MIRA™ Pharmaceuticals

NASDAQ: **MIRA**

June 2025

Management

Erez Aminov
Chief Executive Officer & Excutive Chairman

- Experienced biotechnology investor and adviser with 18+ years of experience
- Founder of Locate Venture Corp, a strategy and investment consulting firm which has advised multiple, early-stage life sciences companies including Telomir Pharma and Tyna Pharma on fundraising and strategic partnerships.
- Collaborated with major universities like University of Miami, Bascom Palmer Eye Institute, and helped form strategic partnerships.

Itzchak Angel, PhD
Chief Scientific Advisor

- Over 40 years of experience in guiding medical, pharmaceutical, drug, and business development in both large and emerging companies.
- Expertise in small molecules, botanical drugs, biotechnology products, delivery systems, medical devices, and drug-device combinations.
- Former Head of Pharmacology at Synthelabo (Sanofi-Aventis, Paris, France) where he participated in research and development of drugs such as Xatral (alfuzosin), Ambien (zolpidem) and Mizollen (mizolastine).

Alan Weichselbaum, CPA, MBA
Chief Financial Officer

- Seasoned Financial Executive with 30+ years of experience in corporate finance, capital markets, and strategic advisory; currently CFO of both MIRA and Telomir Pharmaceuticals.
- Board and Advisory Leadership as Director of FinWise Bancorp (Nasdaq: FINW) and founder of The Wexus Group, advising growth-stage companies on capital structuring and exit strategies.
- Capital Markets Expertise gained through senior Wall Street roles, hedge fund management, and leadership in institutional transactions across public and private markets.

Alex Weisman, PhD
Scientific Advisor

- Occupied executive positions of VP R&D and Chief Scientist at numerous Israeli and international pharmaceutical companies. Currently serve as an advisor and management team member for companies developing new products for the chemicals, pharmaceuticals, and food industries.
- More than 30 years of experience in the development, characterization, scale-up, technology transfer, troubleshooting, production and registration of novel and generic drugs, and other pharmaceutical and chemical products.

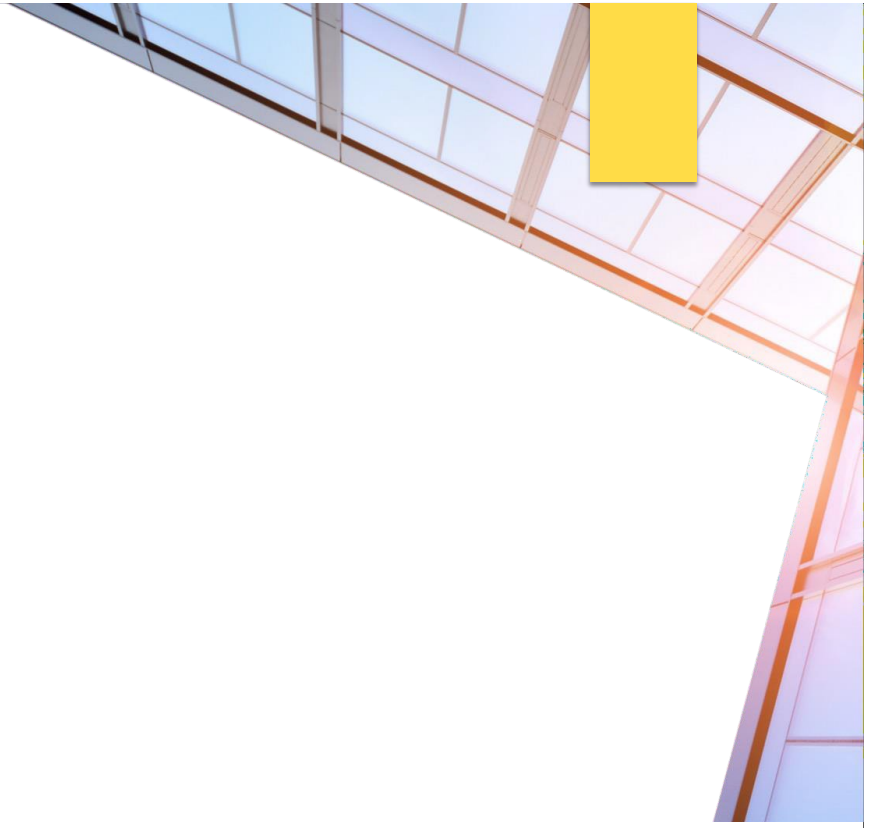
Corporate Overview

- We are MIRA Pharmaceuticals — a clinical-stage biotech developing oral therapies that target the brain, behavior, and metabolism.
- Our pipeline includes:

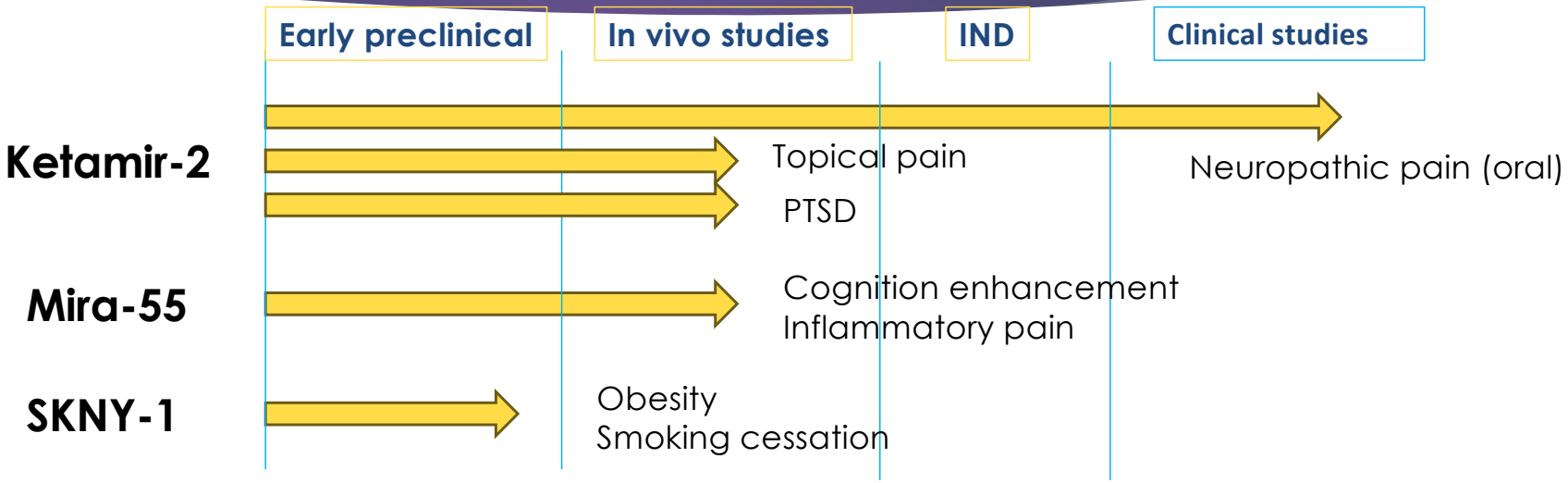
- Ketamir-2 – a next-generation oral ketamine analog with improved bioavailability, selectivity, and safety profile. It is currently in Phase 1 clinical trials for neuropathic pain and treatment-resistant depression.

- MIRA-55 – a synthetic cannabinoid designed to reduce anxiety and improve cognition in aging populations, showing preclinical activity across models of memory, pain, and behavioral regulation.

- SKNY-1 – a THCV-derived compound designed for obesity and smoking cessation. It modulates CB1, CB2, and MAO-B with receptor selectivity that minimizes psychiatric risk and supports metabolic balance.



Our pipeline



What is MIRA-55?

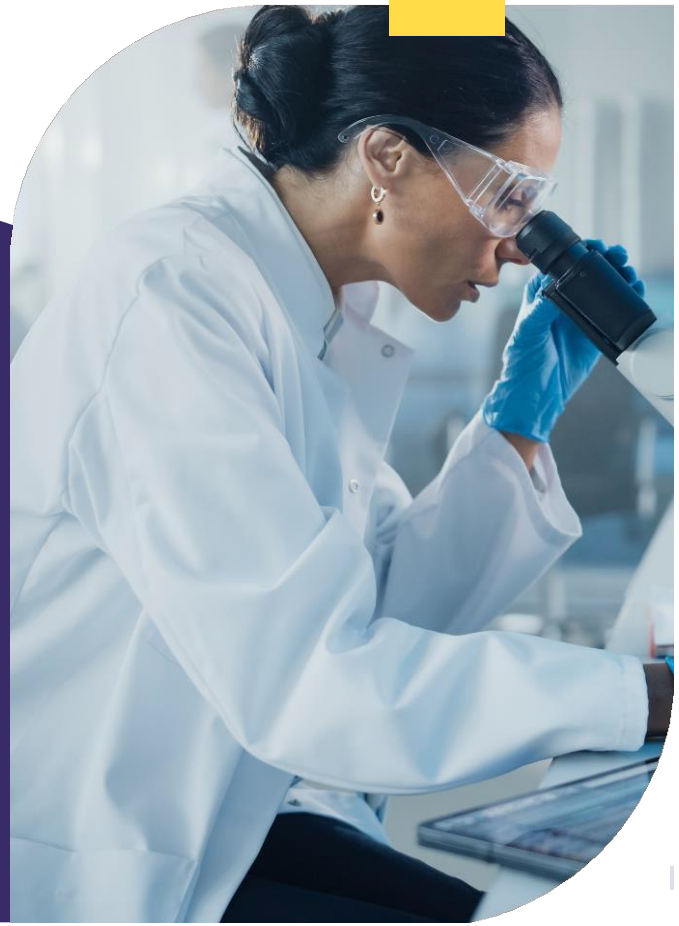
Key Differentiating Factors

THC

- Schedule 1, which means no accepted medical purpose
- Negative side effects
- Legal/regulatory hurdles
- Heightened competition
- Shipping/manufacturing issues

