Hope
Science
Life

NASDAQ: **NRXP**

NRx Pharmaceuticals
October 2025

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NRx (Nasdaq:NRXP) – A microcap company expecting 2025 Revenue

Suicidal Depression

2025 Filing

NRX-100
(IV Ketamine)

- **NDA filing H2 2025**
- **FDA Fast Track** granted for treatment of suicidal depression August 2025
- Patented preservative-free presentation
- $4.3 million filing fee waiver granted by FDA
  Expected PDUFA in 2025
- Application for Commissioner's National Priority Voucher
- Efficacy data from four studies and Real World Data from 180,000
- **$2+ billion addressable market**

Bipolar Depression

2026 Filing

NRX-101
(Oral DCS/Lurasidone)

- **Breakthrough Therapy** designation granted
- Only oral antidepressant to decrease suicidality and/or akathisia in clinical trials
- NDA/Accelerated Approval for bipolar patients with akathisia; **est. PDUFA 2025**
- ~600,000 patient initial addressable market
- Potential use to augment Transcranial Magnetic Stimulation
- > **$2+ billion addressable market**

Interventional Psychiatry

2025 Revenue

HOPE Therapeutics

- **First 9 clinics Q4 2025**
- Rollup of profitable interventional psychiatry clinics with 2025 profit
- Focus on combining neuroplastic drugs with TMS and Hyperbaric Oxygen
- Acquisition finance from commercial banks and strategic investor

NRx (Nasdaq:NRXP) – New Developments with Revenue Implications

Suicidal Depression

Filed 2025

KETAFREE™
(IV Ketamine)

- **ANDA under review**
- Distinct formulation from NRX-100
- Patented preservative-free presentation
- Citizens Petition to remove Benzethonium Chloride from IV ketamine
- US-based manufacture
- Innovative, diversion-resistant packaging
- **$750 million current generic market with chronic drug shortage**

PTSD

IND in progress

NRX-100
(IV Ketamine for PTSD)

- **IND in progress**
- IV ketamine now shown to reduce CAPS-5 score in PTSD in addition to treating depression and suicidality
- Real World Data in 8,000 patients confirm earlier clinical trials data
- **12 million Americans have PTSD with no approved drug**
- **Secretary of Veterans Affairs has stated that Veteran Suicide is Priority Number 1**

Depression and PTSD

IND in progress

NRX-102
(Extended Release DCS)

- **New finding that low-dose DCS doubles the effect of Theta-burst TMS**
- DCS has potent neuroplastic effects that are synergistic with TMS
- Breakthrough Therapy Designation planned
- NRx has 10 years of expertise in unique challenges of manufacturing DCS drug ingredient and formulating for human use
- > **$1+ billion addressable market**

Suicide is a National Crisis

Suicide kills >50,000 Americans every year
Disproportionately affecting people with Bipolar Disorder

Over
49,000
people died by suicide in 2022

1 death every **11** minutes

Many adults think about suicide or attempt suicide

13.2 million
Seriously thought about suicide

3.8 million
Made a plan for suicide

1.6 million
Attempted suicide

Suicide takes our best and brightest

https://www.cdc.gov/suicide/facts/index.html#:~:text=In%202021%2C%20an%20estimated%2012.3,and%201.7%20million%20attempted%20suicide.&text=Suicide%20affects%20people%20of%20all%20ages.

For the first time, we are starting to understand Suicidality

In our lifetimes, we have seen breakthroughs in cancer, heart disease and many other lethal conditions

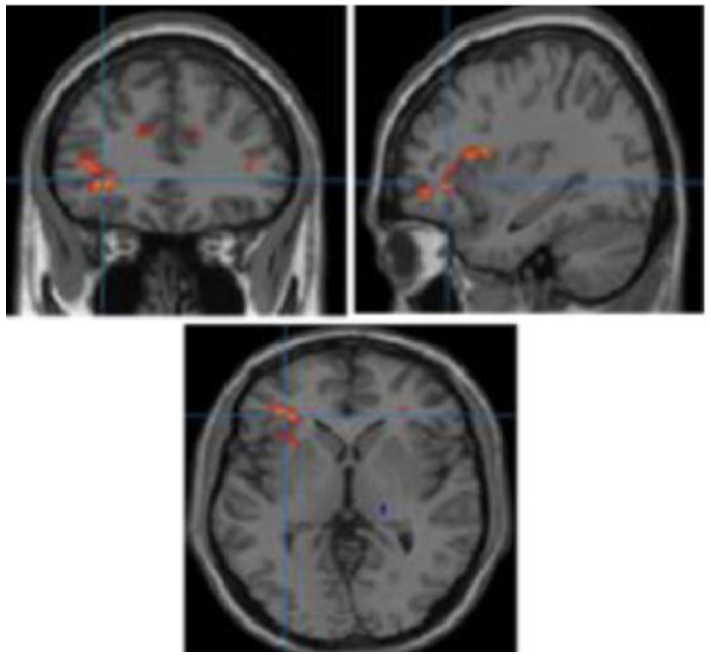
We have also seen a rise in suicidal depression and PTSD

