PHARMATHER

KETAMINE EVOLVED.

11/2025 | PHARMATHER HOLDINGS LTD.

OTCQB: PHRRF | CSE: PHRM

Forward-looking statements

This presentation of PharmaTher Holdings Ltd. ("PharmaTher") contains "forward-looking information", which may include, but is not limited to, statements with respect to anticipated business plans or strategies of PharmaTher, the anticipated date of completion of research studies, the timing of any drug trials, the success of its clinical trials, the ability to enter into licenses, acquisitions or collaborations to enhance its drug development platform, the success of any such licenses, acquisitions or collaborations and the ability to use the information relating to, or obtain patents or other intellectual property protection on, data and clinical trials generated directly by PharmaTher or through such licenses, acquisitions or collaborations, and the success or stage of development of discoveries or medicines. Often, but not always, forward-looking statements can be identified by the use of words such as "plans", "expects", "is expected", "budget", "scheduled", "estimates", "forecasts", "intends", "anticipates", or "believes" or variations (including negative variations) of such words and phrases, or state that certain actions, events or results "may", "could", "would", "might" or "will" be taken, occur or be achieved. Forward-looking statements involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of PharmaTher to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Factors that could cause actual results to differ materially from those anticipated in these forward-looking statements are described under the caption "Risk Factors" in Company's management's discussion and analysis for the year ended May 31, 2025 dated September 26, 2025, which is available on the Company's profile at www.sedarplus.ca. Forward-looking statements contained herein are made as of the date of this presentation and PharmaTher disclaims, other than as required by law, any obligation to update any forward-looking statements whether as a result of new information, results, future events, circumstances, or if management's estimates or opinions should change, or otherwise. There can be no assurance that forward-looking statements will prove to be accurate, as actual results and future events could differ materially from those anticipated in such statements. Accordingly, the reader is cautioned not to place undue reliance on forward-looking statements.

Our Foundation

We are unlocking the therapeutic potential of **ketamine** for neuropsychiatric disorders

- **De-risked supply and revenue:** FDA-approved ketamine ANDA now being monetized, securing product supply for next-generation ketamine programs
- **Deep ketamine know-how:** Advanced ketamine research across mental health, neurological, and pain disorders
- **Innovative delivery platforms:** Developed multiple drug-delivery forms of ketamine (injectables, patch, pump)
- **IP and regulatory assets:** Granted FDA orphan drug designations and multiple USPTO patents for ketamine-based therapies
- **Clinical and regulatory pathfinder:** Established clinical proof-of-concept to enable a rapid path to late-stage trials via the 505(b)(2) pathway

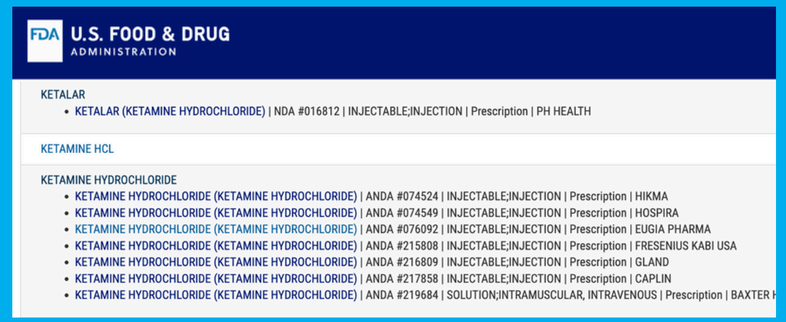
Evolving Ketamine Market

Similar to GLP-1s evolving to long-acting delivery for obesity

Pfizer acquired Metsera for $10 Billion

Generic ketamine

- In 1970, FDA approved as a general anesthetic
- Highly competitive/saturated with 8 ANDAs and numerous 503A/B pharmacy compounders



FDA U.S. FOOD & DRUG ADMINISTRATION

KETALAR
- KETALAR (KETAMINE HYDROCHLORIDE) | NDA #016812 | INJECTABLE;INJECTION | Prescription | PH HEALTH

KETAMINE HCL

KETAMINE HYDROCHLORIDE
- KETAMINE HYDROCHLORIDE (KETAMINE HYDROCHLORIDE) | ANDA #074524 | INJECTABLE;INJECTION | Prescription | HIKMA
- KETAMINE HYDROCHLORIDE (KETAMINE HYDROCHLORIDE) | ANDA #074549 | INJECTABLE;INJECTION | Prescription | HOSPIRA
- KETAMINE HYDROCHLORIDE (KETAMINE HYDROCHLORIDE) | ANDA #076092 | INJECTABLE;INJECTION | Prescription | EUGIA PHARMA
- KETAMINE HYDROCHLORIDE (KETAMINE HYDROCHLORIDE) | ANDA #215808 | INJECTABLE;INJECTION | Prescription | FRESENIUS KABI USA
- KETAMINE HYDROCHLORIDE (KETAMINE HYDROCHLORIDE) | ANDA #216809 | INJECTABLE;INJECTION | Prescription | GLAND
- KETAMINE HYDROCHLORIDE (KETAMINE HYDROCHLORIDE) | ANDA #217858 | INJECTABLE;INJECTION | Prescription | CAPLIN
- KETAMINE HYDROCHLORIDE (KETAMINE HYDROCHLORIDE) | ANDA #219684 | SOLUTION;INTRAMUSCULAR, INTRAVENOUS | Prescription | BAXTER