MIRA-55

- Pure Synthetic
- Based on preclinical studies, better side effect profile (e.g. decreased anxiety across the dose range, improved rather than impaired cognition)
- Being developed to be a prescription medication



Therapeutic Focus Areas

MIRA-55 is under evaluation for two key therapeutic areas with high disease burden and significant unmet needs

Cognitive Impairment

- Cognitive Impairment encompasses conditions marked by notable decline in **one's cognitive abilities** including Alzheimer's disease and dementia
- **~16 million people** in the US are living with cognitive impairment[4]
- Current treatments for cognitive impairment can not restore lost function and instead **transiently delay the progression** of the disease.

Anxiety and Cognitive Decline in the Elderly

- Anxiety disorders are chronic conditions marked by an excessive & persistent sense of apprehension, with physical symptoms such as sweating, palpitations, and feelings of stress
- **~40 million US adults** have an anxiety disorder[2], including phobias, Social Anxiety Disorder, PTSD, Generalized Anxiety Disorder, and Panic Disorder[3]
- Standard pharmacological options include SSRIs, SNRIs, and TCAs (all of which take weeks for the anxiety to respond)*

1. International Association for the Study of Pain.; 2. Anxiety Disorders | NAMI: National Alliance on Mental Illness; 3. Anxiety Disorders Facts and Statistics | The Recovery Village Drug and Alcohol Rehab; 4. https://www.cdc.gov/aging/pdf/cognitive_impairment/cogimp_policy_final.pdf. *SSRIs - Selective serotonin reuptake inhibitor; SNRIs - Serotonin-norepinephrine reuptake inhibitor, TCAs - Tricyclic antidepressants, IQVIA Analysis, Mira Analysis, MIRA-55 for specific therapeutic indications is in early stage pre-clinical development. There is no assurance that MIRA-55 will proceed through development or will receive FDA approval for marketing.

Large Patient Populations with Limited Treatment Options

MIRA-55 addresses a multibillion-dollar opportunity in anxiety and cognitive decline — with up to 14 million patients actively seeking safer, more effective therapies.

- **Mild Cognitive Impairment & Early Dementia**:

-33M eligible; 4.95–6.6M addressable based on diagnosis and treatment rates

- **Anxiety Disorders**:

-40M eligible; 6.0–8.0M patients addressable in the U.S. alone

- **Clinical Urgency:**

-Healthcare professionals seek faster-acting, low-side-effect alternatives to benzodiazepines and SSRIs

- **Global Barriers**:

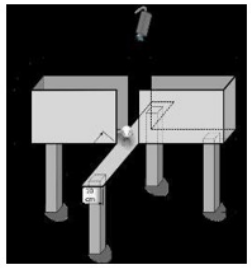
-In many countries, cannabis-based treatments are unavailable or culturally restricted — leading to reliance on suboptimal medications like NSAIDs or mood stabilizers

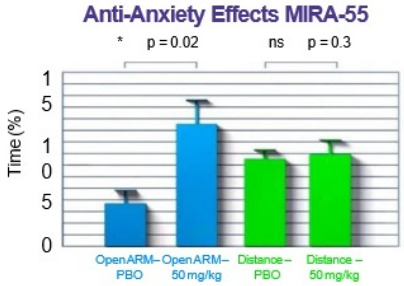
MIRA-55 Reduces Anxiety Without Sedation or Intoxication

In the Elevated Plus Maze, mice treated with MIRA-55 spent more time exploring open areas — a clear sign of reduced anxiety — without showing signs of sedation.

- **Validated Model:** The Elevated Plus Maze tests anxiety by measuring time spent in open vs. closed arms
- **Improved Behavior:** MIRA-55 significantly increased time in open arms vs. placebo (p = 0.02)
- **No Sedation:** Mice showed no decrease in mobility or exploratory activity
- **Clinical Relevance:** Suggests potential as a non-intoxicating treatment for anxiety disorders

Elevated Plus Maze (EPM) for Anxiety

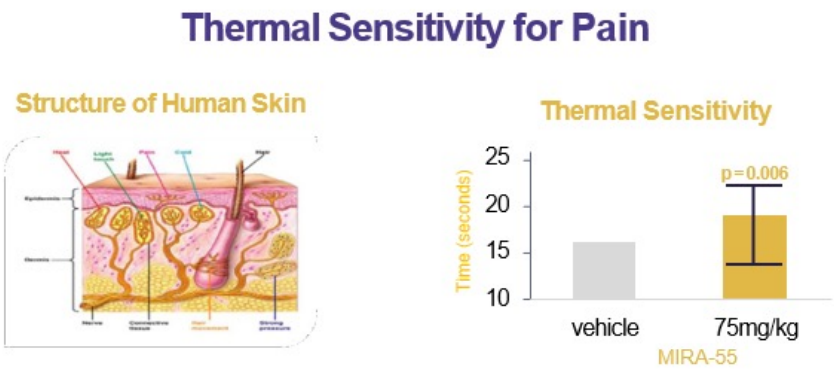




MIRA-55 Shows Significant Pain Relief in Thermal Sensitivity Model

Mice treated with MIRA-55 took longer to react to heat — a clear sign of reduced pain sensitivity compared to placebo.

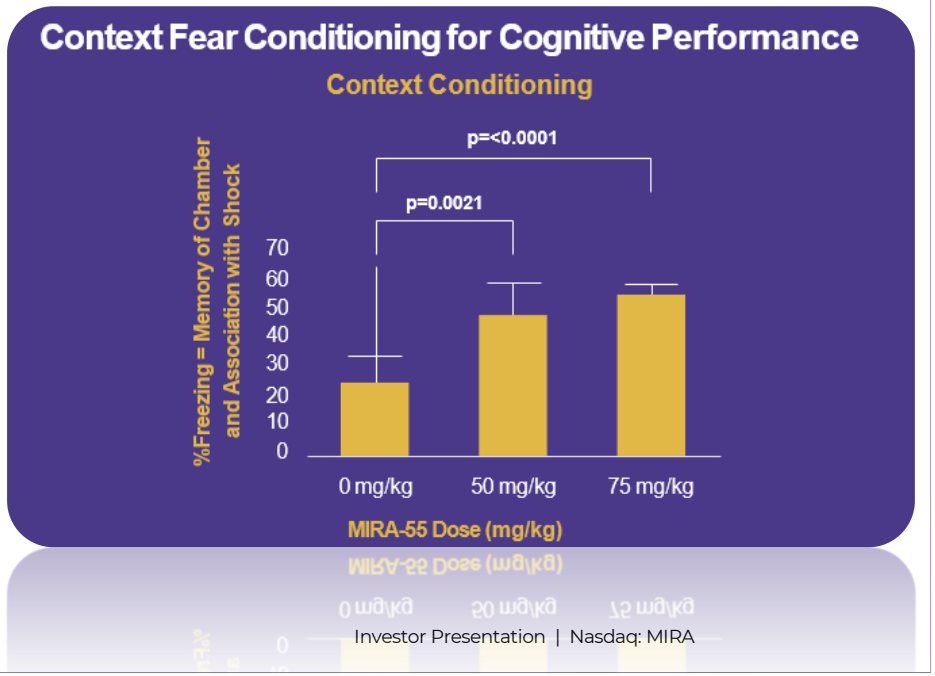
- **Validated Model:** Mice were placed on a heated plate and observed for paw-lift response time
- **Reduced Pain Sensitivity:** MIRA-55 increased response latency significantly (p = 0.006)
- **Mechanism-Free Advantage:** Relief occurred without sedation, intoxication, or opioid-like effects
- **Therapeutic Implication:** Supports MIRA-55's potential as a safe, non-opioid option for managing inflammatory or sensory pain



MIRA-55 Enhances Memory Recall in Contextual Fear Conditioning

In a validated cognitive model, MIRA-55 significantly improved memory performance — suggesting enhanced associative learning with no sedative tradeoffs.

- **Model Overview:** Mice were trained to associate a chamber with a mild shock; freezing behavior was used to assess memory
- **Stronger Recall:** MIRA-55 significantly increased freezing time vs. placebo ($p = 0.0021$, $p < 0.0001$)
- **Unique Effect:** Enhancement occurred independently of anxiety reduction — uncommon for cannabinoid-based compounds
- **Cognitive Potential:** Highlights MIRA-55's differentiated value as both an anxiolytic and cognitive enhancer



Regulatory Pathway to Commercialization

To develop, MIRA-55 as a commercialization asset, we are proceeding on a well-established regulatory pathway designed to establish its safety and efficacy

1

Pre-Clinical Testing

Focus on pre-clinical testing including genetic toxicology, safety pharmacology and general toxicology testing to enable the filing of an IND application with the USFDA.

