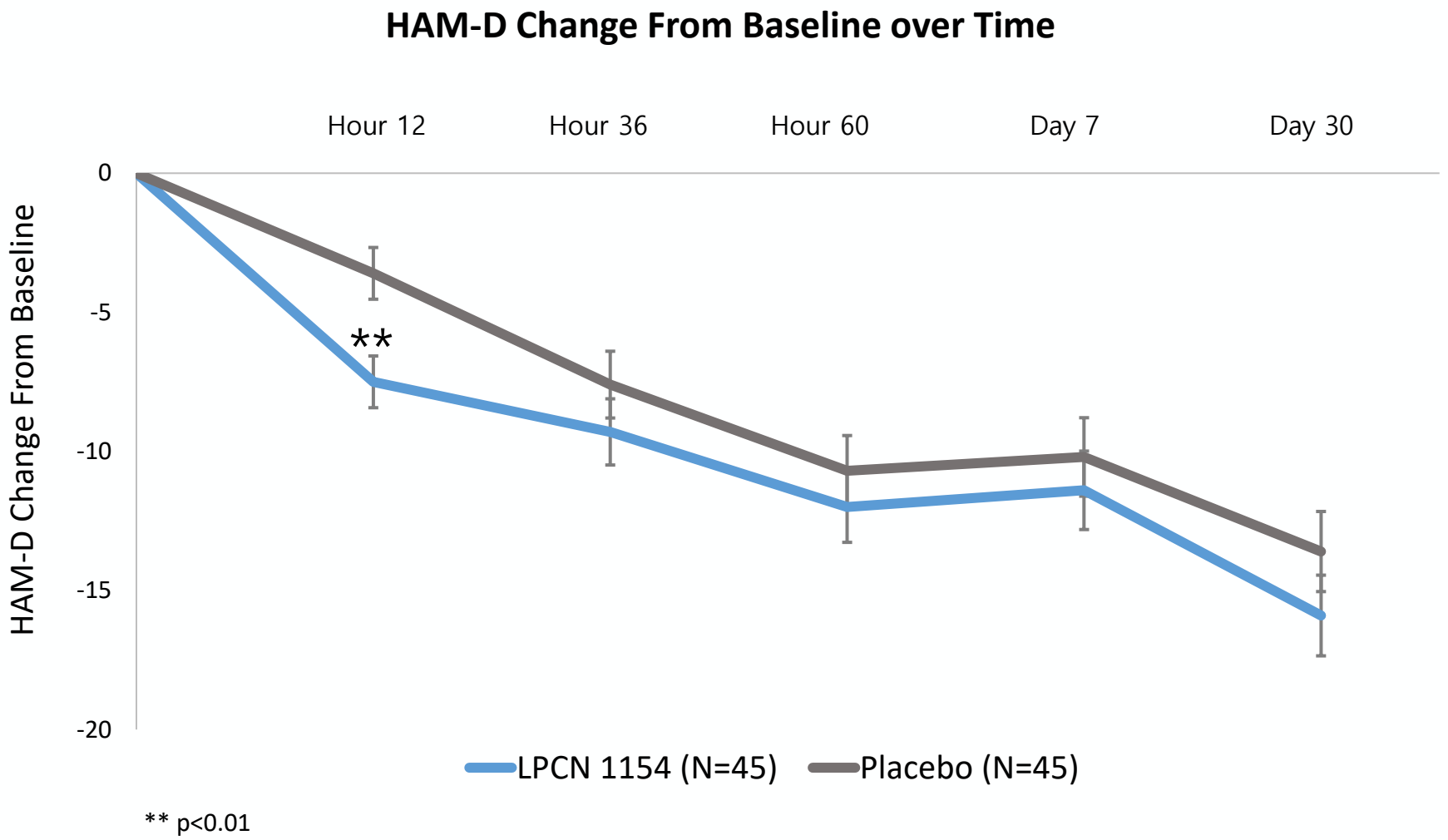
NSS: Not Statistically Significant. Mixed model for repeated measures, least squares means placebo-adjusted difference. P-values are nominal except for Hour 60 Overall Population.