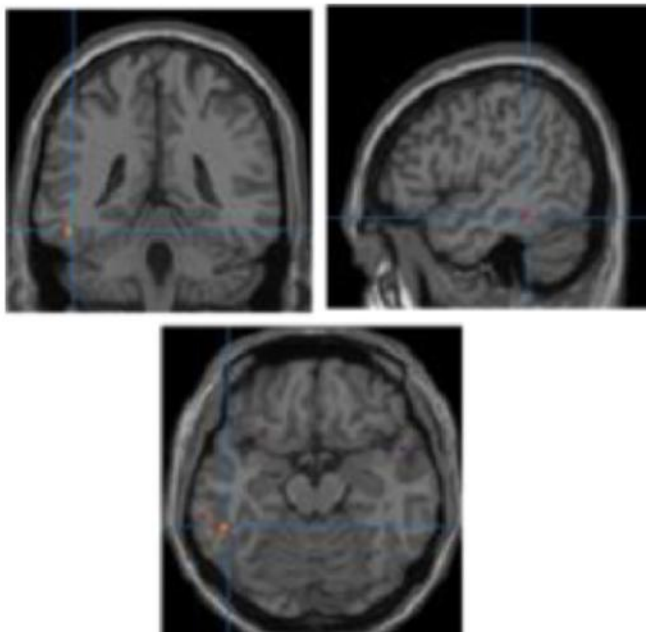
In the last 15 years, science is unlocking the key to Suicide

- Suicidal Depression is a “short circuit” in the brain that we can treat
- We have identified the receptor in the brain (NMDA) and recognized that NMDA antagonist drugs create new connections (neuroplasticity)
- Ketamine and other drugs target this receptor and achieve a 50% or higher clinical response rate
- Transcranial Magnetic Stimulation (TMS) also targets the brain pathways driving suicide and achieve a similar response rate
- Only through combining neuroplastic drugs with other neuroplastic treatments – TMS, Hyperbaric Oxygen, and future treatments can you create a durable and sustainable path to recovery
- We are building the first national network of interventional psychiatry clinics to deliver these treatments in a scalable and sustainable business model

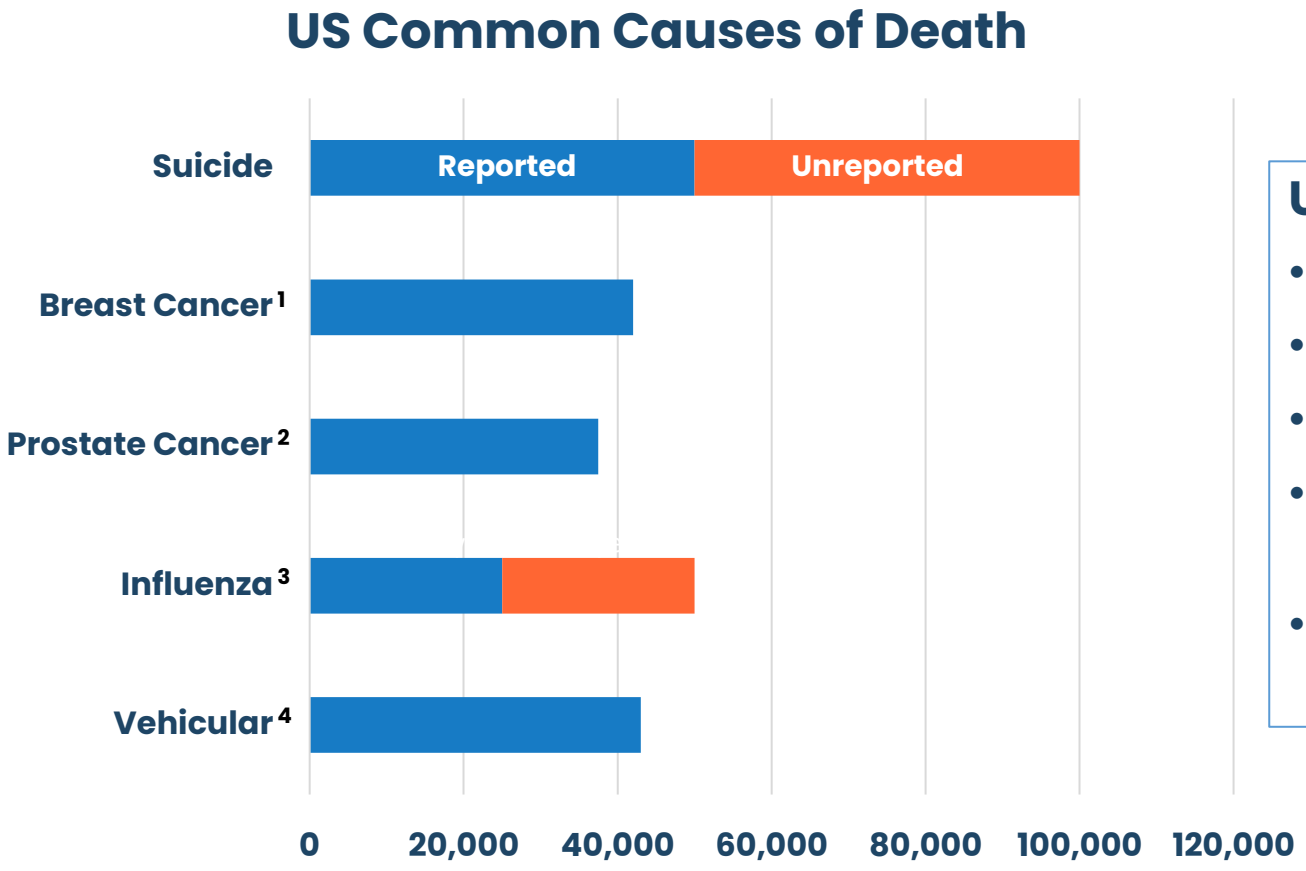
Functional Magnetic Resonance Imaging (FMRI)