2

Clinical Trials

Clinical testing and trials based on guidance from FDA with a focus on our initial prioritized indications while preserving optionality to add 1 or 2 more indications with strategic partners.

Ketamir-2: A Novel Oral Approach to Treating Neuropathic Pain

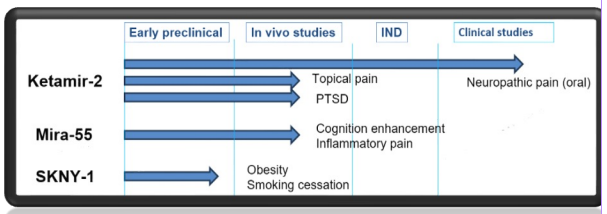
An advanced ketamine analog with fewer side effects, better safety, and clinical-stage momentum.

- **What is Ketamir-2?**
  A next-generation oral ketamine analog with improved **bioavailability**, **selectivity**, and **safety profile**, specifically engineered for **neuropathic pain** and **treatment-resistant depression**.

- **Neuropathic Pain: A Major Unmet Need**
  Affects **7–10% of the global population**, including patients with diabetic neuropathy, postherpetic neuralgia, and MS-related pain. Current treatments are often ineffective or come with significant side effects and addiction risks.

- **Why It Matters to Pharma Leaders:**
  Existing therapies (e.g., anticonvulsants, SNRIs, opioids) offer limited efficacy and poor tolerability. **A rapid-acting, oral, non-controlled alternative** like Ketamir-2 has disruptive potential in this stagnant treatment space.

- **Current Status:**
  Undergoing a **Phase I clinical trial** at Hadassah Medical Center in Israel, showing promising early tolerability and safety.



Emerging Pipeline With Broad Strategic Potential
Mira is advancing oral therapies across CNS, pain, and metabolic disorders, including:
MIRA-55 for cognition and inflammatory pain
SKNY-1 for obesity and smoking cessation

Diverse, mechanism-driven programs with near- and mid-term partnering potential.

Neuropathic Pain: High Prevalence, Low Satisfaction, and Urgent Demand

An underserved patient population where existing treatments fall short — and the risk of addiction runs high.

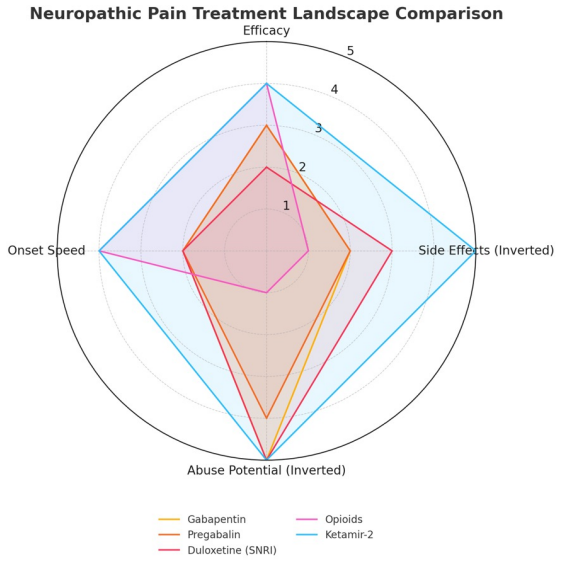
Key Therapeutic Area

- **Widespread and Costly**
  Neuropathic pain affects **7–10% of the population globally**, often linked to diabetes, MS, shingles, and nerve injury. It's one of the most common forms of chronic pain.

- **Current Treatments Are Insufficient**
  First-line therapies like **gabapentin**, **pregabalin**, and **SNRIs** offer **limited relief** and come with **CNS side effects**, sedation, or tolerance concerns. **Opiates** are a last resort, burdened by addiction risk.

- **No Oral, Rapid-Acting, Low-Abuse Option Exists Today**
  There's a significant **gap in the market** for a therapy that is **oral**, **non-addictive**, and provides **fast-acting, targeted relief** without psychomimetic or sedative effects.

- **Opportunity**
  Entering this space positions any firm as a leader in **next-generation non-opioid pain therapeutics**, aligned with both public health priorities and long-term CNS portfolio expansion.



Precision Targeting at the NMDA Receptor — Without the Collateral Effects

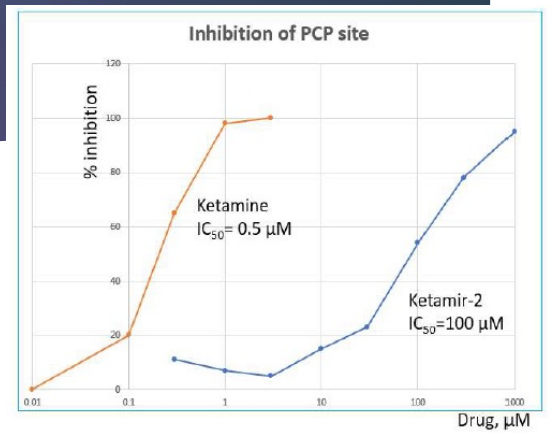
A novel oral NMDA antagonist with selective PCP-site binding and none of ketamine's psychomimetic baggage.

- **Low-Affinity, Highly Selective NMDA Modulation**
  Ketamir-2 acts as a **low-affinity antagonist** at the **PCP-site of the NMDA receptor**, with an IC_{50} of ~100 µM — avoiding the broader binding that drives ketamine's side effects.

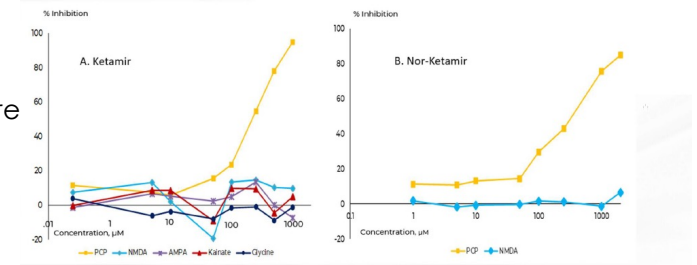
- **No Off-Target Binding to Problematic Sites**
  Unlike ketamine, Ketamir-2 **does shows no binding** to: AMPA, Kainate, Sigma, Glycine or Glutamate receptors
  → This greatly **reduces psychosis-like effects, sedation, and misuse potential**.

- **Improved Safety Profile Confirmed in Nor-Ketamir Metabolite**
  Its active metabolite shows similarly selective NMDA antagonism (IC_{50} ~300 µM), **reinforcing a consistent, predictable pharmacodynamic profile.**

- **Differentiated CNS Action Without Hyperactivity or Euphoria**
  In vivo data confirms no hyperlocomotion or euphoria, highlighting Ketamir-2's differe CNS profile in schizophrenia-relevant behavioral models.



Binding and inhibition data for Ketamir-2 and Nor-Ketamir at the NMDA PCP-site. No significant activity at other glutamatergic receptor sites.



CNS Differentiation Without Hyperlocomotion or Euphoria

Unlike ketamine, Ketamir-2 does not induce hyperactivity — a key signal of reduced psychomimetic liability.

- Preclinical locomotor activity testing confirms **no increase in spontaneous movement** with oral or injected Ketamir-2
- In contrast, ketamine (20 mg/kg, i.p.) significantly elevated horizontal locomotion
- Supports **low risk of psychomotor activation**, dissociation, or abuse liability
- Further differentiates Ketamir-2 from existing NMDA-targeting compounds
- Reinforces safety seen in Phase 1 NeuroCart and subjective e-diary reports

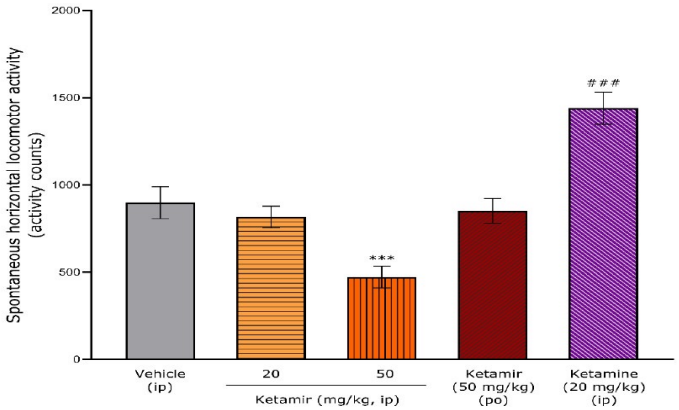


Figure: Spontaneous hyperlocomotion in mice (1 hour)
Results are expressed as mean±SEM
*****: p<0.001 for ketamir(50 mg/kg, ip) vs vehicle (ip) by one-way ANOVA test followed by a Dunnett's multiple comparisons test**
###: p<0.001 for ketamine (20 mg/kg, ip) vs vehicle (ip) by two-tailed Student's t test for

Ketamir-2 Demonstrates Potent Pain Relief in Validated Animal Models

Effective across sexes, models, and doses — with statistically significant reversal of neuropathic pain.