*Post hoc analysis

Primary Endpoint: HAM-D CFB at Hour 60

Primary endpoint not met



https://clinicaltrials.gov/study/NCT06979544

Mixed model for repeated measures, least squares means placebo-adjusted difference. P-values are nominal except for Hour 60 Overall Population.

Patients with PPD and Psychiatric Conditions

Appropriate for Subgroup Analysis

- ✓ Well defined condition characterized via standardized tool, MINI
  - Validated structured clinical interview for DSM and ICD psychiatric disorders
  - Commonly used in clinical trials
  - FDA agreed on using MINI to diagnose major depressive episode in this study
- ✓ Prone to higher severity and chronicity
  - The risk of PPD was more than 20 times higher for women with a depression history, compared to women without[1]
- ✓ High prevalence of psychiatric conditions in patient with PPD
  - ✓ 65 - 82% prior history of depression[2,3]
- ✓ This group often show lower placebo effect
- ✓ Aligns with known antidepressant effects of brexanolone
  - IV administered brexanolone demonstrated substantially higher treatment effect in patients with prior personal PPD history[4]

1. *Depress Anxiety. 2017 Feb;34(2):178-187*
2. *BMC Pregnancy Childbirth. 2014 Dec 10:14:402*
3. *J Clin Psychiatry. 2020 Jan 21;81(1):19m12929*
4. *Lancet* 2018; published online Aug 31. http://dx.doi. org/10.1016/S0140-6736(18)31544-7.

