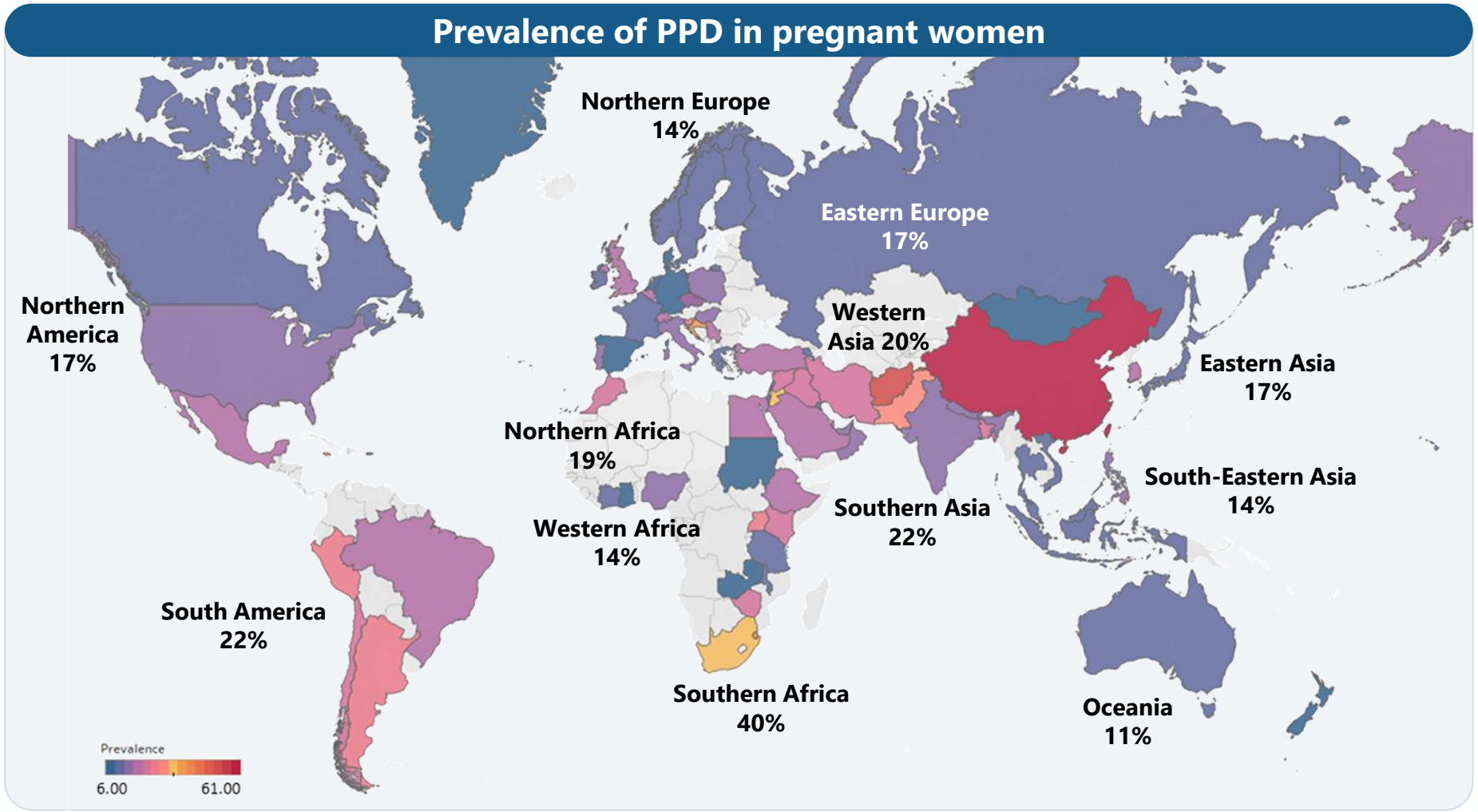
LPCN 1154 (BRLIZIO™)

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)