- **Chung Model (Rats – Visual 1):**
  - Male and female rats with spinal nerve ligation
- - Ketamir-2 produced **dose-dependent reversal** of allodynia
- - Stronger or equal to Ketamine; **better than Pregabalin/Gabapentin**
- - **Significant analgesic effects observed at 30–300 mg/kg ($p < 0.01$ to $p < 0.001$), with full reversal at 300 mg/kg.**

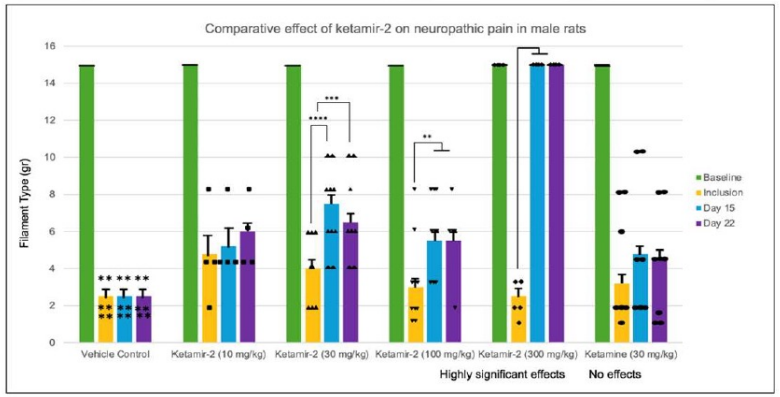


Figure 1. Comparative effects in male rats

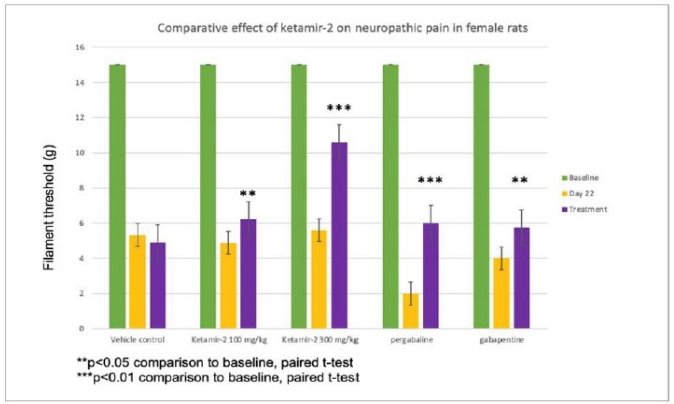


Figure 2. Comparative effects in female rats

Ketamir-2 Promotes Antidepressant-Like Behavior Without Stimulant Effects

Demonstrates increased movement and velocity without hyperactivity — mirroring classical antidepressant responses in the Open Field Test

- **Open Field Test** is a validated model for screening **antidepressant and anxiolytic activity**.
- **Ketamir-2 treatment** led to a **significant, dose-dependent increase in total distance moved** (Panel A) and **velocity** (Panel B).
- This pattern aligns with **classical antidepressant effects**, suggesting improved mood and motivation.
- **No significant effect** was observed with **ketamine (30 mg/kg PO)** — underscoring Ketamir-2's differentiation.
- Trend toward increased time in the center of the field (Panel C) suggests potential anxiolytic activity.
- Behavioral effects observed with Ketamir-2 occurred without signs of psychomotor overstimulation.

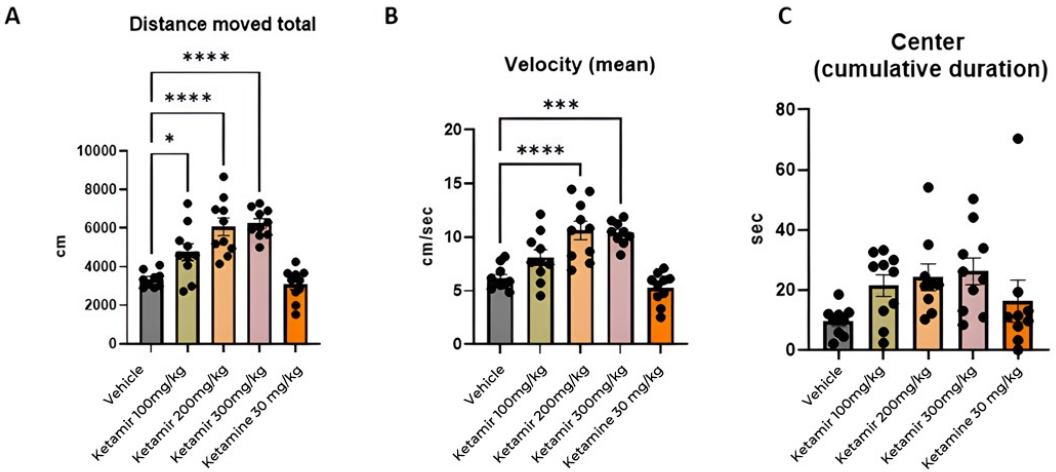


Figure: Open field parameters. (A) Distance moved (cm); (B) mean velocity (cm/seconds) and (C) cumulative time spent in center (seconds). Significance values were obtained through One-Way ANOVA

Ketamir-2 Shows Anxiolytic-Like Effects in Elevated Plus Maze

Demonstrates increased movement and time in center — consistent with reduced anxiety and enhanced exploratory behavior

- **Elevated Plus Maze** is a classical assay used to assess **anxiolytic and antidepressant activity** based on exploratory behavior.
- Mice treated with Ketamir-2 moved significantly **farther** (Panel A) and **faster** (Panel B) than vehicle controls — reflecting increased mobility.
- Time spent in closed arms decreased (Panel C), suggesting reduced anxiety and greater willingness to explore open spaces.
- **Ketamir-2 effects were dose-dependent,** with increased activity seen at 100–300 mg/kg.
- Ketamine (30 mg/kg PO) showed no significant improvement, further differentiating Ketamir-2's anxiolytic potential.
- These findings reinforce Ketamir-2's behavioral signature consistent with **clinical antidepressant and anxiolytic profiles**.

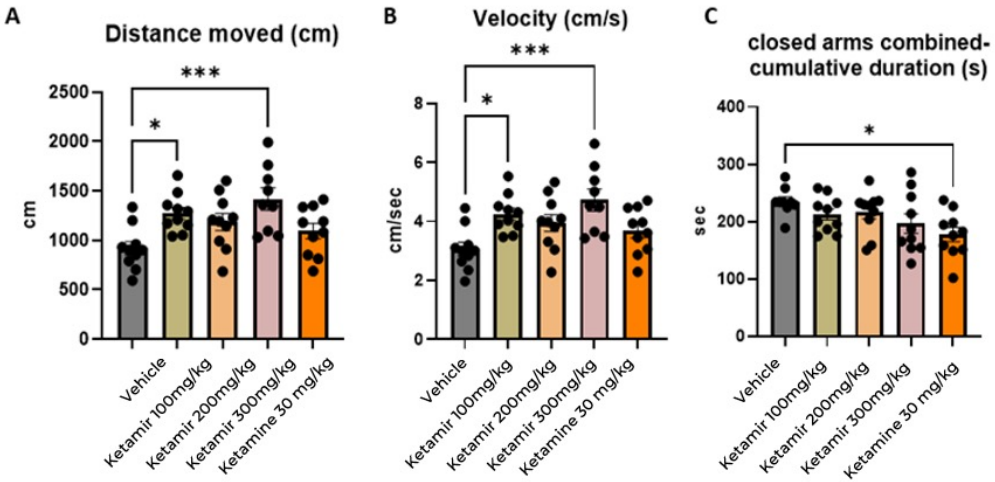


Figure Elevated plus maze (EPM) parameters. (A) Distance moved (cm); (B) mean velocity (cm/seconds), (C) cumulative time spent in open arms (seconds. Significant values were obtained through One-Way ANOVA

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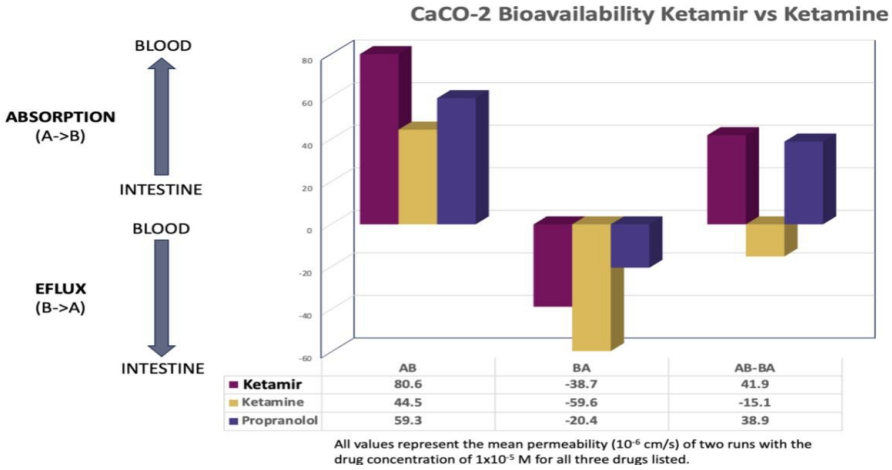
Ketamir-2 Shows Superior Oral Bioavailability and Brain Penetration Potential

Not a substrate of P-gp efflux transporter — enabling improved absorption and CNS exposure compared to ketamine

- Caco-2 assay results confirm Ketamir-2 is **not a substrate for P-glycoprotein (P-gp)**, unlike ketamine.
- Ketamir-2 showed high intestinal **absorption (AB: 80.6 × 10^{-6} cm/s) and low efflux (BA: –38.7),** similar to the oral reference drug **propranolol**.
- In contrast, ketamine demonstrated higher **efflux than absorption**, a classic P-gp interaction profile.
- **Net absorption (AB–BA)** for Ketamir-2 was 41.9, compared to –15.1 for ketamine, supporting significantly better permeability.
- **Predicted oral bioavailability of ~80%,** exceeding that of ketamine's oral or intranasal routes.
- Supports potential for **convenient, at-home, oral administration** — improving treatment access and patient autonomy.