PPD with History of Psychiatric Conditions

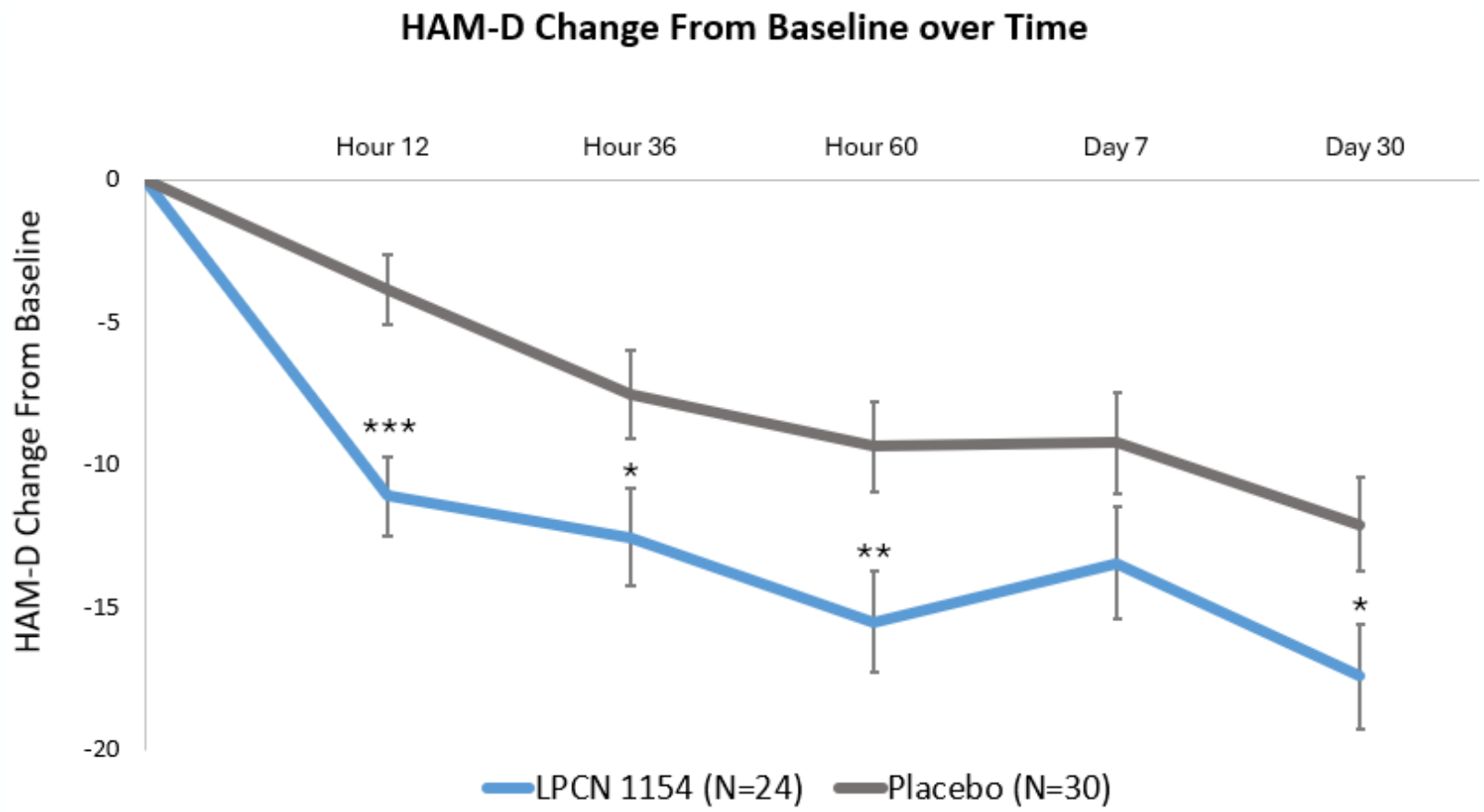
Baseline demographics

Characteristics	LPCN 1154	Placebo	Overall
N	24	30	54
Age (years) (Mean, SD)	31.0 (5.5)	30.8 (6.6)	30.9 (6.1)
BMI (kg/m2) (Mean, SD)	31.6 (6.6)	30.1 (6.7)	30.8 (6.6)
Ethnicity (HISP; %)	41.7	50.0	46.3
Race (White; %)	50.0	60.0	55.6
AD use at baseline (%)	12.5	13.3	13.0
HAM-D at baseline (Mean, SD)	28.9 (3.5)	28.6 (3.5)	28.7 (3.5)
History of psychiatric condition (based on MINI) (N, %)	24 (100)	30 (100)	54 (100)

- Similar characteristics as overall study population, including baseline HAM-D
  - Slightly lower number of Hispanic participants (46% vs 62%)

PPD with History of Psychiatric Conditions

HAM-D Change from Baseline



* p<0.05; ** p<0.01; *** p<0.001

https://clinicaltrials.gov/study/NCT06979544

Mixed model for repeated measures, least squares means placebo-adjusted difference. P-values are nominal except for Hour 60 Overall Population.

Overall Population Safety

LPCN 1154 was well tolerated

Parameter	LPCN 1154 N=45 n (%)	PLACEBO N=45 n (%)	Overall N=90 n (%)
Any TEAE	8 (17.8)	8 (17.8)	16 (17.8)
Any treatment-related TEAE	5 (11.1)	3 (6.7)	8 (8.9)
Any severe TEAE	2 (4.4)	0 (0.0)	2 (2.2)
Any serious TEAE	1 (2.2)	0 (0.0)	1 (1.1)
TEAEs in ≥ 2 participants in LPCN 1154 arm			
Headache	2 (4.4)	3 (6.7)	5 (5.6)
Dizziness	2 (4.4)	0 (0.0)	2 (2.2)
Somnolence	2 (4.4)	0 (0.0)	2 (2.2)
Nausea	2 (4.4)	0 (0.0)	2 (2.2)

- 100% of participants completed dosing
- No treatment-related severe or serious TEAEs
- All dizziness, somnolence, and nausea were mild-moderate and resolved without intervention

https://clinicaltrials.gov/study/NCT06979544

TEAE: Treatment-emergent adverse event (any AE that occurred after first dose of study drug)

Hypothesis Generating Results Support LPCN 1154's Potential as a RAAD

Clinically meaningful signals

✓ Consistent efficacy signal in patients with PPD and history of psychiatric conditions

- HAM-D placebo adjusted change from baseline less than or equal to 4 at all timepoints
- Supporting secondary responder and remission endpoint trends
- Numerically superior to placebo across multiple scales (HAM-D, MADRS, HAM-A) at all time points

✓ Preliminary competitive label differentiation

- Onset as early as 12 hours, short treatment duration, ease of access, sustained durability, and superior safety

