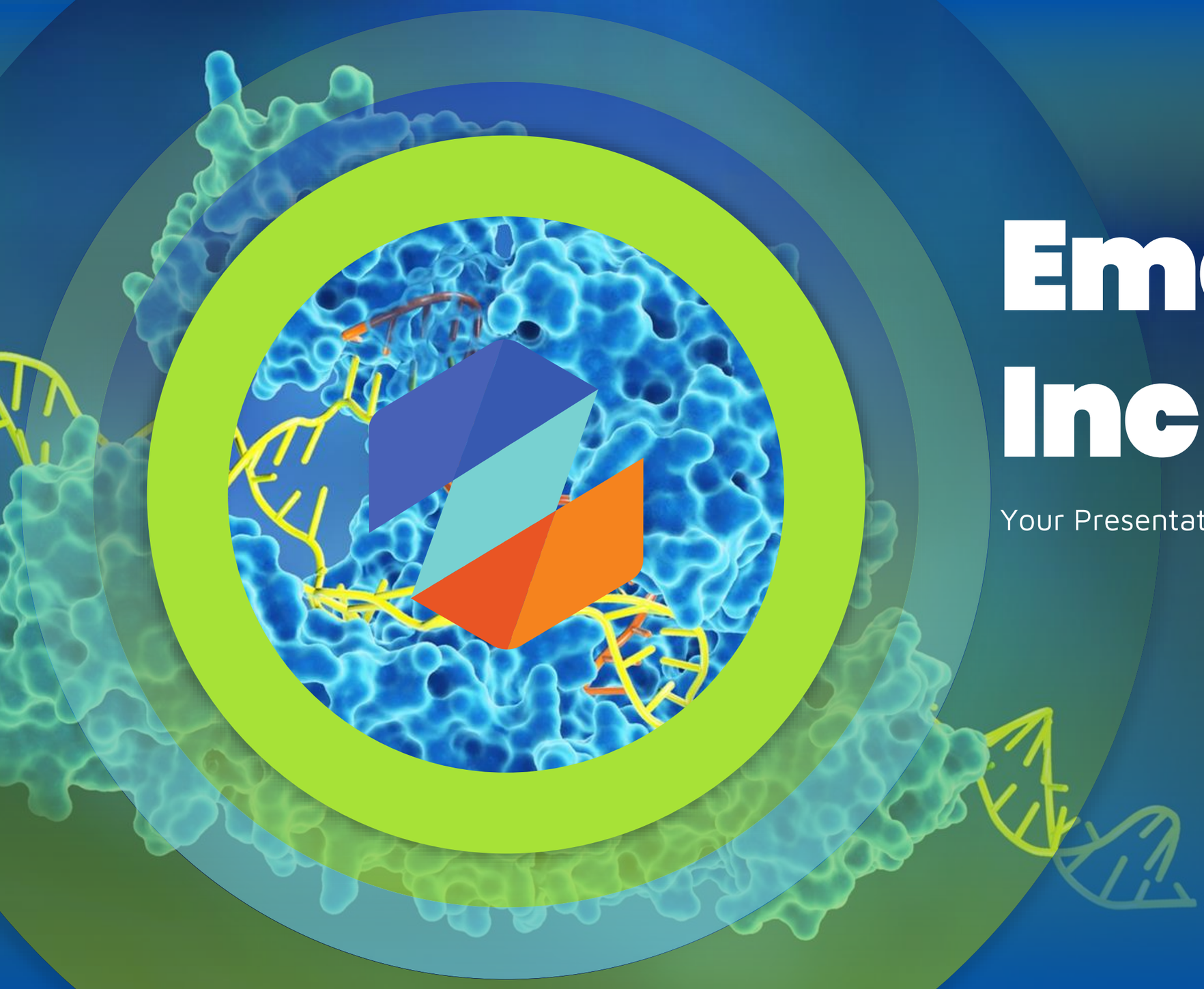


Emerzene Inc

Your Presentation Start Here

OUR MISSION

Optimal pain relief without addiction risk.

Today's pain therapy comes with a tremendous burden..