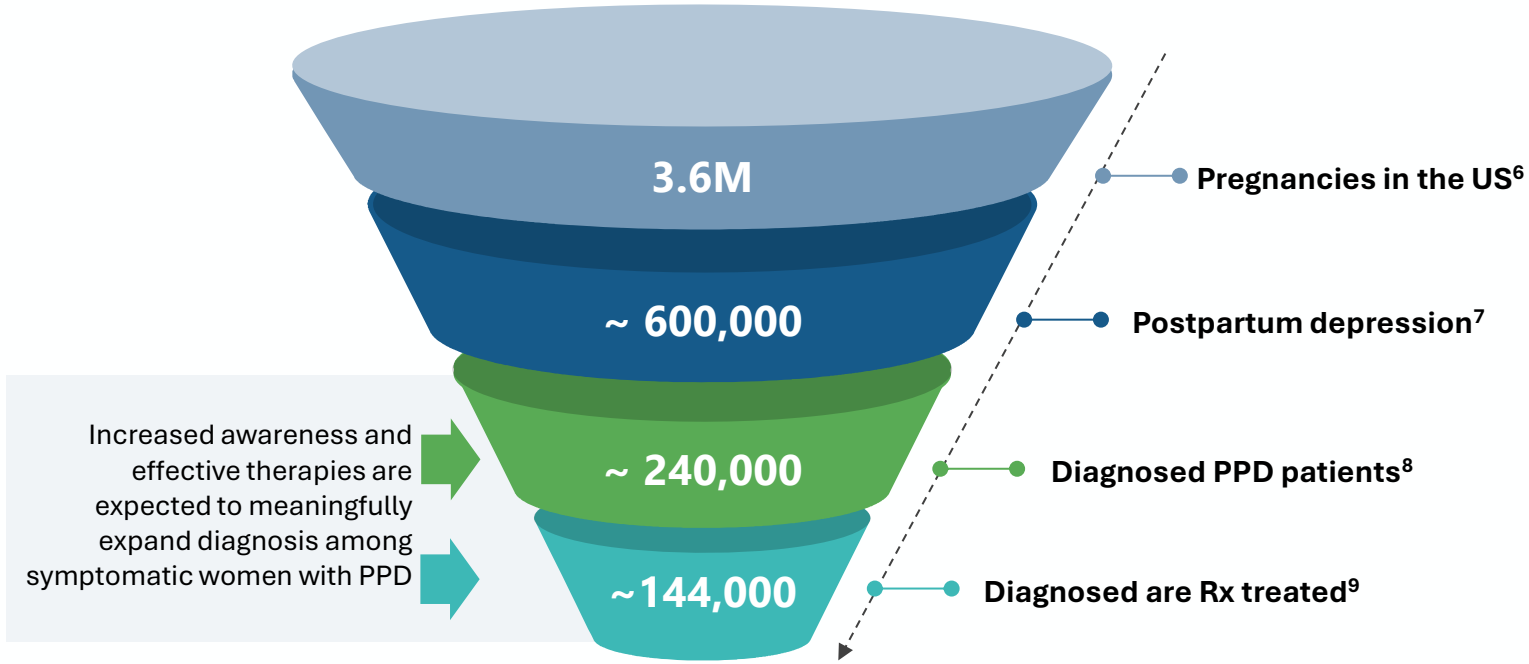
1. Wang et al. Translational Psychiatry (2021) 11:543

PPD – 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

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

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

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

LPCN 1154 -Target Product Attributes Addresses Unmet Medical Need

Strong potential to set the benchmark for first-line therapy

Oral Dosage Form Comprising Brexanolone

48-hour outpatient dosing

Rapid relief

Superior tolerability

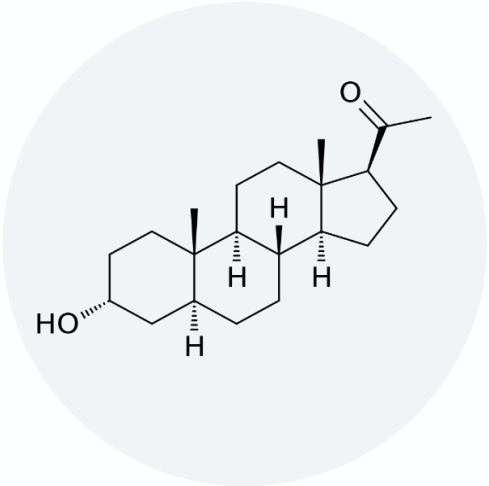
Identical to endogenous allopregnanolone

