



***Unlocking the Potential of
Ketamine***

Corporate Presentation

February 2024

PharmaTher Holdings Ltd.

PharmaTher.com

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 PharmaTher’s management’s discussion and analysis for the three months ended August 31, 2023 (“MD&A”), dated October 26, 2023, 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.



Summary

- ◆ Focused on unlocking the potential of Ketamine
- ◆ FDA approval goal date for KETARX™ is April 29, 2024*
- ◆ Multiple approvals for KETARX™ in 2024 (i.e. EU, JP, China, IN, SA, CAD)
- ◆ Novel ketamine product and clinical pipeline
- ◆ Diversified commercial lines (i.e. Sales, Spin-off, partnerships)
- ◆ Funded to multiple milestones in 2024
- ◆ Attractive valuation in psychedelics

*See February 12, 2024 press release update



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Unlocking the Potential of Ketamine

Next Generation Ketamine Products

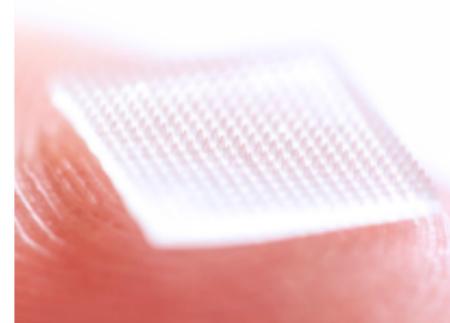
KETARX™

IV / Injectable



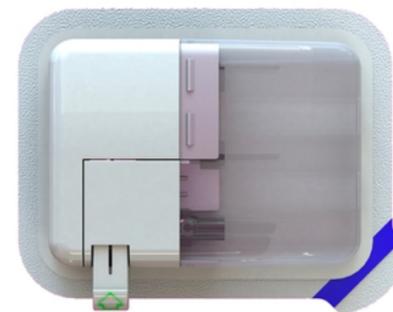
KET-101

Microneedle Patch



KET-102

Sub-Q Pump



KET-103

Oral Enteric Coated

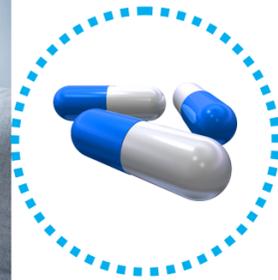


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Strategy

- ◆ Global commercialization of **KETARX™**
- ◆ Advance novel uses and delivery forms of **KETARX™**
- ◆ Clinical partnerships with **KETARX™**
- ◆ Development partnerships with **PharmaPATCH**
- ◆ Spin-off **Sairiyo Therapeutics Inc.** into a public company

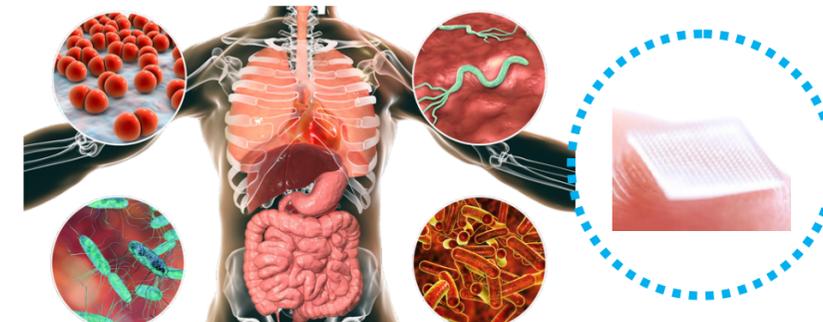
Target Markets



700 Million
Mental Health



1.5 Billion
Pain



2 Billion
Medical Countermeasures



10 Million
Neurological



500 Million
Surgeries & Procedures

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Expected Milestones in 2024

Approvals

- ◆ Q2: FDA approval of KETARX™
- ◆ Q3: Health Canada approval of KETARX™
- ◆ Q4: EMA approval of KETARX™
- ◆ Q4: Multiple approvals of KETARX™ (JP, IN, CH, AUS, SA)
- ◆ Q4: FDA approvals of KETARX™ (Multiple dosages)