Opiate Use & Abuse could not be separated

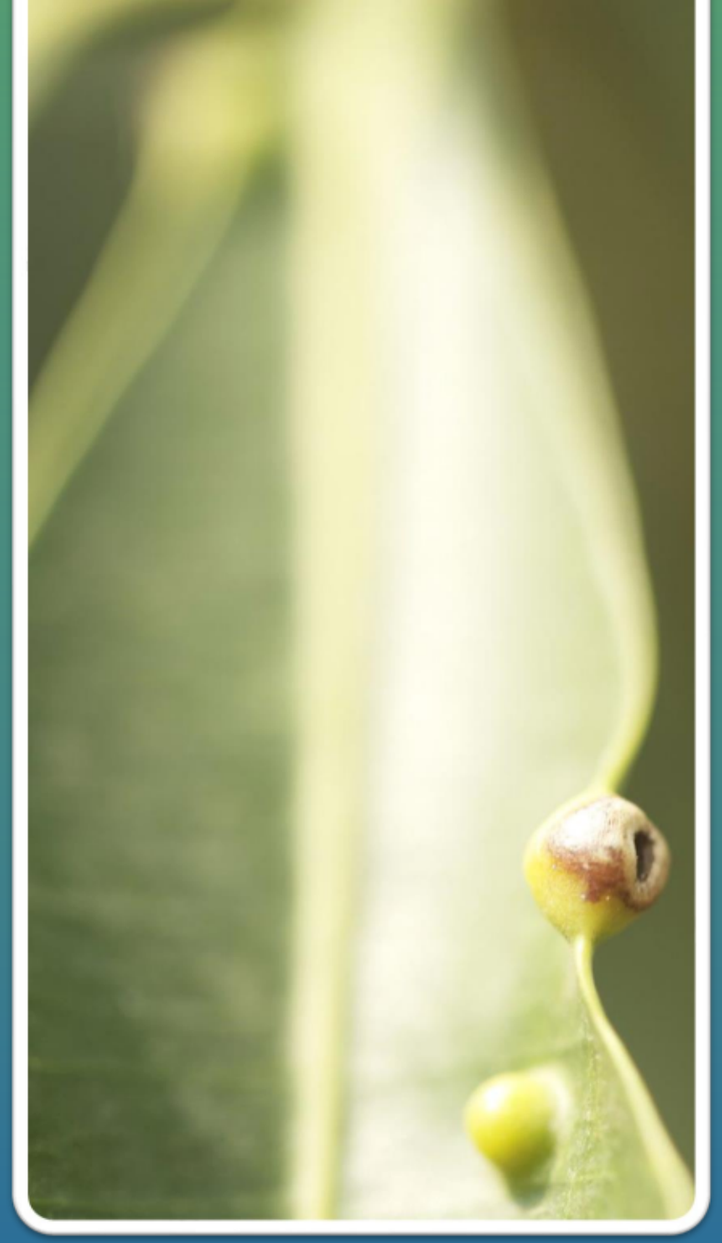
International Narcotics Control Board 2021 press release "3/4 of world population has limited or no access to pain relief medication". Major problem in many low-income countries where affordability is low.

CDC of the United States estimated 100,306 drug overdose deaths during the 12-month period ending in April 2021, an increase of 28.5 per cent over the year before.

Most overdose deaths involved synthetic opioids, primarily illicitly manufactured fentanyl and methamphetamine.