Fixed dose without titration or taper required

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

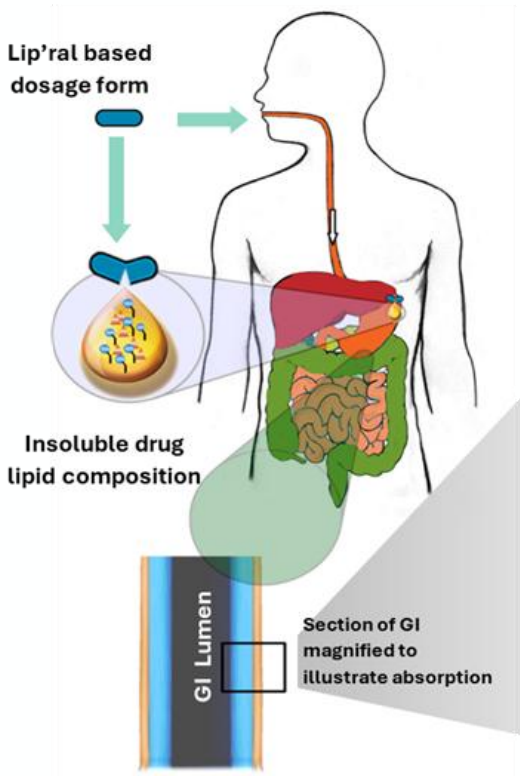
Overcoming brexanolone oral delivery challenges