Commercial

- ◆ Q2: U.S. Launch of KETARX™ in the U.S.
- ◆ Q3: Partnership of KETARX™ for Parkinson's Disease
- ◆ Q2: Spin-off Sairyo Therapeutics Inc. into a public co.
- ◆ Q1-4: International partnerships for KETARX™
- ◆ Q1-4: PharmaPATCH partnerships

Clinical

- ◆ Q2: Results of Phase 2 Study for Rett Syndrome
- ◆ Q3: Results of Phase 2 Study for ALS
- ◆ Q3: Start Phase 3 Study of KETARX™ for Parkinson's
- ◆ Q3: Start Phase 2a Study of KET-103 (Oral Ketamine)



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About Ketamine



Not approved for sale

- ◆ 50 years of clinical use with known safety and efficacy
- ◆ FDA approved for anesthesia and procedural sedation
- ◆ NMDA receptor antagonist responsible for anesthetic, analgesic and anti-depressant activity
- ◆ FDA approved delivery methods: IV, injection and intranasal
- ◆ Growing use in mental health, pain and abuse disorders
- ◆ Experimental use in neurological disorders

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KETARX™ Opportunity



Not approved for sale

◆ Initial target for anesthesia, sedation and pain relief

- Commercial sales in the U.S. and international regulatory submissions in 2024

◆ Favorable market dynamics for ketamine

- Rising demand as an alternative to opiates
- Listed on the FDA drug shortages list and WHO Essential Medicines List
- Growing adoption and validation in mental health and pain
- Big pharma interest

◆ Opportunities via 505(b)(2) pathway

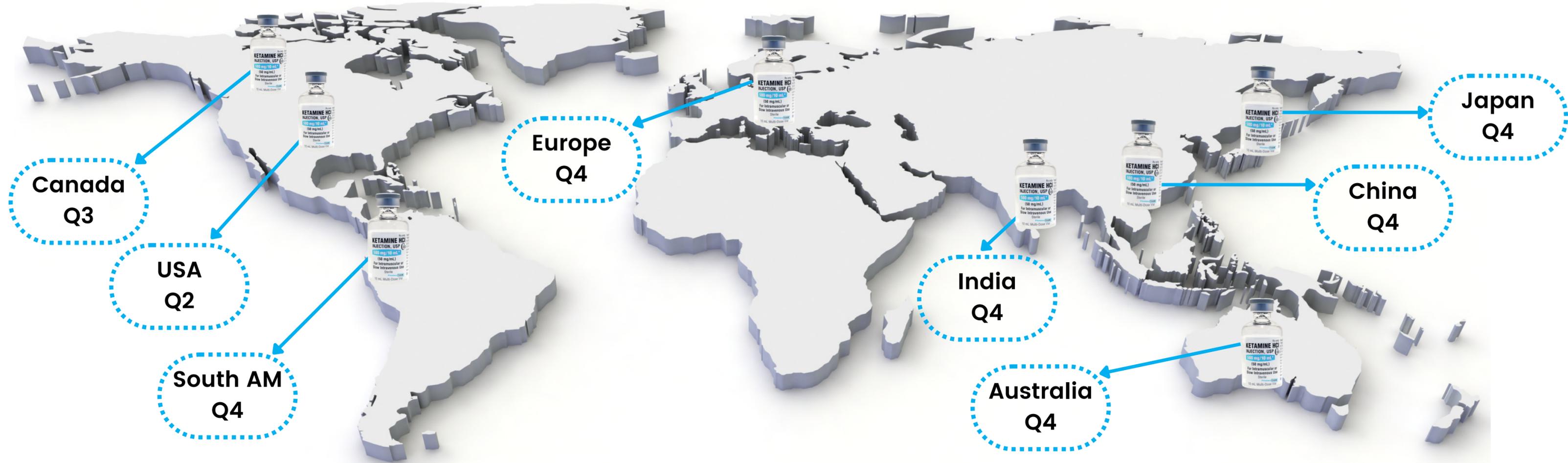
- Depression, Parkinson's disease, Rett Syndrome, CRPS, and ALS