SPRAVATO®

- In 2019, FDA approved esketamine nasal spray for TRD and MDD with acute suicidal thoughts or actions
- TTM sales: ~$1.7B*

* Global market, end of Q2-25 per J&J

Clinical-stage

1. Orals
2. Intranasal
3. Patch / Pump
4. Injectables / IV
5. Hydronorketamines

Our Belief: Long-acting Ketamine is the Future

Potential to help change the way neuropsychiatric disorders are treated

Long-acting ketamine potential

- Maintain therapeutic drug levels over extended periods
- Improved safety
- Eliminate/reduce dissociative affects, abuse & diversion
- Lowever clinic burden
- Higher patient compliance
- Expands new indications where steady exposure is critical

Neuropsychiatric disorders market potential

U.S. = ~$37B in 2025

Global = ~$145B in 2024

Potential indications for LAI Ketamine:
Depression, Post-traumatic stress disorder (PTSD), anxiety, schizophrenia, Addiction/Substance use, bipolar disorders, Obsessive-compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), migraine, seizures, Eating disorders, epilepsy, stroke, Alzheimer's disease and other dementias, Multiple sclerosis, Parkinson's disease.

Our Solution: KET-100

Patented microsphere-based long-acting injectable ketamine

Patent: US 12,233,165
(Expires October 2, 2042)

Microsphere formulations comprising ketamine and methods for making and using the same

1. **Proven Regulatory and Clinical Track Record**
   - FDA-accepted delivery technology; approved drugs using similar technology (Lupron Depot®, Risperdal Consta®, Sandostatin LAR®)
2. **Flexible Release Kinetics**
   - Drug release can be tuned from days to several months
3. **Controlled and Predictable Release**
   - Reducing side effects (dissociation, sedation, dizziness)
4. **Established U.S.-based Manufacturing**
   - Scalable & reproducible, lowering manufacturing risks
5. **Versatility in Drug Types and Routes**
   - Delivered subcutaneously or intramuscularly

Potential Differenitation of KET-100 vs Others

Lower clinic burden, steadier PK, better adherence, scalable economics

KET-100: LAI Ketamine (+monthly)

✓ Set-and-forget monthly dosing
✓ No clinic or short visit: ~30–60 min, minimal observation
✓ Steady exposure → fewer peak-trough swings
✓ Lower acute AEs (dissociation, BP spikes) vs. bolus formats
✓ High adherence: HCP-administered, infrequent dosing
✓ No Spravato® REMS; standard monitoring only
✓ Lower diversion risk
✓ Predictable payer spend; frees clinic chairs
✓ Strong IP moat via formulation + new label

Spravato® & Other ketamine formats (IV, pump, patch, oral)

- High visit burden: 2–8 hrs per clinic visit (REMS for Spravato)
- Spravato (2x/w first month, 1x/w second month, 2x/m ongoing)
- Frequent dosing to maintain effect (weekly/biweekly or more)
- Cmax spikes → more dissociation & BP elevations
- Technique/device variability (nasal anatomy, pump, patch flux)
- Higher diversion risk for take-home forms
- Clinic bottlenecks (chairs, staff)
- Variable payer economics due to visit/device cadence

Clinic time:	KET-100: ■■■■■ (low)	Others: ■■□□□ (high)
Adherence / persistence:	KET-100: ■■■■■ (high)	Others: ■■■□□ (moderate)
Peak–trough swings:	KET-100: ■□□□□ (low)	Others: ■■■■□ (higher)
Abuse/diversion risk:	KET-100: ■□□□□ (low)	Others: ■■■□ (moderate–high)
Payer & ops scalability:	KET-100: ■■■■■ (strong)	Others: ■■□□□ (limited)

For discussion only. Comparative assessments reflect typical use patterns; program-specific data may vary.