	AB	BA	AB-BA
Ketamir	80.6	-38.7	41.9
Ketamine	44.5	-59.6	-15.1
Propranolol	59.3	-20.4	38.9

All values represent the mean permeability (10^{-6} cm/s) of two runs with the drug concentration of $1x10^{-5}$ M for all three drugs listed.

Figure: Data obtained from the CaCO-2 model of intestinal absorption. Propranolol, a commonly prescribed beta-blocker that is taken orally and used to treat hypertension, is included as a positive control. The intestinal absorption (AB), Intestinal efflux (BA) and net absorption (AB-BA) are shown.

Ketamir-2 Summary: Preclinical Profile Supports Further Development

Mechanistically selective, orally bioavailable, and non-genotoxic — with consistent activity across models of depression, anxiety, and neuropathic pain

Chemistry & Formulation (CMC)
-Ketamir-2 is a stable crystalline analog of ketamine, developed as a hemi-pamoate salt
-Synthesized via a cost-efficient, high-yield process
-Formulated into stable 50 mg and 300 mg oral capsules

Pharmacology
-Acts as a low-affinity, selective PCP-site NMDA antagonist
-Demonstrates potent activity in models of neuropathic pain, depression, and anxiety

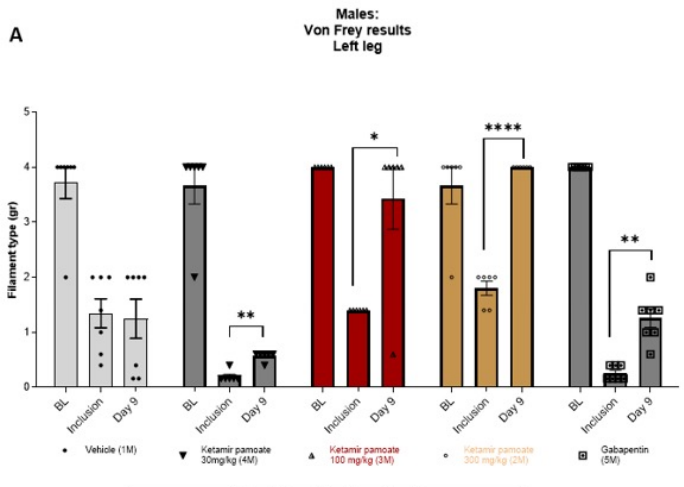
ADME & Bioavailability
-Not highly protein-bound across preclinical species (mouse, rat, dog, monkey, human)
-Not a P-glycoprotein substrate, supporting improved brain penetration
-Metabolized via N-demethylation (primarily CYP2B6 & CYP3A4)
-Shows rapid oral absorption and short half-life; metabolite has longer half-life and CNS exposure
Predicted oral bioavailability ~100%

Safety & Toxicology
-Highly selective across a broad receptor panel
-Non-genotoxic in standard assays
-NOAELs: 300 mg/kg/day in rats; 200 mg/kg/day in dogs

Comparative effects of several oral doses of Ketamir-2 to Gabapentin in the PTX model of Neuropathic pain in male mice.

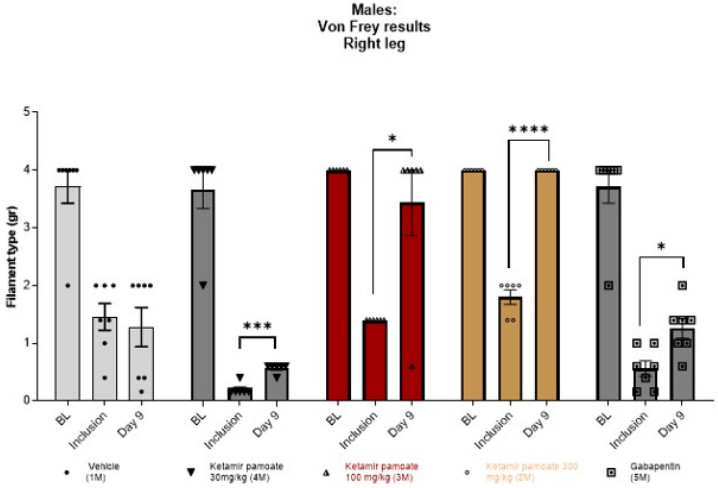
Male mice were evaluated in the right and left legs 9 days following PTX treatment. As can be seen a marked allodynia was observed. We can see a significant effect as from 30 mg/kg PO and a full reversal to basal le levels at 100 and 300 mg/kg Po. Ketamir-2 out performed gabapentin (100 mg/kg po) in this study.

A



Paired t test (Day 8 vs. Day 9)		
Table Analyzed	P value	P value summary
Ketamir pamoate 300 mg/kg (2M)-L leg	<0.0001	****
Ketamir pamoate 100 mg/kg (3M)-L leg	0.0157	*
Ketamir pamoate 30mg/kg (4M)-L leg	0.0041	**
Gabapentin (5M)-L leg	0.0018	**

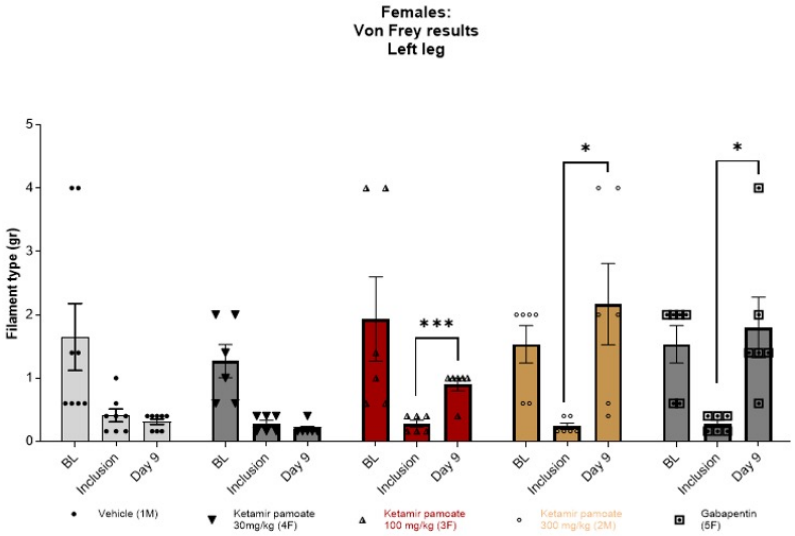
B

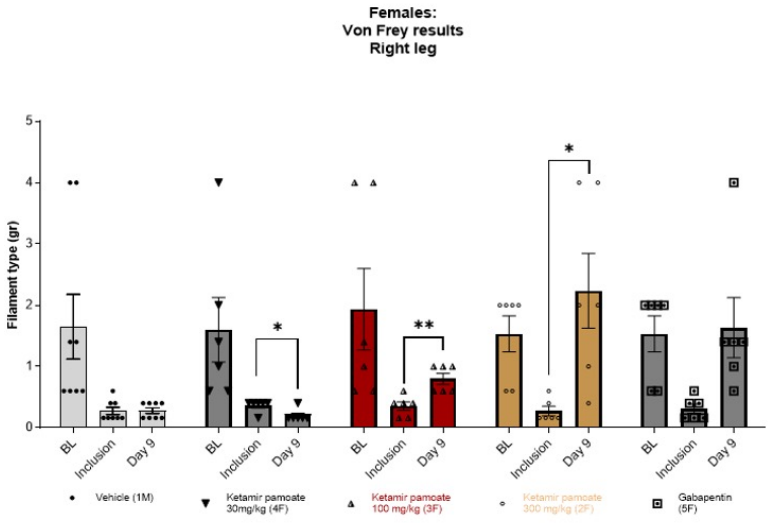


Paired t test (Day 8 vs. Day 9)		
Table Analyzed	P value	P value summary
Ketamir pamoate 300 mg/kg (2M)-R leg	<0.0001	****
Ketamir pamoate 100 mg/kg (3M)-R leg	0.0157	*
Ketamir pamoate 30mg/kg (4M)-R leg	0.0005	***
Gabapentin (5M)-R leg	0.018	*

Comparative effects of several oral doses of Ketamir-2 to Gabapentin in the PTX model of Neuropathic pain in female mice

Female mice were evaluated in the right and left legs 9 days following PTX treatment. As can be seen a marked allodynia was observed with higher sensitive than male mice.. We can see a significant effect as from 100 mg/kg PO and a full reversal to basal le levels at 300 mg/kg Po. Ketamir-2 slightly out performed gabapentin (100 mg/kg po) in this study.