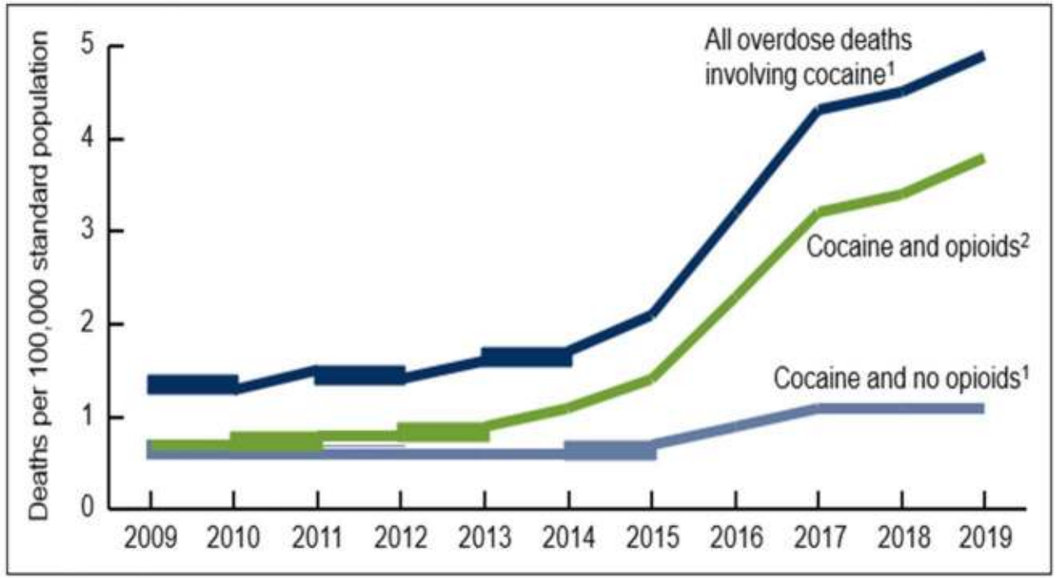
Worldwide, about 0.5 million deaths are attributable to drug use. More than 70% of these deaths are related to opioids. (World Health Organization, August 2021).

Opioids affect the parts of the brain that control breathing – a condition known as Opioid Induced Respiratory Depression (OIRD)



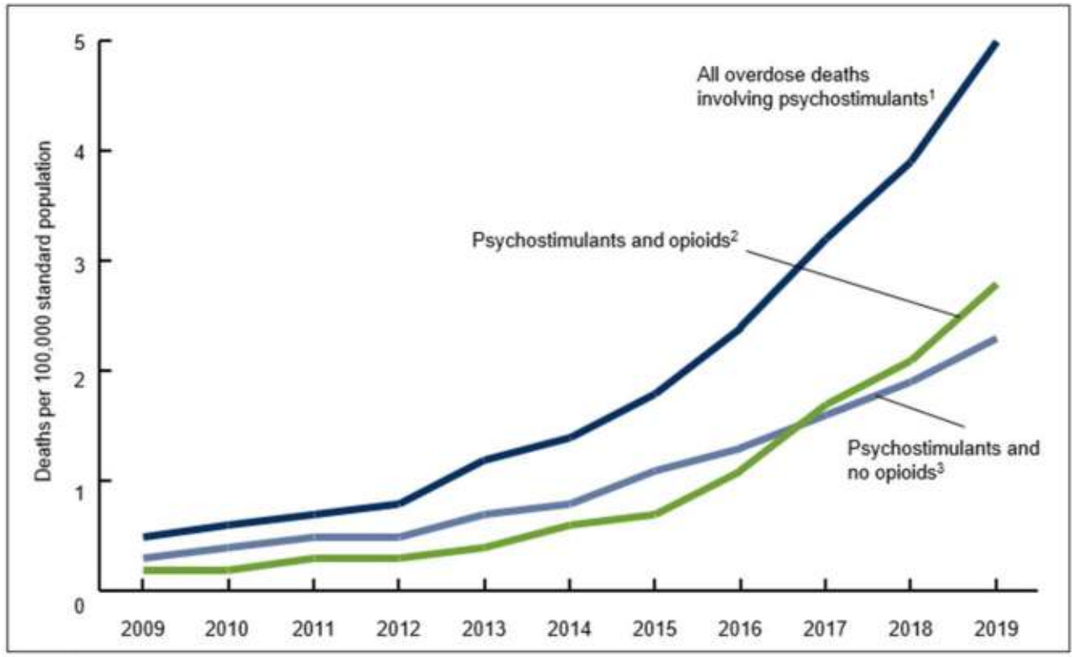
Current Pain relief options seems like a nightmare

Age-adjusted rates of overdose deaths - cocaine & other opioids: United States, 2009–2019