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Expected Approvals in 2024

Global Opportunity for KETARX™



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KETARX™ Pipeline

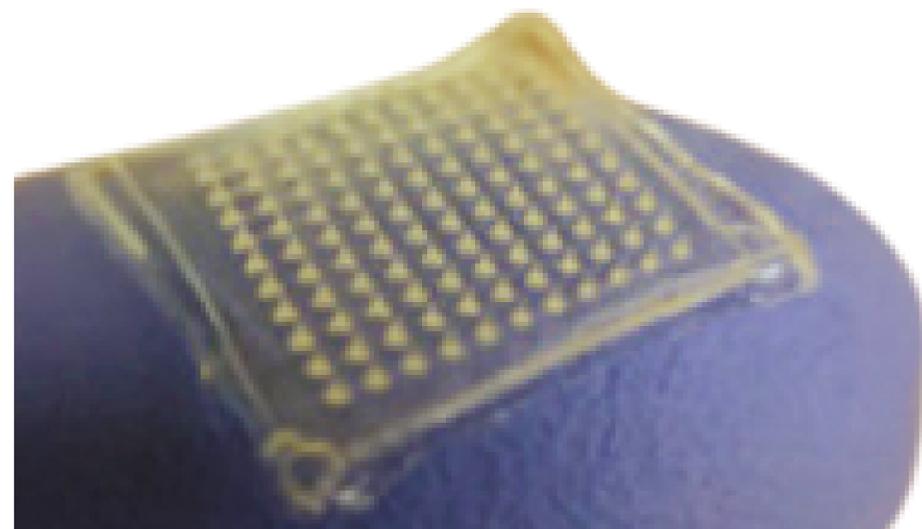
Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Status
Anesthesia & Sedation	[Dark Blue bar spanning Pre-clinical, Phase 1, Phase 2, and Phase 3]				<ul style="list-style-type: none"> FDA application review
Parkinson's Disease	[Dark Blue bar spanning Pre-clinical and Phase 1; Light Blue bar spanning Phase 2]				<ul style="list-style-type: none"> Preparing for Phase 3 study
Rett Syndrome	[Dark Blue bar spanning Pre-clinical and Phase 1; Light Blue bar spanning Phase 2]				<ul style="list-style-type: none"> Granted FDA Orphan Status Awaiting for Phase 2 top-line results
Amyotrophic Lateral Sclerosis	[Dark Blue bar spanning Pre-clinical and Phase 1; Light Blue bar spanning Phase 2]				<ul style="list-style-type: none"> Granted FDA Orphan Status FDA IND accepted for Phase 1/2
Complex Regional Pain Syndrome	[Dark Blue bar spanning Pre-clinical and Phase 1; Light Blue bar spanning Phase 2]				<ul style="list-style-type: none"> Ready for Phase 2
Depression	[Dark Blue bar spanning Pre-clinical; Light Blue bar spanning Phase 1 and Phase 2]				<ul style="list-style-type: none"> Evaluation of Preclinical studies



PharmaPATCH

Delivering Psychedelics, Stem Cells and Gene Therapy

- Pain-free, easy administration, improves compliance
- Use in clinics, hospitals, and home
- Tamper-proof potential to avoid patient misuse, abuse, and diversion