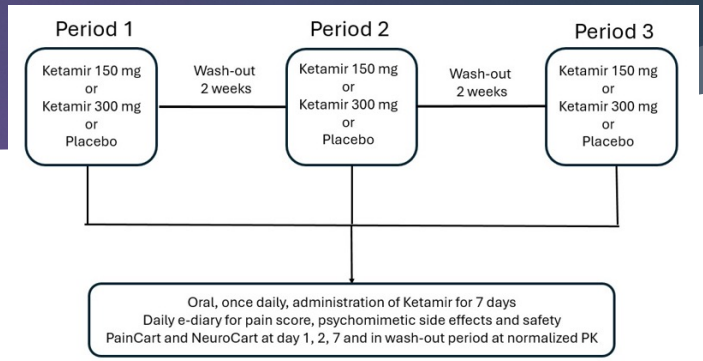
Paired t test (Day 8 vs. Day 9)		
Table Analyzed	**P value**	**P value summary**
Ketamir pamoate 300 mg/kg (2F)-L leg	0.0372	*
Ketamir pamoate 100 mg/kg (3F)-L leg	0.001	***
Gabapentin (5F)-L leg	0.0206	*

Paired t test (Day 8 vs. Day 9)		
Table Analyzed	**P value**	**P value summary**
Ketamir pamoate 300 mg/kg (2F)-R leg	0.0324	*
Ketamir pamoate 100 mg/kg (3F)-R leg	0.0067	**
Ketamir pamoate 30mg/kg (4F)-R leg	0.025	*

Ongoing Phase 1 Trial: Cohort 3 Complete, Preparing for Cohort 4

To date, 18 participants have completed dosing with no serious or dose-limiting adverse events reported.

- **Phase 1 trial is ongoing** — Cohort 3 has completed dosing with **no serious or dose-limiting adverse events reported to date**
- Preparation for **Cohort 4** is underway
- Randomized crossover design with three treatment periods: 150 mg, 300 mg, and placebo — each administered once daily for 7 days
- Evaluations include e-diary pain scores, NeuroCart cognitive testing, psychomimetic assessments, safety labs, and ECGs
- Dose escalation to 600 mg is underway, with SAD Cohort 4 initiating shortly.



SAD	Dose level, mg (once daily oral dosage)	Number of participants	
		Ketamir hemipamoate	Placebo
Cohort 1	50mg, 1X50mg capsule	6	2
Cohort 2	150mg, 3X50mg capsule	6	2
Cohort 3	300mg, 1X300mg capsule	6	2
Cohort 4	600mg, 2X300mg capsule	6	2
MAD			
Cohort 5	150mg, 3X50mg capsule for 5 days	6	2
Cohort 6	300mg, 1X300mg capsule for 5 days	6	2
Cohort 7	600mg, 2X300mg capsule for 5 days	6	2
Total Participants		**42**	**14**

Ketamir-2 Development Pathway Toward Phase IIa in Neuropathic Pain

A strong foundation from preclinical and Phase 1 data supports rapid advancement into diabetic neuropathy patients.

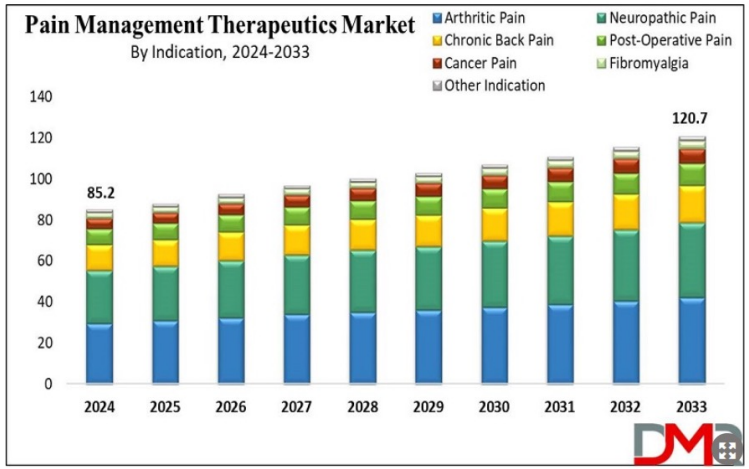
Market Opportunity:

-Pain therapeutics market expected to exceed **$120B by 2033**

-Neuropathic pain remains a large, underserved segment

-Ketamir-2 offers an oral, CNS-safe alternative with clear differentiation

-Well-positioned for strategic collaboration to co-develop Ketamir- 2 through Phase II and beyond



Phase IIa Study Design Overview:

Phase 1 (Mira-001) underway:

300 mg cohort complete, 600 mg cohort initiating

Milestones:

- MAD study concludes Q2 2025
- Repeat SAD study begins Q3 2025

Phase IIa Study (Start: Q4 2025) — Painful Diabetic Polyneuropathy (PDPN)

Primary Endpoints:

- AE/SAE frequency
- Vital signs, ECGs
- PainCart battery for pain modeling
- NeuroCart cognitive tests
- VAS (mood, alertness, calmness)
- CADSS-6 for dissociative symptoms
- Daily pain & tolerability scores (e-diary)

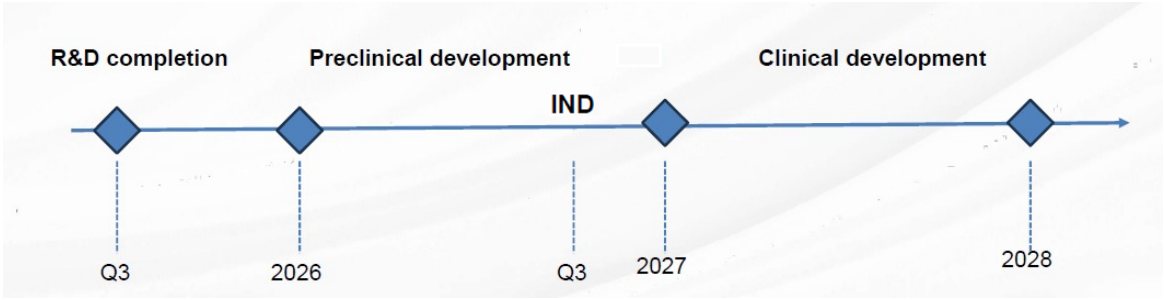
Secondary Endpoints:

- PK of Ketamir-2 and metabolite
- Measured in plasma and urine

A Next-Generation Approach to Obesity & Smoking Cessation

Unlocking Metabolic and Behavioral Health Innovation Through SKNY-1

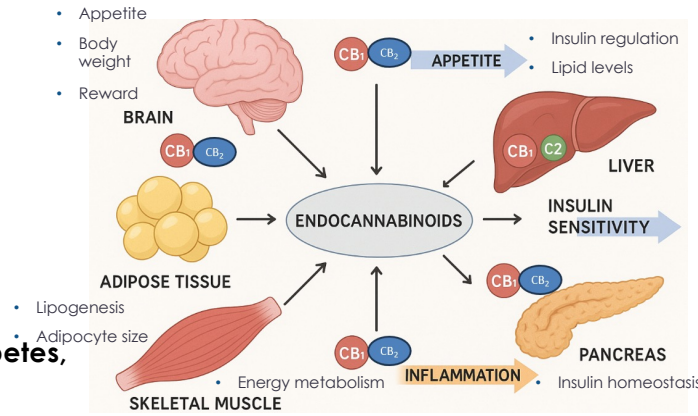
- **Oral small molecule THCV analog with non-controlled status**
- **Multi-mechanistic profile**: CB1 antagonist, CB2 partial agonist, MAO-B inhibition
- Designed to address **obesity, smoking cessation, insulin resistance**, and other metabolic disorders
- **Differentiated safety and receptor bias** avoids CNS liabilities of earlier CB1 drugs
- **IND planned for Q3 2026,** development-ready for strategic partnerships



The Endocannabinoid System: A Master Regulator of Metabolism and Craving

CB1 and CB2 receptors influence appetite, insulin sensitivity, lipid metabolism, and reward — making them ideal targets for obesity and addiction.