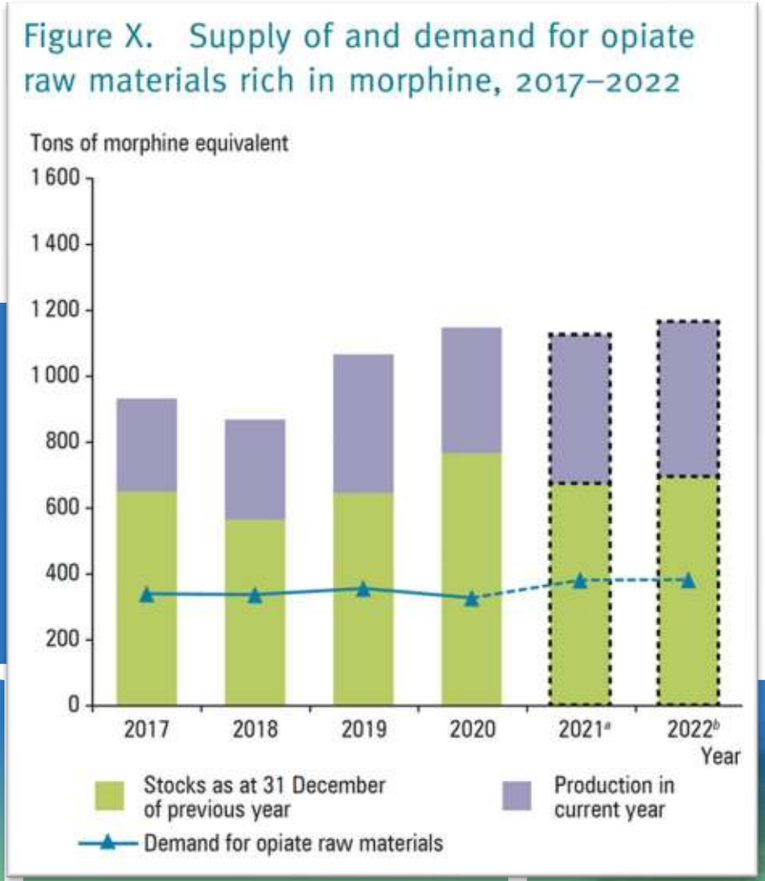
Access data table for Figure 1 at: https://www.cdc.gov/nchs/data/databriefs/db406-tables-508.pdf#1.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

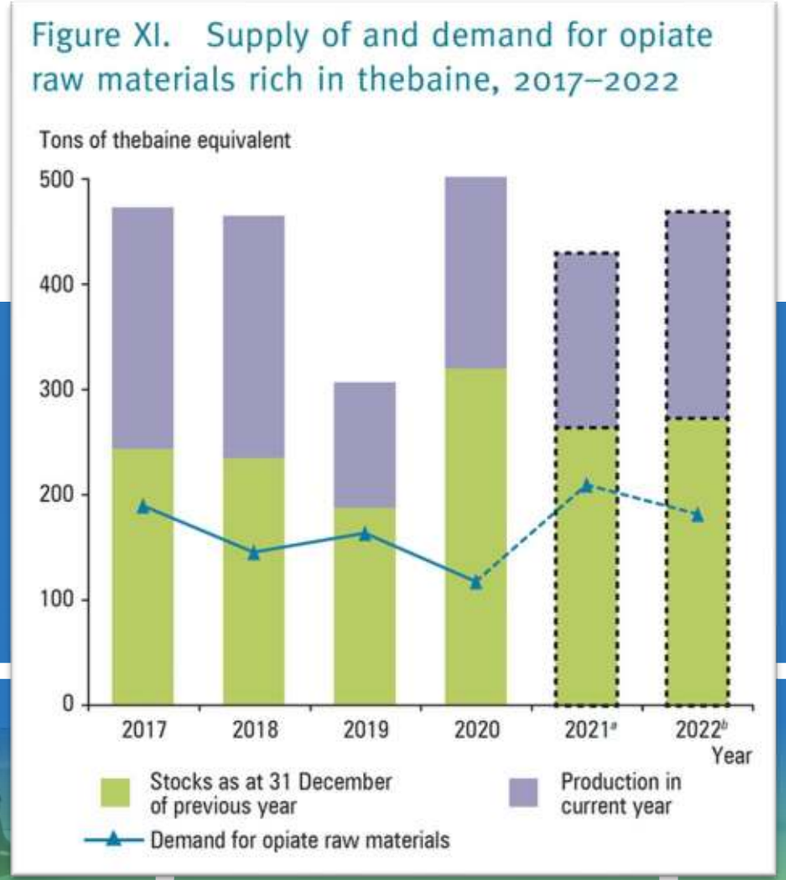
Rate of overdose deaths involving psychostimulants, by concurrent involvement of opioids: United States, 2009–2019



SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

Without alternatives, supply & demand for morphine and thebaine are sky high





Our Solution

Pain relief without addiction risk

- World's first patented Papaver related genetics
- Strains high in minor alkaloids – Noscapine, Etorphine
- Improved Agronomy methods and crop physiology aspects documented through doctoral studies
- Perennial variety - Prolific flowering in the first year
- High disease resistance to Downy Mildew
- Excellent Crop establishment methods have been designed
- Patented unique extraction process without solvents.
- High yield variety with 5-6 capsules per plant
- Create a safe & organic alternative to the synthetic opioid crisis

Agronomic adv. of our variety

Species	Papaver bracteatum	Papaver somniferum
Growing cycle	Perennial, Multiple crops with one planting.	Annual. Need to replant every year. Labor and cost intensive
Yield & Disease resistance	4-5 capsules per plant. Six times the yield of traditional somniferum. Highly resistant to DM	One capsule per plant. Highly susceptible to DM, PM, Stem & Capsule rot, Damping off.
Opiates derived	Complete absence of Morphine Pathway. Thebaine, Noscapine, Oripavine	Morphine, Codeine
Demethylation of the enol ether	Blockage of this process results in no morphine	Presence of Morphine, easily convertible to illicit drugs
Receptor activity leading to addiction	Thebaine acts on κ and δ receptors	Morphine acts on μ

Economics of P. bracteatum

Revenue Streams[1]

- Opiates for treating Cancer, anti-tussive
- Seeds used in food industry (cakes)

Robust Growth

- Drought tolerant
- Cold tolerant
- Natural disease resistance

Excellent Cover Crop

- Perennial crop, no operating cost
- Improved soil health & nutrient runoff management

Carbon Savings

- Attractive carbon profile
- Cover crop during winter, also additional carbon sequestration with zero tillage

Scalability

- Small acreage today
- Little to no land usage costs during second year and less fertilizer inputs

Improvement Potential

- Little history of selective breeding/gene editing
- Enhanced seed viability and vigor. 5-6 capsules per plant

Genetic Engineering

- Founder – proprietary oil & yield trait targets
- Readily segregated from traditional poppy with wide spectrum of opiates

Economics

- Highly valuable (minor opiates)
- Huge upside potential & attracts honeybees for pollination

Compelling Proof-of-Concept

- Gene Silencing of the enzymes responsible for the biosynthesis of Thebaine to Morphine at specific growth stages.
- Vernalization requirement and effect of Phyto-hormones to induce flowering.
- Breaking Seed dormancy and optimal germination requirements.
- Altering the TyDC/DODC genes responsible for DAHP Synthase, 3-Dehydroquinate Synthase, 3-Dehydroquinate Synthase-Shikimate Dehydrogenase, Shikimate Kinase, 5-Enoylpyruvylshikimate-3-Phosphate (ESPS) Synthase.
- O3- and O6-demethylation reactions are catalyzed by Fe (II)/α-ketoglutarate-dependent dioxygenase, previous hypothesis was that an enzyme would be responsible for demethylation steps (NIH Grant work in Submission)
- Production of morphinan alkaloids is associated with cell differentiation and morphogenetic processes. Alkaloid synthesis is dependent on the presence of laticifers (NIH Grant work – Research in progress).

First-Generation Programs

01

Altering the expression of 7-O-methyltransferase (7OMT) and 3′-hydroxyl-N-methylcoclaurine 4′-O-methyltransferase (4′OMT2) genes in different tissues.

02

Manipulating genes responsible for the epimerization of (S)-reticuline to (R)-reticuline and the conversion of (S)-reticuline to (S)-scoulerine.