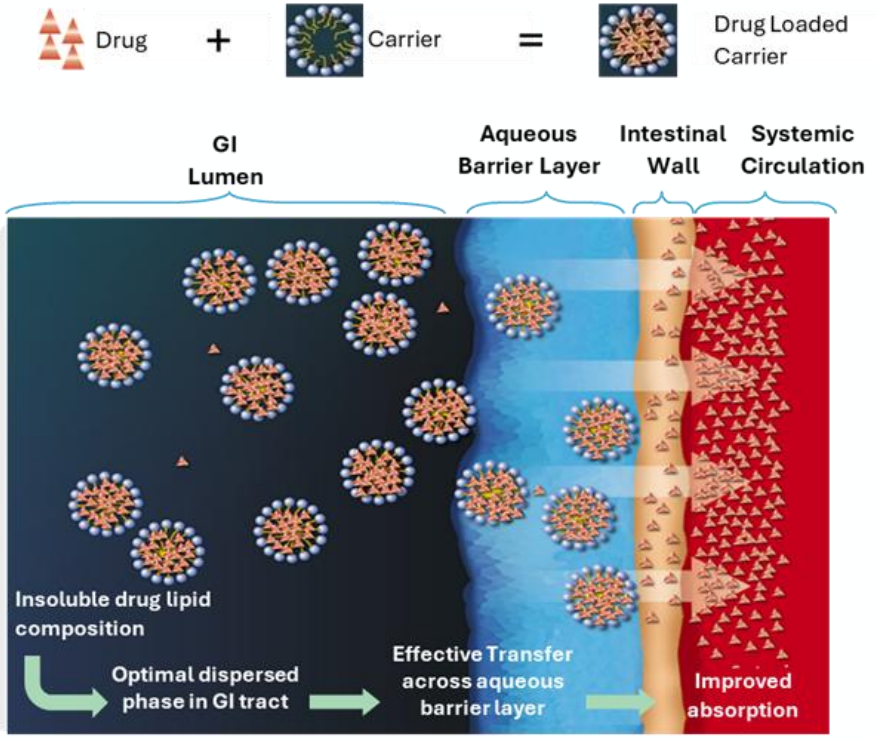
Brexanolone



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

Oral enablement



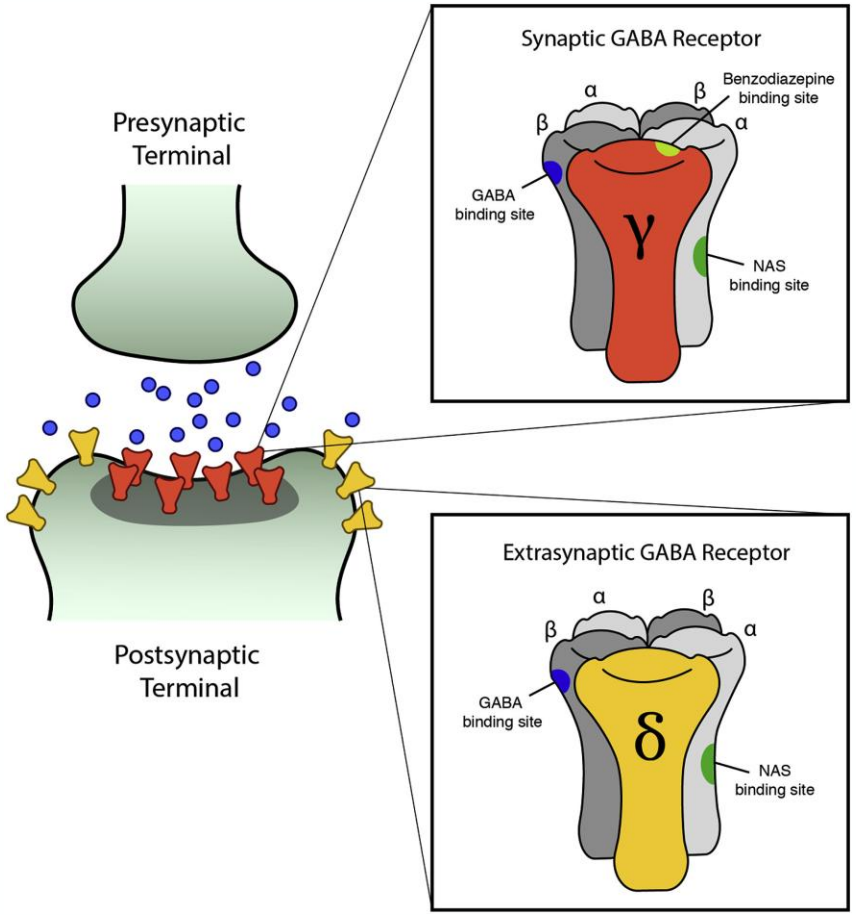


Source: Giliyar et al. Drug Delivery Technology, Jan 2006, Vol 6 No.1

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.

IV Brexanolone (Zulresso®) provides rapid symptom relief and required a 60-hour inpatient IV infusion with intensive monitoring. The therapy has been discontinued.

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®)*	**IV Brexanolone** *(Zulresso®)*[8]	***SSRIs / SNRIs*** *Off-Label Use*
Description	**Bioidentical NAS**	Synthetic NAS Derivative	Bioidentical NAS	Synthetic SSRI/SNRI
CNS depressant AEs	**TBD**[6]	High[4]	Serious	Moderate[7]
Onset of Action	**TBD**[6]	Days	Hours	Weeks
Treatment Duration	**48 Hours**	14 Days	60 Hours	Months
Response Rate at Day 3	**TBD**[6]	Up to 41%	81%[9]	N/A

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.
Response Rate defined as a reduction of HAM-D score of at least 50% compared with baseline
*Projected based on Zulresso published reports (Brexanolone Briefing Book, November 2, 2018 and Meltzer-Brody et al. Lancet. 2018 Sep 22;392(10152):1058-1070)