✓ Amenable to additional development paths - MDD/TRD

LPCN 1154 - Significantly Better Tolerated

Comparison to Zurzuvae safety*

Adverse Reaction	LPCN 1154A (N=45)	Placebo (N=45)	Zuranolone (N=171)	Placebo (N=169)
Key Adverse Reactions				
Somnolence and sedation	4%	0%	19-36%	6-11%
Dizziness	4%	0%	8-13%	6-9%
Fatigue	0%	0%	5%	1-2%
Diarrhea	0%	0%	5-9%	2-3%
Memory impairment	0%	0%	3%	0%
Tremor	0%	0%	2%	0%
Anxiety	0%	0%	2%	1%

Dose reductions

- 1% with LPCN 1154 due to rash
- Up to 14% with Zuranolone
  - Due to somnolence and dizziness

Treatment discontinuations

- 0% with LPCN 1154
- Up to 4.1% with Zuranolone
  - Majority due to nervous system AEs

- No treatment-related SAEs with LPCN 1154
- One SAE of confusional state reported with Zurzuvae in Phase 3 PPD trials
  - "In each clinical study, some Zurzuvae-treated patients developed confusional state. One of these cases was severe, and was also associated with somnolence, dizziness, and gait disturbance"

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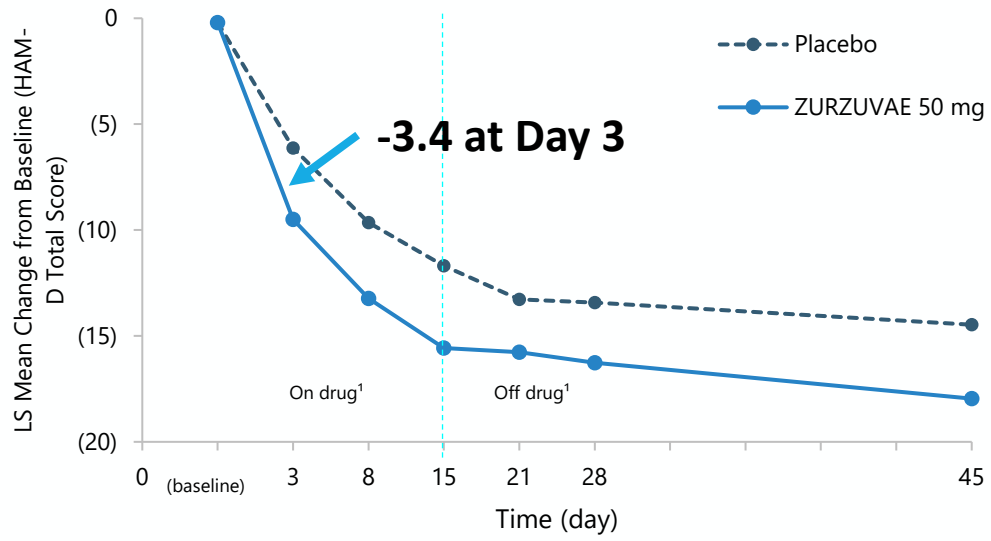
* Per label; two separate studies

LPCN 1154 Demonstrated Differentiated Efficacy Signal

Zuranolone

Mean CBL in HAM-D Total Score Over Time (Days) in Study [1]