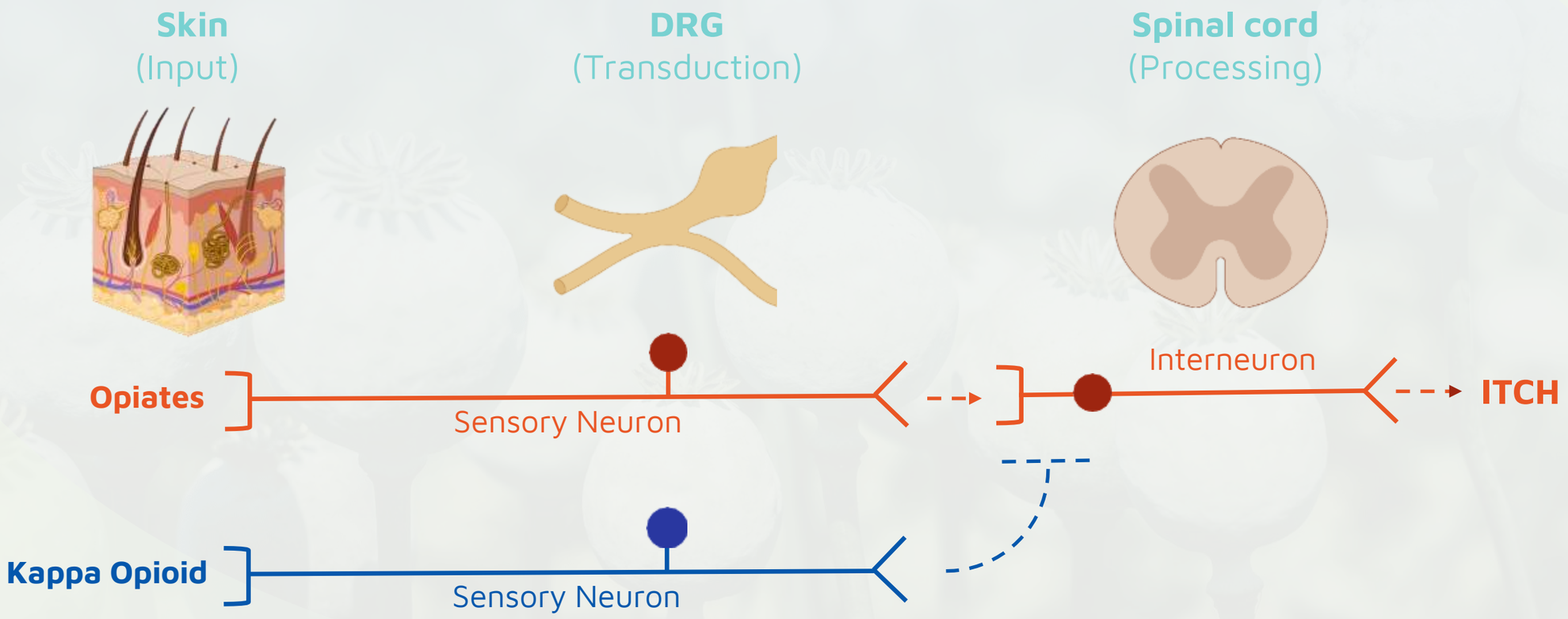
03

Presence of DNA sequences to orient correctly and dimerize with the provided spacer length. Application of CRISPR/Cas9 system helps without requiring protein dimerization.

04

Post transcriptional TRV-mediated gene silencing in a tissue specific manner to control the amount of alkaloid biosynthesis.

Thebaine is a partial opioid agonist, it has a much lower potential for dependence and misuse than pure agonists like heroin or morphine



Kardon et al. *Neuron* 2014
Snyder et al. *Neuron* 2019

CRISPR/CAS9 Gene Editing Platform

MILLIPORE SIGMA (DIV. OF MERCK)

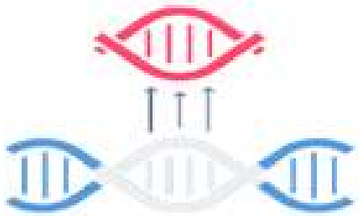
Gene Correction

Correct point mutations or short DNA stretches in endogenous locus

Disrupt

Gene Replacement

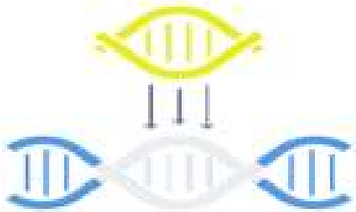
Replace gene driven by own promoter



Delete

Target Gene Insertion

Knock-in promoter gene expression cassette info safe harbor location



Correct or Insert

POWER OF CRISPR

Nobel-Prize Winning Genome Editing Technology

- Precise and modular approach for editing the genome
- Discovery of potential new pathogen resistant strains & Improving quality
- Locates a genetic sequences To make a permanent change
- Overcomes key challenges associated with traditional plant breeding methods
- High level of specificity to make one or multiple edits
- Provide foundation capabilities for derivative tools

History & Partners

01 **2011** – Dr Raj Madam Graduated from University Tasmania. Ph.D in Genetics.