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1. Zulresso label
2. Brexanolone Briefing Book, November 2, 2018
3. In adolescent patients per sNDA 211371 S-007 Multi-disciplinary Review and Evaluation ZULRESSO)
4. Zurzuvae label; Somnolence (36%), dizziness (13%), dose Reduction (14%), and discontinuation (2%),
5. Kristina M. Deligiannidis et al., JAMA Psychiatry. 2021 Sep; 78(9): 1–9
6. Subject to ongoing P3 trial results; all participants have completed dosing with no drug discontinuations, drug-related SAEs, loss of consciousness, or excessive sedation reported
7. https://www.uptodate.com/contents/image?imageKey=PSYCH%2F143603
8. IV brexanolone therapy has been discontinued
9. https://www.sciencedirect.com/science/article/pii/S0165032722011570; cumulative response rate

LPCN 1154 – Dosing Regimen Confirmation Study Results

Results inform dosing regimen for Phase 3 safety and efficacy confirmatory study (NCT06979544)

Bioequivalent to Zulresso

PK Parameter	LPCN 1154	IV Brexanolone	GMR Test vs. Reference (90% CI)
C_{max} (ng/mL)	120	115	105% (92-118)
$AUC_{0-\infty}$ (h*ng/mL)	4884	5019	97% (89-107)
AUC_{0-t} (h*ng/mL)	4266	4784	89% (81-98)

Brexanolone was well tolerated independent of route

- No sedation or somnolence events observed
- All events were mild to moderate
- No severe or serious AEs
- Reported study related events were venipuncture site related, arthralgia, fatigue, dizziness, headache, back pain, hematoma, and pelvic pain

LPCN 1154 multi-dose regimen resulted in bioequivalent blood levels compared to IV brexanolone administered per label at 90 µg/kg/hr

n=23; Outlier participant presented PK results for the IV administration period greater than 70 standard deviations away from the PK data set mean for all PK parameters included above

GMR = Geometric Mean Ratios, CI = Confidence Interval, t = 100 hours for AUC_{0-t}

LPCN 1154 Phase 3 Safety and Efficacy Study (NCT06979544)

Based on FDA feedback – outpatient setting with no medical monitoring requirement

Study design

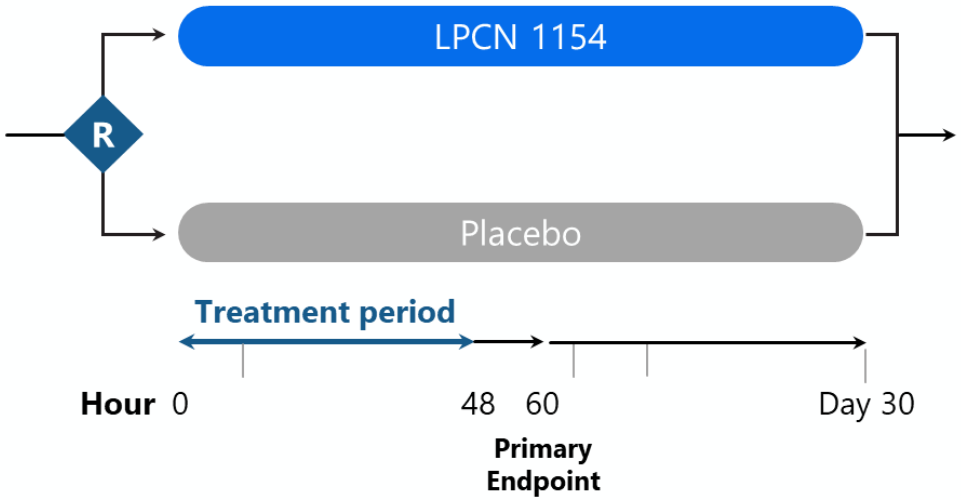
Two arm, outpatient, randomized, blinded, placebo-controlled in women with postpartum depression

Inclusion criteria

Severe PPD

Age ≥15 yrs

N= ~80 women



Endpoints

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

Additional endpoints: MADRS, HAM-A (anxiety), safety and tolerability, etc.