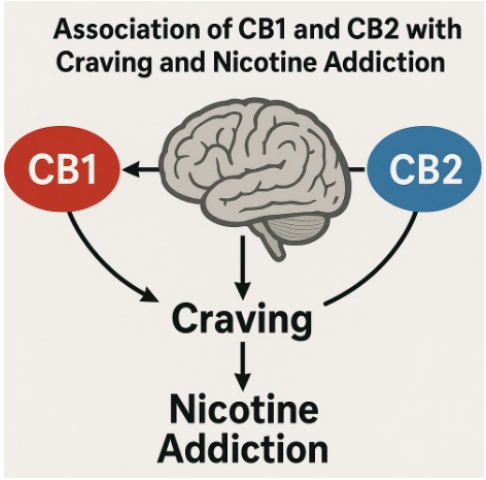
- CB1 and CB2 receptors are found throughout the brain and peripheral tissues
- CB1 activity in the brain regulates **appetite, craving, and reward**
- CB1 in adipose tissue and muscle drives **lipogenesis and energy metabolism**
- CB2 is involved in **immune modulation, inflammation**, and **insulin sensitivity**
- Targeting both CB1 and CB2 offers a systemic strategy for treating **obesity, diabetes, and addiction**



Multi-Target Mechanism to Address Complex Metabolic and Behavioral Conditions

SKNY-1's unique combination of activities enables broad therapeutic coverage across obesity, addiction, and metabolic dysregulation.

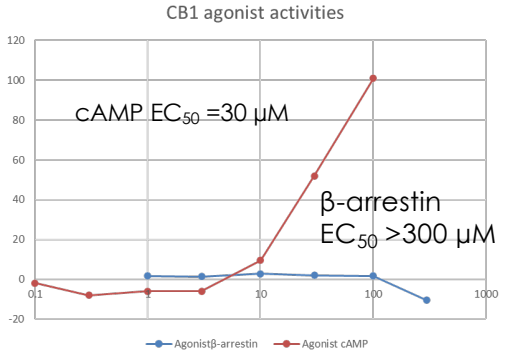
- **CB1 Antagonism**: Reduces appetite, body weight, and craving by dampening central reward signaling
- **CB2 Partial Agonism:** Modulates inflammation, improves insulin sensitivity, and reduces peripheral immune activation
- **MAO-B Inhibition:** Enhances dopamine tone to support mood and motivation without dopaminergic overstimulation
- **No CB1 Agonism or G-protein bias:** Limits CNS liability, hallucinations, or psychomotor side effects
- **Peripheral Selectivity**: Designed to act outside the brain while avoiding CB1-associated psychiatric risks

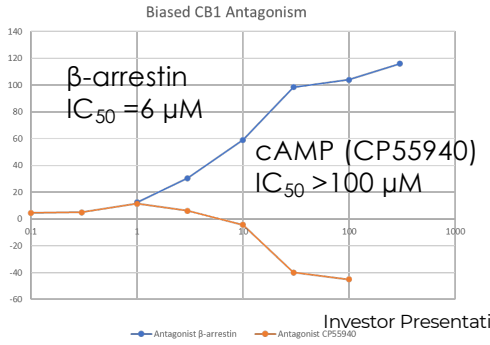


A Safer Path Forward: Receptor Bias Minimizes Psychiatric Side Effects

SKNY-1's peripheral action and arrestin bias offer safety advantages over earlier CB1-targeting drugs.

- **Biased CB1 Modulation**: Selectively blocks β-arrestin signaling without blocking CB1 agonists, while showing only low-affinity G-protein (cAMP) activity — preserving key metabolic signaling and avoiding CNS overstimulation
- **Avoids CNS Over-Inhibition:** Reduces psychiatric risks linked to earlier CB1 drugs like Rimonabant (e.g., depression, anxiety)
- **No CB1 Agonist Activity:** Minimizes risk of CNS stimulation, hallucinations, or reward-related liability
- **Peripheral Selectivity:** Engineered to act outside the brain, further limiting central nervous system exposure
- **Clean MAO Profile:** Selectively inhibits MAO-B (linked to dopamine regulation and addiction) with minimal MAO-A activity

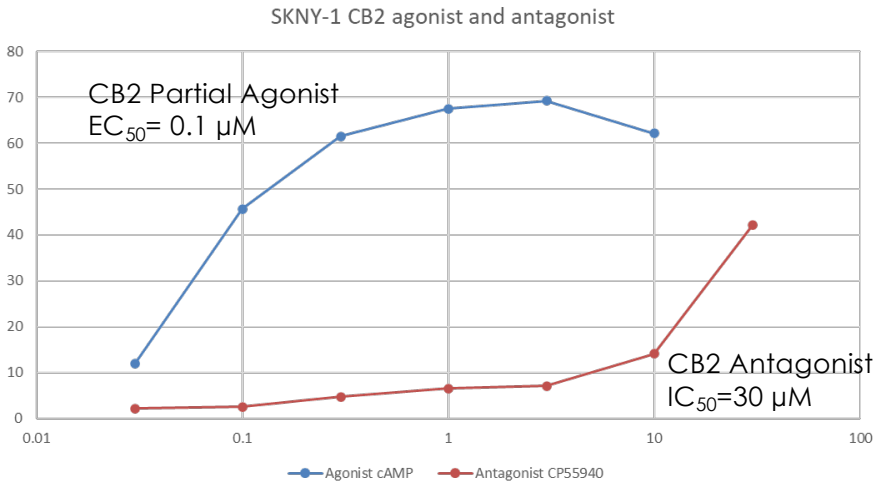




SKNY-1: Tackling Obesity with a Differentiated Mechanism

Designed to modulate appetite and metabolism without the psychiatric baggage of first-generation CB1 blockers.

- Selective modulation of CB1 receptor without β-arrestin activation — may reduce CNS-related side effects
- Demonstrates partial agonist behavior at CB2 (~60% maximal effect)
- At higher concentrations, SKNY-1 shows CB2 antagonism — indicating a dose-dependent dual profile
- MAO-B inhibition (without affecting MAO-A) supports dopaminergic balance — key in appetite, craving, and addiction
- Combined activity offers a novel strategy for treating obesity, especially in patients with metabolic and behavioral complexity



Avoiding the Pitfalls of First-Generation CB1 Blockers

Designed to retain metabolic benefit while minimizing psychiatric burden

- **Earlier CB1 blockers like Rimonabant** were effective in reducing weight and improving metabolic parameters — but failed due to **CNS-related psychiatric side effects** (e.g., depression, anxiety)

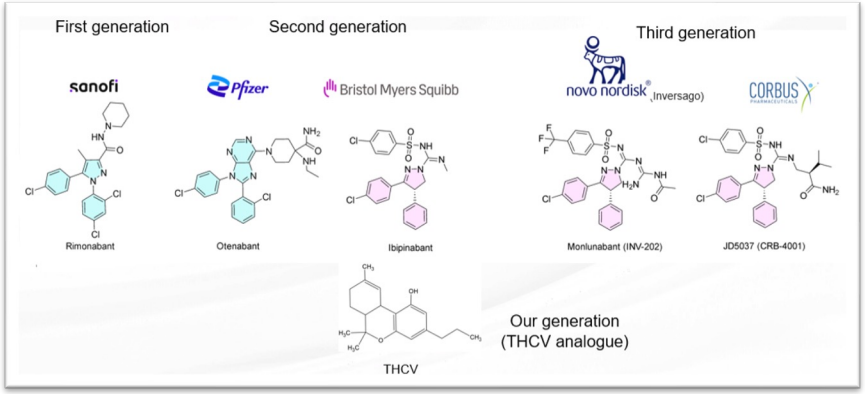
SKNY-1 avoids this fate through:

-No G-protein antagonism — avoids full CB1 shutdown

-Selective β-arrestin antagonism — preserves key metabolic signaling

-Peripheral action — limits CNS penetration and reduces psychiatric risk

- **MRI-1891**, a later-generation CB1 antagonist, also showed β-arrestin selectivity — but with **greater G-protein antagonism and CNS liability** compared to SKNY-1
- **SKNY-1 stands apart** as a **moderate β-arrestin antagonist** with **no G-protein antagonism** and **enhanced CB2 activity**, positioning it as a next-generation metabolic modulator with **improved safety margins**

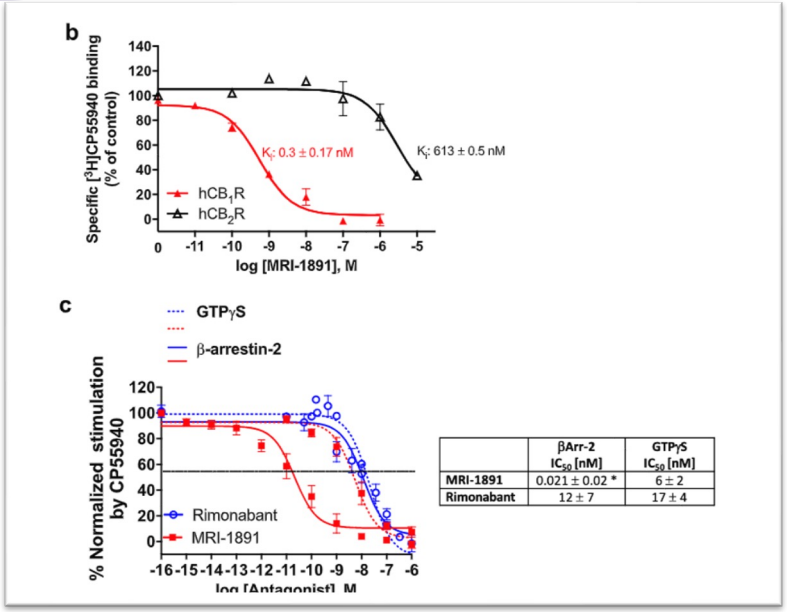


SKNY-1 represents a next-generation evolution in CB1/CB2 modulation — advancing the THCV class with improved safety and metabolic targeting.