Our Pipeline and Opportunity

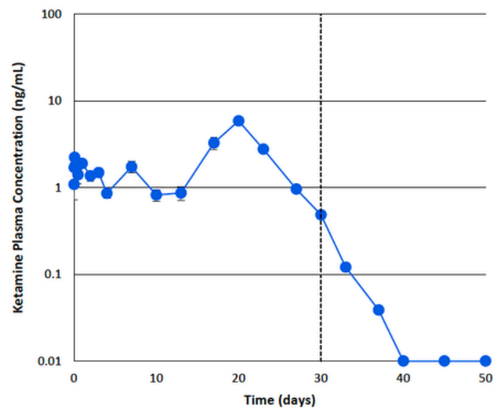
Expedited development opportunities via the 505(b)(2) pathway

Drug	Indication	IND-enabling	Phase I/II	Phase III	Market size
KET-100	**Treatment-resistant depression**	FDA PIND meeting			>$6B market >20M population
KET-100	**Major depressive disorder**	FDA PIND meeting			>$4B market >15M population
KET-002 Racemic ketamine IV	**Levodopa-induced Parkinson's Disease**	Adaptive Phase 2/3 ready			>$1B market 1M population
KET-003 Racemic ketamine IV	**ALS**	PI funded			>$250M market <200K population

Current | 12-18 Months

KET-100 Preclinical Overview

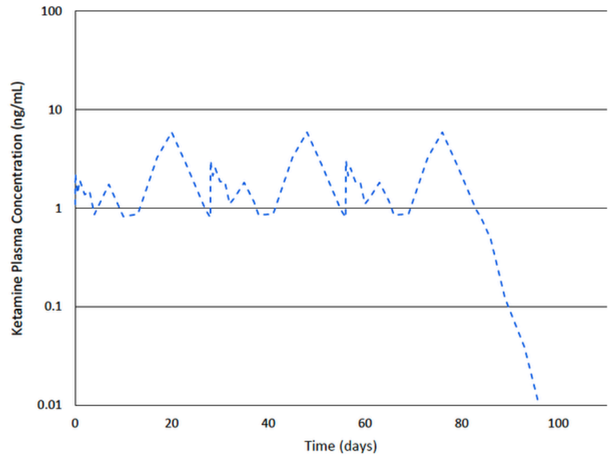
In-Vivo Release of Ketamine-Loaded Microspheres in Dogs



Study Parameters	
Microsphere drug loading	14.4 wt%
Dog dose	15 mg API/kg
# of animals	5 dogs
C_{max}	5.93 ng/mL
T_{max}	20 days

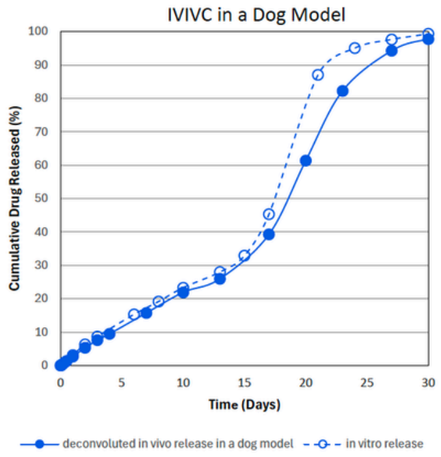
- in vivo release profile of 30 days in dog model was achieved
- Release profile is very steady and linear; blood level targets can be varied based on overall dosing levels to target a specific therapeutic window

Simulated Repeat Dosing (3 Months)



- Dosing schedule:
  - 15 mg of ketamine/kg/month in a dog model
  - 28-day injection intervals
  - Dosing levels can be adjusted to account for different dosing schedules
- C_{max}=5.9 ng/mL (Day 20)
- C_{min}= 0.8 ng/mL (Day 28)

In Vitro – In Vivo Correlation in an Animal Model



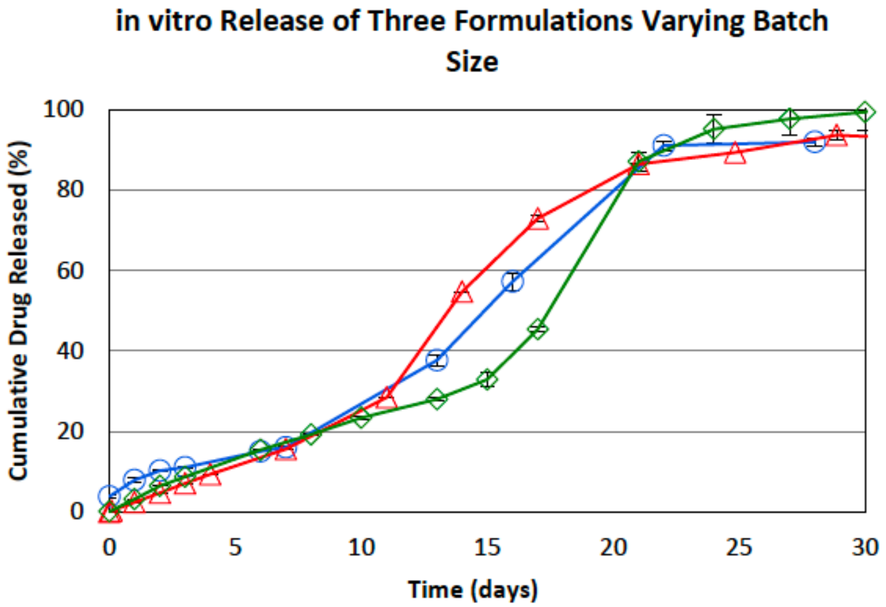
- Dog model dosing of 15 mg/kg/month
- Good correlation between in vitro testing and in vivo animal model release profiles
  - Allows for robust testing of every formulation
- In vitro – in vivo correlation also confirmed in a rat model with good results