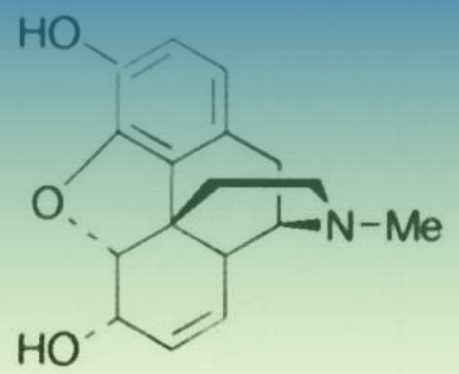
02 **2016 – 2019** Our first R&D license from Agriculture Victoria making us the third company in Australia to hold a cultivation license. Pilot crop grown in Melbourne, Australia.

03 **2019 – 2022** Renewal of our license and focused on R&D of gene editing. Innovation Patents issued in 2020.

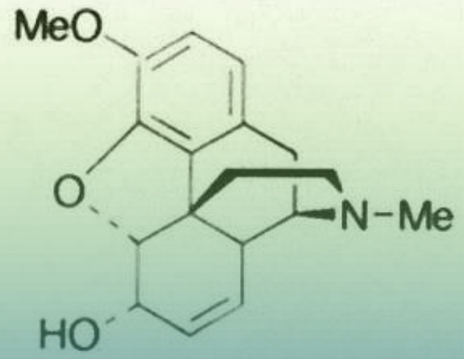
04 **2022 – 2025** Renewal of our license for the third time – Focus on CRISPR enhancements. Licensing with Merck – Germany in final stages

05 **2022** – Partnerships with Phytal (Netherlands), ICON PLC (London)& Millipore Sigma (Merck Germany).

OUR SEED INVENTORY



Morphine



Codeine

01 **Thebaine:**

Ideal starting material for many pain-relieving and abuse deterrent Active Pharmaceutical Ingredients.

02 **Papaverine:**

Industry produces synthetically, we have access to organic plant-based API's.

03 **Oripavine:**

Alkaloid raw material widely used to produce (API's) such as Naloxone and Naltrexone.

04 **Noscapine:**

Has Anti-cancer properties.

GLOBAL SUPPLIERS WITH LICENSE

Sunpharma	Recently acquired GSK's opiate business
Tasmanian Alkaloids	Owned by Johnson and Johnson
TMO	Turkeys Opiates Board (TMO) is a state owned enterprise that manufacture manly Thebaine & Moprhine for the US Market
G.O.A.F	Unlike other NRM manufacturers, India's Government Opium and Alkaloid Factories (GOAF) exports morphine in the form of opium
Alcaliber	Spanish company founded in 1973. Processing based on cultivation in Spain with ~80% of production destined for export. Maintains a global market share of approximately 15%
Francopia	Owned by Sanofi
Macfarlan Smith	Owned by Johnson Matthey
Emerzene	Owned by Dr. Raj Madam, 1st and foremost plant based organic manufacturer

API Development

Natural Narcotics | Synthetic and semi-synthetic narcotic derivatives

Agricultural Production	Narcotic Raw Material (NRM)	Active Pharmaceutical ingredient (API)	Final Dosage Formulation (FDF)
			
API	Morphine Codeine	Morphine Sulphate Codeine phosphate	MS Contin Panadeine Panadeine Forte
	Thebaine	Oxycodone HCl Hydrocodone Buprenorphine	Oxycontin Vicodin Endone Tylenol
	Oripavine	Naloxone Naltrexone Buprenorphine HCl	Suboxone Subutex Narcan

OUR VALUE PROPOSITION

Financial Snapshot

- **2021 Global Thebaine Market**
  - Traditional Thebaine API production ranges from 30 to 35 kilograms for every 1 to 2 tons of biomass
  - Our Proprietary genetics yield 120-135 milligrams per capsule of Opiate.