Microneedle patch

Validating Studies

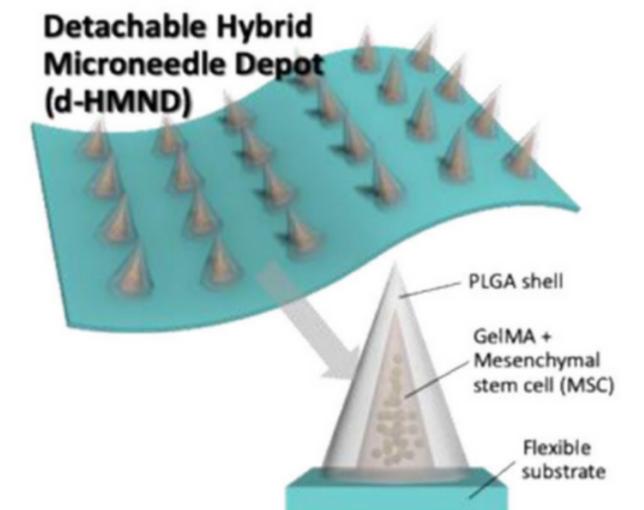
Advanced functional materials

Author Manuscript

HHS Public Access

A Patch of Detachable Hybrid Microneedle Depot for Localized Delivery of Mesenchymal Stem Cells in Regeneration Therapy

KangJu Lee, Yumeng Xue, [...], and Ali Khademhosseini



Nanoscale



COMMUNICATION

View Article Online
View Journal

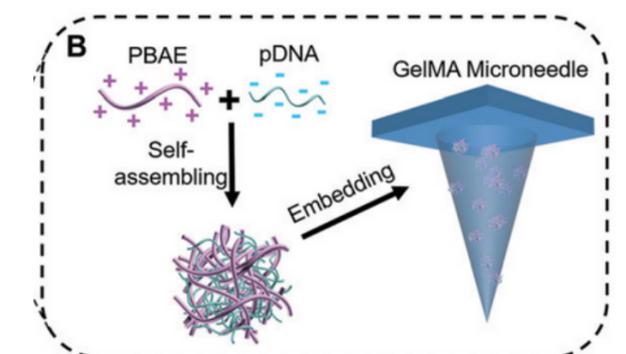
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Biodegradable microneedle patch for transdermal gene delivery†

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PharmaPATCH Pipeline

Drug	Purpose	Pre-clinical	Phase 1	Phase 2	Phase 3	Status
Ketamine	MCMs					<ul style="list-style-type: none"> • Manufacturing scale up and prep regulatory submission for Phase 2 study
Psilocybin	TBD					<ul style="list-style-type: none"> • Scale up ready for clinical trial
MDMA	TBD					<ul style="list-style-type: none"> • Scale up ready for clinical trial
DMT	TBD					<ul style="list-style-type: none"> • Scale up ready for clinical trial
LSD	TBD					<ul style="list-style-type: none"> • Scale up ready for clinical trial
PP-010	Gene Delivery					<ul style="list-style-type: none"> • Preclinical research
PP-020	Stem Cells					<ul style="list-style-type: none"> • Preclinical research



Investment: Sairiyo Therapeutics Inc.

PharmaTher owns 49% with potential to own up to 90%

- Developing patented Enteric-coated Cepharranthine (CEP-001)
- Cepharranthine with 70 years of safety and efficacy
- Approved in Japan for antivenom, hair loss and malaria
- Mode of action:** Antiviral, anti-inflammatory, anti-oxidative, immunoregulatory, antitumor, anti-pathogen, and antinociceptive activities
- Potential indications:** Medical countermeasures (COVID-19, biotreats) cancers, and inflammatory disorders



Problem: Low bioavailability (~6%) limiting its potential

CEP-001: Enteric Coated Cepharanthine

Advancing a reformulated version of Cepharanthine

- Granted U.S. Patent No. 10,576,077 (Expires 2036)
- U.S. Defence invested +\$3.5 million for Ebola

~10X improved bioavailability

Generic Version



~ 6% bioavailability

CEP-001



~ 70% bioavailability

Research in COVID & Cancer

ADVANCED BIOLOGY

Perspective | Free Access

Cepharanthine: A Promising Old Drug against SARS-CoV-2

Huahao Fan, Shi-ting He, Pengjun Han, Bixia Hong, Ke Liu, Maochen Li, Shuqi Wang, Yigang Tong