Placebo (n)	96	95	90	83		85
ZURZUVAE 50 mg (n)	98	93	93	84		84

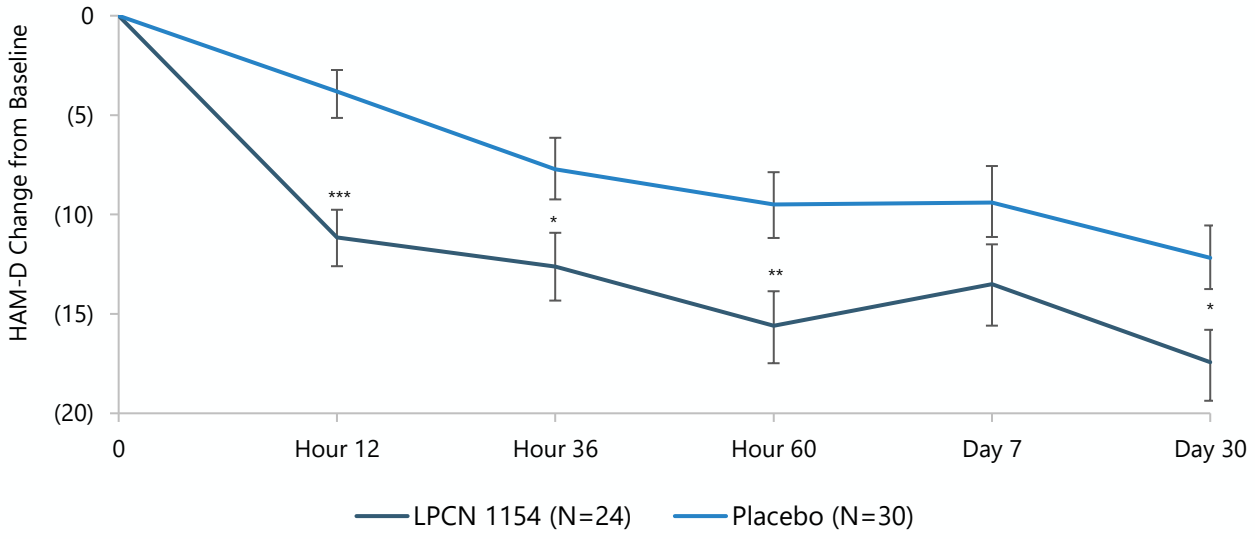
Differential HAMD-17 Total Score at Day 15*

Study Number	Mean Placebo Subtracted Difference (95% CI)
1	-4.0 (-6.3, -1.7)
2	-4.2 (-6.9, -1.5)

LPCN 1154: PPD with History of Psychiatric Conditions

Mean CBL in HAM-D Total Score Over Time

HAM-D Change from Baseline Over Time



Timepoint	Hour 12	Hour 36	Hour 60	Day 7	Day 30
Placebo-Subtracted Difference (95% CI)	-7.2 (-10.8, -3.7)	-5.0 (-9.6, -0.5)	-6.1 (-10.7, -1.5)	-4.2 (-9.4, 1.0)	-5.3 (-10.2, -0.5)

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No head-to-head clinical trials have been conducted. Data are derived from published reports of different clinical trials at different points in time, with differences in trial design, size, and patient populations.

*CBL in the HAMD-17 Total Score at Day 3 was 3.4 units

[1] Both phases were double-blind.

LPCN 1154 – Differentiated Target Attributes as a Rapid-Acting PPD treatment*

Potential to meet RAAD criteria

FDA Criteria for Rapid-Acting Anti-Depressants (RAAD)

For rapid-acting antidepressants, the timing of effect considerations include the following:

- Efficacy generally should be demonstrated within 1 week for a rapid-acting antidepressant. Some novel antidepressants are thought to be effective within hours or days. In such cases, an earlier primary efficacy endpoint would be appropriate.
- Durability of effect beyond the initial response should be characterized. To demonstrate both early onset of action and durability of effect, a primary efficacy endpoint early in the course of treatment would be chosen, with continued observation of drug–placebo differences over time.

Efficacy demonstrated within 1 week

Rapid relief as early as **12 hr** over Zurzuvae of 3 days

Rapid time to response **2.6 days** over Zurzuvae of 9 days

Durability of effect beyond the initial response

Effect lasts ~1 month post treatment

+ Superior tolerability

Bioidentical, **low** CNS depressant effect (<5%), and devoid of psychotomimetic effects

