LPCN 2101

Treatment of Epilepsy

Drug-Resistant Epilepsy (DRE)

A significant clinical challenge in epilepsy care with high social and occupational limitations[1]

DRE is defined by **ILAE** as the failure of two appropriate anti-seizure medications (ASMs) to achieve sustained seizure freedom

Prevalence	Affects 30-40% of epilepsy patients in the U.S. [2]
Clinical Impact	Increased risk of injury, hospitalization, mortality, and mental health issues[1]
Economic Burden	Contributes heavily to the $24.5 billion annual epilepsy-related healthcare costs[4]
Treatment Challenges	Limited success with medications and need for early identification Probability of achieving seizure freedom diminishes substantially with each subsequent AED regimen tried[5]

1. Pharmacol Rev. 2020 Jul;72(3):606–638
2. Front Neurol. 2022 Nov 3;13:1023832.
3. https://www.epilepsy.com/treatment/medicines/drug-resistant-epilepsy?
4. Epilepsia. 2022;63(8):2144–2154
5. JAMA Neurol. 2017 Dec 26;75(3):279–286

Unmet Needs in DRE

Seizure freedom without adverse effects, while improving the patient's quality of life

Limitations of Current Options

- **30–40% of patients still do not achieve freedom from seizures, despite being on multiple medications**
- Many patients with DRE go through multiple ASMs with limited success
- Rescue treatments (primarily benzodiazepines) do not prevent future seizures, they only stop the current episode
- High risk of seizure recurrence within hours or days after a cluster
- Seizures may cause physical injuries, and a minority may last long (status epilepticus) or recur in clusters and can be life-threatening

Unmet Needs

- **Medications with novel mechanism of action, especially for patients who experience recurrent seizure clusters or DRE**
- Minimal cognitive, mood, or systemic side effects
- Address associated comorbidities like depression, anxiety, and cognitive impairment
- Transition effectively to maintenance therapy and sustain seizure control after acute treatment
- Prevent status epilepticus and prevent patients from using emergency room for seizure management

Ioannou et al. Brain Behav. 2022 Sep;12(9):e2589
Mesraoua et al. J Neurol Sci. 2023 Sep 15:452:120766

LPCN 2101 – NAS for Epilepsy Treatment

Positive Allosteric Modulator (PAM) of the $GABA_A$ receptor

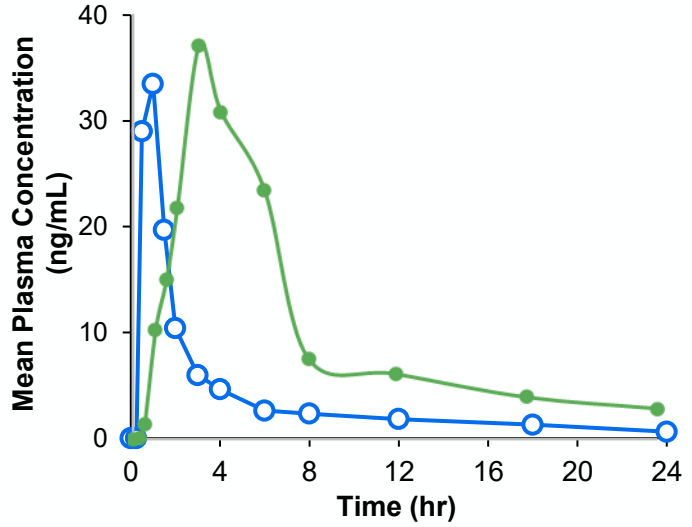
Product Candidate Differentiation

- Novel MOA specifically addressing DRE
- Active molecule is bioidentical to endogenous NAS
- Potential to address psychiatric comorbidities (depression, anxiety, sleep disorders)

Anti-Seizure Activity in Preclinical Models

- Effective in most of the tonic and/or clonic, focal, and generalized seizure animal models[1-3]
- Maintained effectiveness upon chronic dosing [6]
- Potentially synergistic with benzodiazepines[4,5]

First Oral Enablement Phase 1 Results



From separate studies in post-menopausal women with Lip'ral based oral dosage forms

1) Kokate et al., 1996. Neuropharmacology. 2) Carver and Reddy, JPET 2016. 3) Ekaminski et al. epilepsia, 2004. 45(7): p. 864-7. 4)Bruun et al., 2015 Neuropharmacology. 5) Chuang and Redy, 2020, J Pharmacol Exp Ther. 6) Kokate et al., JPET, 1998. *horizontal screen test

LPCN 2101 Development Status

Phase 2 ready

Preclinical PK	Preclinical Toxicity	Phase 1 Studies	Next Steps
✓ First oral enablement demonstrated ✓ Achieved ~10x of estimated highest target therapeutic level	✓ Chronic administration was safe and well tolerated	✓ IND cleared ✓ Confirmed oral enablement ✓ Well-tolerated	○ Initiate P2 study