KET-100 Clinical and Commercial Scale-up

Lot Number	22	23	24
Symbol	○	△	◊
Batch Size (g) (total solids)	15	50	1200
Drug Load (wt%)	14.5	13.5	14.4

*all other microsphere parameters held constant

- Increasing batch size has little to no effect on drug loading and release profile
  - Small changes in release duration can be overcome with minor polymer or particle size changes
- 1200 g batch size = approximately 1500 vials
- On-going work to scale-up batch size to 5000 g (commercial scale)



KET-100 Expected FDA Approval Timeline

- FDA PIND Meeting*
- Complete Ph2 study

- EoPh2 FDA meet
- Complete Ph3 study

- NDA Submission (1H-28)
- Commercial scale-up

Potential Pharma partnership or acquisition

FDA Approval (1H-29)

- Commercial sales
- Label expansions
- Int'l regulatory approvals

** Assume TRD indication*

2026 | 2027 | 2028 | 2029 | 2030

Regulatory and IP Portfolio

FDA Orphan Drug Designation

7 years exclusivity

1. Amyotrophic lateral sclerosis
2. Complex Regional Pain Syndrome
3. IR injury solid organ transplants
4. Status Epilepticus
5. Rett Syndrome

PATENTED

KET-100
U.S. Patent No. 12,233,165
expiring Oct 2, 2042

Parkinson's Disease
U.S. Patent No. 11,426,366
expiring May 5, 2036

Amyotrophic lateral sclerosis
U.S. Patent No. 12,128,012
expiring May 14, 2041

Our Monetizing Assets

Providing non-dilutive funding opportunities

Ketamine ANDA

CAPLIN POINT® Laboratories

Website

- Subsidiary of Caplin Point Laboratories Limited (BSE: CAPPL (524742), NSE: CAPLIPOINT); Market cap ~ US$1.7Bn & Sales of ~ US$232Mn
- We are entitled to receive sales milestones of up to $25M & profit sharing with no ceiling for 7 years

Cepharanthine

Sairiyo Therapeutics

Website

- Clinical-stage, patented, orally bioavailable version of Cepharanthine
- U.S. Patent No. 10,576,077 (Exp 2036)
- U.S. Defence invested +$3.5m for Ebola
- MoA: Antiviral, anti-inflammatory, anti-oxidative, immuno-regulatory, antitumor
- Phase I/II for infectious diseases & cancers
- We own 49%; seek spin-out or sale

Expected Milestones

Commercial

1. ✓ FDA approval for KETAMINE ANDA in August 2025
2. ✓ Commercial sale of KETAMINE in the U.S.
3. Generic ketamine approvals & sales in Canada, EU, UK, Japan, and APAC
4. Multiple pharma partnerships for clinical programs
5. Spin-out or sale of Sairiyo Therapeutics

Clinical*

1. KET-100: Phase 2 top line results for TRD
2. KET-100: Phase 2 top line results for MDD
3. KET-002: Phase 3 top line results for Parkinson's disease
4. KET-003: Phase I/II top line results for ALS

** Pending funding and/or pharma partnerships, and health regulatory acceptance to proceed with studies*

Leadership

Fabio Chianelli

Founder, Chairman, CEO

- Founder, CEO, President at Revive Therapeutics Ltd.

Dr. Bev Incledon

Director

- CSO, Ironshore Therapeutics

(Acquired by Collegium for $525M in 2024)

Carmelo Marrelli

Chief Financial Officer

- CFO of various TSX, CSE, OTCQB listed companies

Carlo Sansalone

Director

- Investor, Biotech and Real estate
- President, Sanscon

Capital Structure

PHRRF
OTCQB

PHRM
LISTED ON CSE™

91,019,065

Issued & Outstanding Common Shares

~ 19%

Insiders Ownership

1,500,000

Stock Options Outstanding

16,875,000

Warrants Outstanding

16,875,000 @ CAD $0.80 (expires Sept 2026)

PHARMATHER

Thank you

info@pharmather.com

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