Comparison to Monlunabant: A Safer, More Selective Alternative

SKNY-1 demonstrates a differentiated pharmacological profile compared to third-generation CB1-targeting drugs like Monlunabant (MRI-1891), with important safety and mechanistic distinctions.

- **No G-Protein Coupled Antagonism:** Unlike Monlunabant, SKNY-1 does not exhibit G-protein antagonism — avoiding the mechanism associated with psychiatric side effects in earlier CB1 drugs.
- **Moderate β-arrestin Antagonist:** SKNY-1 shows only moderate antagonism at β-arrestin, whereas Monlunabant exhibits high potency in both G-protein and β-arrestin pathways.
- **Selective and Safer Pharmacology:** This functional bias suggests SKNY-1 preserves necessary metabolic signaling while minimizing central nervous system risks.
- **Avoids Rimonabant-Like Liability:** By sidestepping full CB1 blockade, SKNY-1 may reduce risk of depression, anxiety, or psychomotor disturbances linked to prior generation CB1 antagonists.
- **Distinct Molecular Profile:** SKNY-1's THCV-based structure represents a novel generation of cannabinoid modulators with differentiated CNS safety.

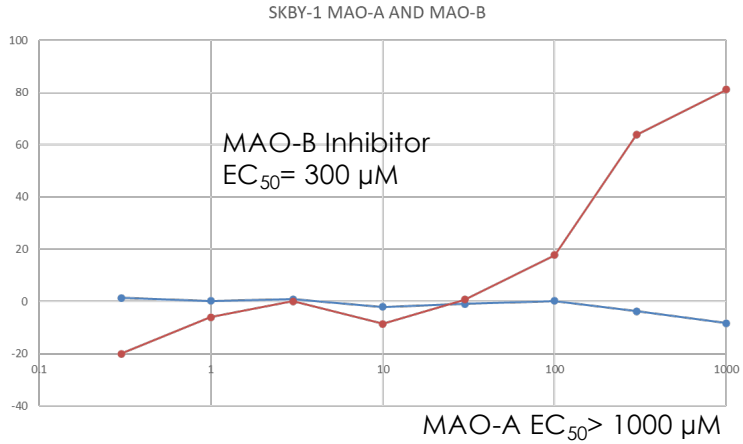


	βArr-2 IC_{50} [nM]	GTPγS IC_{50} [nM]
MRI-1891	0.021 ± 0.02 *	6 ± 2
Rimonabant	12 ± 7	17 ± 4

MAO-B Inhibition: Enhancing Motivation and Reducing Craving

SKNY-1 selectively and weakly inhibits MAO-B — supporting dopaminergic tone with minimal CNS risk.

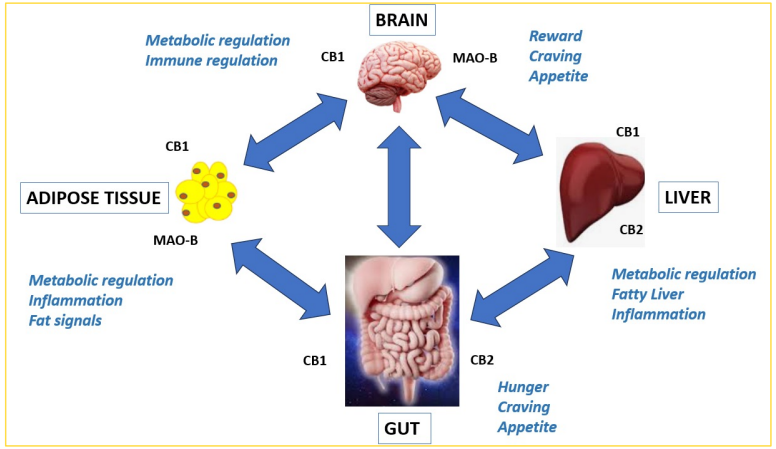
- **Low-Affinity, Selective MAO-B Inhibition:** SKNY-1 inhibits MAO-B (EC_{50} ≈ 300 µM) with minimal effect on MAO-A (EC_{50} > 1000 µM), avoiding off-target serotonergic effects
- **Supports Dopamine Balance:** Sustained dopamine levels may enhance motivation, reduce craving, and improve mood without overstimulation
- **Relevance for Addiction:** MAO-B modulation is linked to reduced nicotine and reward-driven behaviors, making SKNY-1 a strong candidate for smoking cessation
- **Minimizes CNS Liabilities:** Selective inhibition avoids the adverse events associated with non-selective MAO inhibitors
- **Integrative Mechanism:** Enhances SKNY-1's CB-targeting strategy by adding dopaminergic support for metabolic and behavioral indications



SKNY-1's Multi-Tissue Action: A Coordinated Strategy for Obesity and Addiction

A single compound influencing central and peripheral targets — uniting metabolic, behavioral, and inflammatory control.

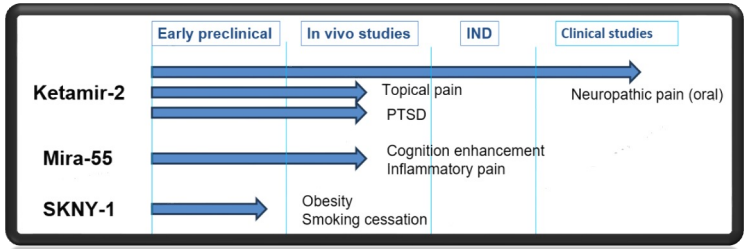
- **Brain:** Modulates CB1 and inhibits MAO-B, impacting appetite regulation, reward signaling, and dopaminergic tone
- **Liver & Adipose Tissue:** Affects CB1 and CB2 to regulate fat storage, lipid metabolism, and reduce inflammation
- **Gut:** CB1 and CB2 activity influence hunger cues, cravings, and appetite suppression
- **Systemic Integration:** SKNY-1's profile links central mechanisms with downstream effects in peripheral tissues
- **Therapeutic Implication:** A promising candidate for multifactorial conditions like obesity, metabolic syndrome, and substance dependence



Advancing SKNY-1 Toward Strategic Partnership and Clinical Validation

Differentiated science, druggable profile, and commercial opportunity converge in SKNY-1

- **Highly differentiated** THCV-analog small molecule with CB1/CB2/MAO-B selectivity
- **Multi-mechanistic action addresses both metabolic and behavioral drivers of obesity and addiction**
- **Peripheral selectivity** and **receptor bias** avoid CNS risks that limited prior-generation CB1-targeting drugs
- **Validated targets** with strong precedent in large markets (e.g., rimonabant, Monlunabant)
- **Preclinical package supports IND** in 2026 with optionality for metabolic, smoking cessation, or CNS pathways
- **Positioned for partnering** to advance SKNY-1 into the clinic and unlock value in multiple indications



Emerging Pipeline With Broad Strategic Potential
Mira is advancing oral therapies across CNS, pain, and metabolic disorders, including:
MIRA-55 for cognition and inflammatory pain
SKNY-1 for obesity and smoking cessation

Diverse, mechanism-driven programs with near- and mid-term partnering potential.

Investment Highlights

KETAMIR-2

Ketamir-2 is a novel oral ketamine analog with improved bioavailability, CNS selectivity, and a clean safety profile.

- Demonstrated potent activity in validated models of **neuropathic pain, depression, and anxiety**
- **No psychomimetic effects, no hyperlocomotion**, and minimal off-target activity
- Currently in **Phase 1 trials** with ongoing dose escalation toward 600 mg
- Predicted **oral bioavailability ~80%**, far exceeding ketamine's oral/intranasal performance
- Not a DEA-controlled substance — favorable for regulatory and commercial pathways

MIRA-55

MIRA-55 is a synthetic cannabinoid designed to reduce anxiety and enhance cognition — without THC-like intoxication.

- Preclinical data shows **reduced anxiety (EPM), improved memory (Fear Conditioning), and pain relief (Thermal Test)**
- Acts without sedation or euphoria — **a rare behavioral profile among cannabinoid analogs**
- Targets ~**14M patients with anxiety or cognitive decline in the U.S.**
- Non-scheduled compound — development-friendly for age-related CNS indications

SKNY-1

SKNY-1 is a THCV-based compound with CB1 antagonist, CB2 partial agonist, and MAO-B inhibition activity — targeting metabolic and behavioral disorders.

- Designed to treat **obesity, smoking cessation, and insulin resistance**
- Demonstrates **peripheral selectivity** and **receptor bias** — avoiding psychiatric side effects seen in earlier CB1-targeting drugs
- Distinct from Rimonabant and MRI-1891: **No G-protein antagonism**, only moderate β-arrestin modulation
- IND expected in **Q3 2026**, with strong partnering potential for metabolic or addiction pipelines

MIRA Pharmaceuticals

Thank you.

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Meeting Presentation