First published: 01 July 2022 | <https://doi.org/10.1002/adbi.202200148> | Citations: 5

SECTIONS

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Abstract

Recently, the inhibiting effects of a clinically approved drug Cepharanthine on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have attracted widespread attention and discussion. However, the public does not understand the relevant research progress very well. This paper aims to introduce a brief history of studies on the effects of cepharanthine against SARS-CoV-2, including "discovery of anti-SARS-CoV-2 activity of cepharanthine in vitro", "potential mechanisms of cepharanthine against SARS-CoV-2", "confirmation of cepharanthine's anti-SARS-CoV-2 activity in vivo", "potential approaches for improving the druggability of cepharanthine" and "clinical trials of cepharanthine treating SARS-CoV-2 infection". Taken together, cepharanthine is believed to be a promising old drug for coronavirus disease-19 (COVID-19) therapy.



Biomedicine & Pharmacotherapy

Volume 165, September 2023, 115107



Review

A mechanistic updated overview on Cepharanthine as potential anticancer agent

Abstract

The antitumor effects of traditional drugs have received increasing attention and active antitumor components extracted from traditional drugs have shown good efficacy with minimal adverse events. Cepharanthine (CEP for short) is an active component derived from the *Stephania* plants of Menispermaceae, which can regulate multiple signaling pathways alone or in combination with other therapeutic drugs to inhibit tumor cell proliferation, induce apoptosis, regulate autophagy, and inhibit angiogenesis, thereby inhibiting tumor progression. Therefore, we retrieved studies concerning CEP's antitumor effects in recent years and summarized the antitumor mechanism and targets, in order to gain new insights and establish a theoretical basis for further development and application of CEP.

Expected Milestones in 2024

- ◆ Q2: Initiate Phase 1/2 Clinical study
- ◆ Q4: Top-line results of Phase 1/2 study

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Regulatory and Patent Portfolio

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Ketamine

- Amyotrophic lateral sclerosis
- Rett Syndrome
- Complex Regional Pain Syndrome
- Ischemia-Reperfusion Injury
- Status Epilepticus (Seizures)

Cepharanthine

- Esophageal Cancer

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Granted Patents, PCTs, Provisional Patents

Delivery

Microneedle patch and hydrogel composites for drugs/APIs
Enteric coated

Method

Compositions and methods for ketamine in Parkinson's Disease, Amyotrophic lateral sclerosis, Rett Syndrome

Formulation

Enteric-coated oral dosage

Strategic Partners



KETARX™

USA Commercialization



KETARX™

Development and
Manufacturing



**Psychedelics, Stem Cells,
Gene Therapy**

PharmaPATCH Development
and Manufacturing



Cepharanthine

49% ownership with
potential to own upto 90%



Ketamine

Rett Syndrome



Ketamine

Amyotrophic Lateral Sclerosis



Ketamine

Parkinson's Disease



Ketamine

Microneedle Patch Research



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Management Team and Board



Fabio Chianelli

Founder, Chairman, CEO

- Founder, CEO, President at Revive Therapeutics Ltd.



Carmelo Marrelli

Chief Financial Officer

- CFO of TSX, CSE, OTCQB listed companies



Dr. Owen Van Cauwenberghe

VP, Pharmaceutical Development

- Director, Research, Eli Lilly CAD
- Director, Pharma R&D, Accucaps



Dr. Bev Incledon

Director

- CSO, Ironshore Pharma
- 25 years drug development



Christian Scovenna

Director

- Entrepreneur and investor

Carlo Sansalone

Director

- Investor, Biotech, and Real estate

Financial Snapshot

PHRRF
OTCQB



88,169,065

Issued & Outstanding Common Shares

~ 19%

Insiders Ownership

5,749,000

Stock options outstanding

16,875,000

Warrants outstanding

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



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THANK YOU

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