- **Emerzene's current inventory**
  - 4 tons of Thebaine rich plant biomass from 2018 and 2019 harvest
  - 1,000 acres of commercially available Thebaine seed
    - Our proprietary Thebaine varietals yield on average 2 tons of biomass per acre
      - 1 ton of biomass produces 50-55 kilograms of Thebaine API

REGULATORY LICENSES FROM AGRICULTURE VICTORIA, AUSTRALIA

OFFICIAL: Sensitive

Agriculture Victoria

Department of Jobs, Precincts and Regions

402 Mair Street
Ballarat, Victoria 3350 Australia
Telephone: +61 3 5336 6844

Reference: Case 082

Dr Phani Raja Kumar Madam
Poppy Genetix Pty Ltd
2/8 Hirst Street
BLACKBURN VIC 3130

Dear Raj,

ALKALOID POPPIES: LICENCE TO CULTIVATE FOR NON-THERAPEUTIC (RESEARCH) USE

I refer to your application received 24 April 2022 seeking a renewal to a licence to cultivate alkaloid poppies for non-therapeutic (research) purposes on a property at 993 Sunny Creek Road, Childers Victoria.

This is to advise that your application has been approved. The licence is enclosed for your records.

The licence-

- expires on 5 June 2025. Should you wish for this licence to continue, an application to renew a licence must be received at least 2 months prior to the date of expiry; and
- applies to the cultivation of alkaloid poppies, on a property at the above address, for non-therapeutic (research) purposes only.

You are reminded that-

- the *Drugs, Poisons and Controlled Substances Act 1981* provides for severe penalties for breaches of a licence condition; and
- the licence may be suspended or cancelled if there is a failure to comply with a licence condition.

You will be sent an invoice for the renewal fee ($589.90) separately. Additionally, upon granting of this licence, and in any given year when alkaloid poppies are cultivated, you will receive an invoice for the annual administration fee. In 2021/22 this fee is $881.40 (GST free).

If you have any concerns or queries, please contact me by telephone 0437 568 091 or by email shane.herbertson@agriculture.vic.gov.au

Australian Government

IP Australia

CERTIFICATE OF GRANT

INNOVATION PATENT

Patent number: 2020101437

The Commissioner of Patents has granted the above patent on 12 August 2020, and certifies that the below particulars have been registered in the Register of Patents.

Name and address of patentee(s):

PHANI RAJA KUMAR MADAM of Blackburn, U 2 8 Hirst St Blackburn VIC 3130 Australia

Title of invention:

REQUIREMENT OF VERNALIZATION TO INDUCE FLOWERING IN NON-ADDICTIVE STRAIN OF PAPAVER BRACTEATUM

Name of inventor(s):

MADAM, PHANI RAJA KUMAR

Term of Patent:

Eight years from 22 July 2020

NOTE: This Innovation Patent cannot be enforced unless and until it has been examined by the Commissioner of Patents and a Certificate of Examination has been issued. See sections 120(1A) and 129A of the Patents Act 1990, set out on the reverse of this document.

Industry Leading Extraction Process

Melbourne & Liechtenstein

EMERZENE TEAM ACROSS THE GLOBE

Dr Raj Madam
Founder & CEO

- Founder of Tulip Sciences, Innovative Natural Sciences
- 15 years experience in Life sciences, Gene editing, Organics and Sustainable agriculture
- PhD in Genetics, Molecular Biology, University of Tasmania, Australia
- Fermentation Biology, MIT

Dr Mary Cole
Chief Scientific Advisor

- 45+ years experience in Plant pathology, microbiology, soil health & sustainability
- Founder of Ag path, Melbourne Australia
- Honorary Professor University of Melbourne & PhD from Monash University
- Founding Director of Wine Food & Agribusiness

Douglas Brien
VP Operations Australia

- 30+ years experience in finance and accounting; Principal Accounting Officer and acting CFO at Poppy Genetix Australia

Thank You