+ Ultrashort treatment duration

48-hour treatment

+ Prompt access

At home use without burdensome monitoring

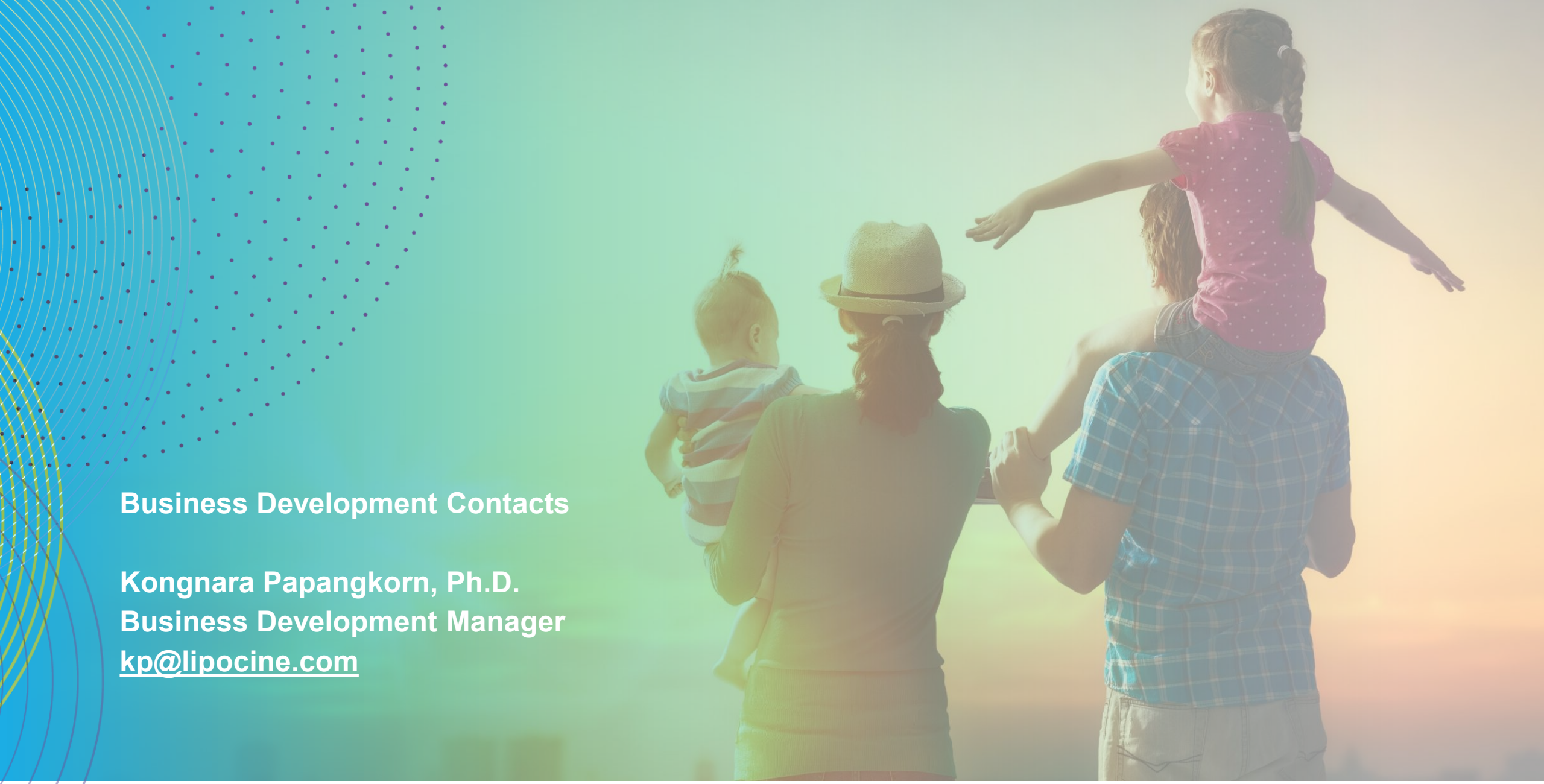
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/major-depressive-disorder-developing-drugs-treatment

*Based on subgroup based hypothesis generating results

LPCN 1154 “Best-in-Class” Oral Treatment for PPD

Key takeaways

- **Credible signal in patients with PPD and history of psychiatric conditions**
  - Next steps: finalize validation study protocol based on FDA feedback
- **Significant market opportunity**
- **Differentiated product attributes addressing unmet needs**
- **Streamlined pathway to NDA submission**
- **Issued and pending patents worldwide**



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