Rationale for Success

- Brexanolone has established efficacy (IV infusion)
- LPCN 1154 has demonstrated comparable exposure to IV infusion
- Study size, duration, and population similar to IV infusion P3 study

LPCN 1154 – Development Status

Streamlined 505(b)(2) pathway to NDA submission targeted mid 2026

Dosing Regimen Confirmation Study

- ✓ Positive Results

Labeling Clinical Studies

- ✓ Food effect study
- ✓ PK study in PPD
- ✓ Metabolite evaluation

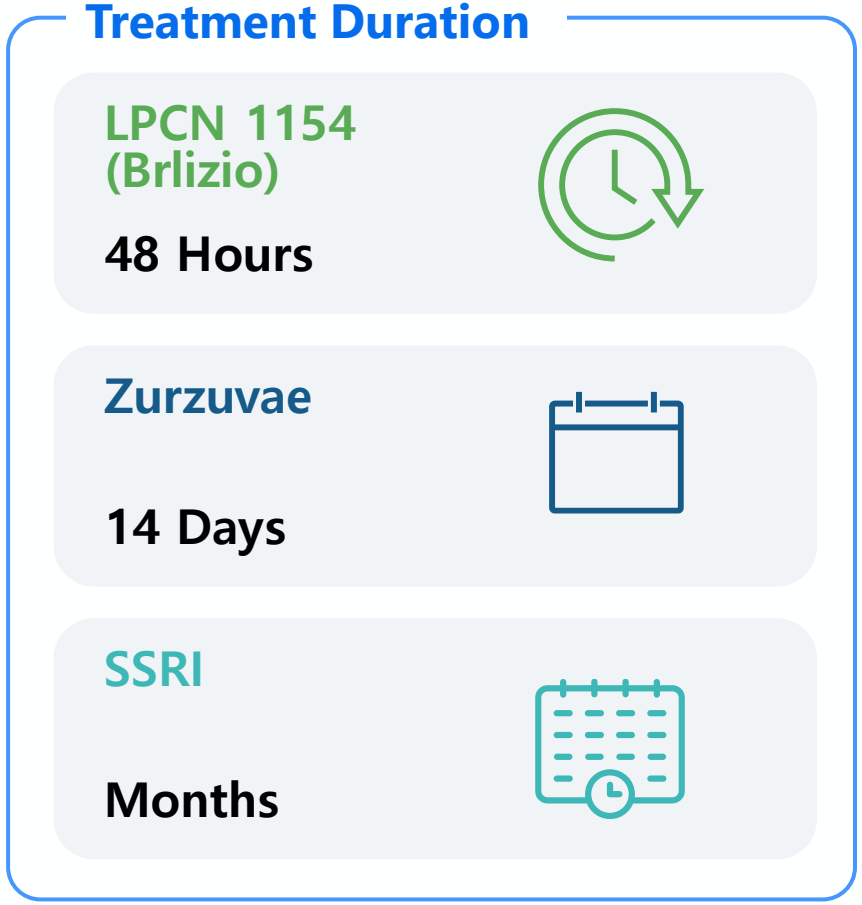
Ongoing P3 Study

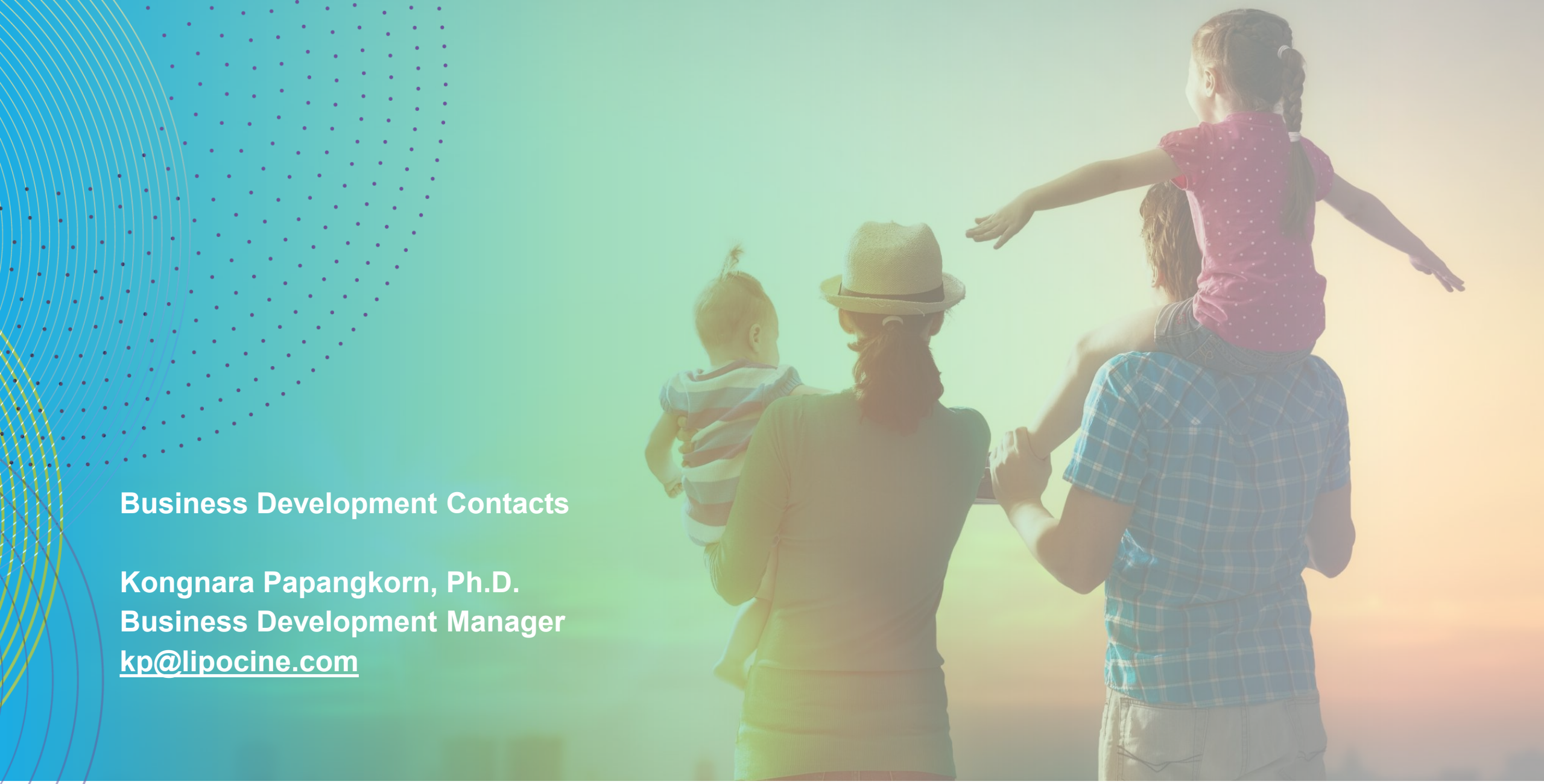
- ✓ Dosing completed
- ✓ Two DSMB data review meetings complete
- ○ Topline results – Early Q2-26

LPCN 1154 – Potential "Game Changer" for Fast Acting Depression Therapy

Key takeaways

- **Large, attractive market opportunity**
- **Differentiated product profile addressing unmet needs**
  - Rapid relief, short treatment duration, superior tolerability
- **Clear, streamlined path to NDA submission**
  - Dosing regimen confirmed
  - Phase 3 safety and efficacy study ongoing
  - Topline data expected early Q2 2026
  - Planned NDA filing mid-2026
- **Issued and pending patent protection globally**
  - Issued patent terms extending to 2044+
- **Platform potential for expansion into additional depressive indications**





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