FMRI in Suicidal Ideation vs. Normal





Suicide is the only major cause of death not to bend the curve



Unlike other common causes of death, suicide

- *Is allocated minimal research funding*
- *Has no approved drugs*
- *Carries enormous social stigma*
- *Can result in incarceration, involuntary treatment with debilitating therapy*
- *Is frequently treated as a psychological, rather than biological disease*

1. https://www.cdc.gov/cancer/breast/basic_info....
2. https://www.cancer.org/cancer/types/prostate-cancer/about/...
3. https://www.cancer.org/cancer/types/prostate-cancer/about/key-statistics.html#:~:text=The%20American%20Cancer%20Society's%20estimates,34%2C700%20deaths%20from%20prostate%20cancer
4. https://www.statista.com/statistics/1124915/flu-deaths-number-us/

125 Drugs for Depression and They All Cause Suicide

For 70 years, we have been looking at the wrong neurochemical pathway (serotonin)

- **No approved drug is shown to decrease suicidal ideation, although esketamine reduces depression in patients with suicidal ideation**
- **Every antidepressant carries a Boxed Warning label against suicide (except esketamine)**
- **All drugs that raise brain serotonin levels cause akathisia, which is closely linked to suicide**

There is now overwhelming evidence that:

- ***NMDA antagonist drugs rapidly reduce suicidal ideation***
- ***Neuroplastic drugs lead to long term remission***

https://www.madinamerica.com/2023/11/the-lie-that-antidepressants-protect-against-suicide-is-deadly/

All Antidepressants Carry Black-Box Warnings for Suicidality and Akathisia

no antidepressant has ever improved either side effect

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LATUDA safely and effectively. See full prescribing information for LATUDA.

LATUDA (lurasidone hydrochloride) tablets, for oral use
Initial U.S. Approval: 2010

WARNINGS:
INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS; AND SUICIDAL THOUGHTS AND BEHAVIORS
See full prescribing information for complete boxed warning.

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.**
- **LATUDA is not approved for the treatment of patients with dementia-related psychosis (5.1).**
- **Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants (5.2)**
- **Monitor for worsening and emergence of suicidal thoughts and behaviors (5.2)**

----------**RECENT MAJOR CHANGES**----------

Boxed Warnings, Suicidal Thoughts and Behaviors (5.2)	m/20xx
Indications and Usage, Bipolar Depression (1.2)	m/20xx
Dosage and Administration, Bipolar Depression (2.1)	m/20xx
Warnings and Precautions (5.2, 5.6, 5.7, 5.9, 5.10, 5.11, 5.13, 5.14)	m/20xx

Akathisia occurs in up to 15% of patients on antidepressants

Akathisia is the side effect of antidepressants most closely linked to suicide

The New York Times

By Roni Caryn Rabin

Sept. 11, 2017

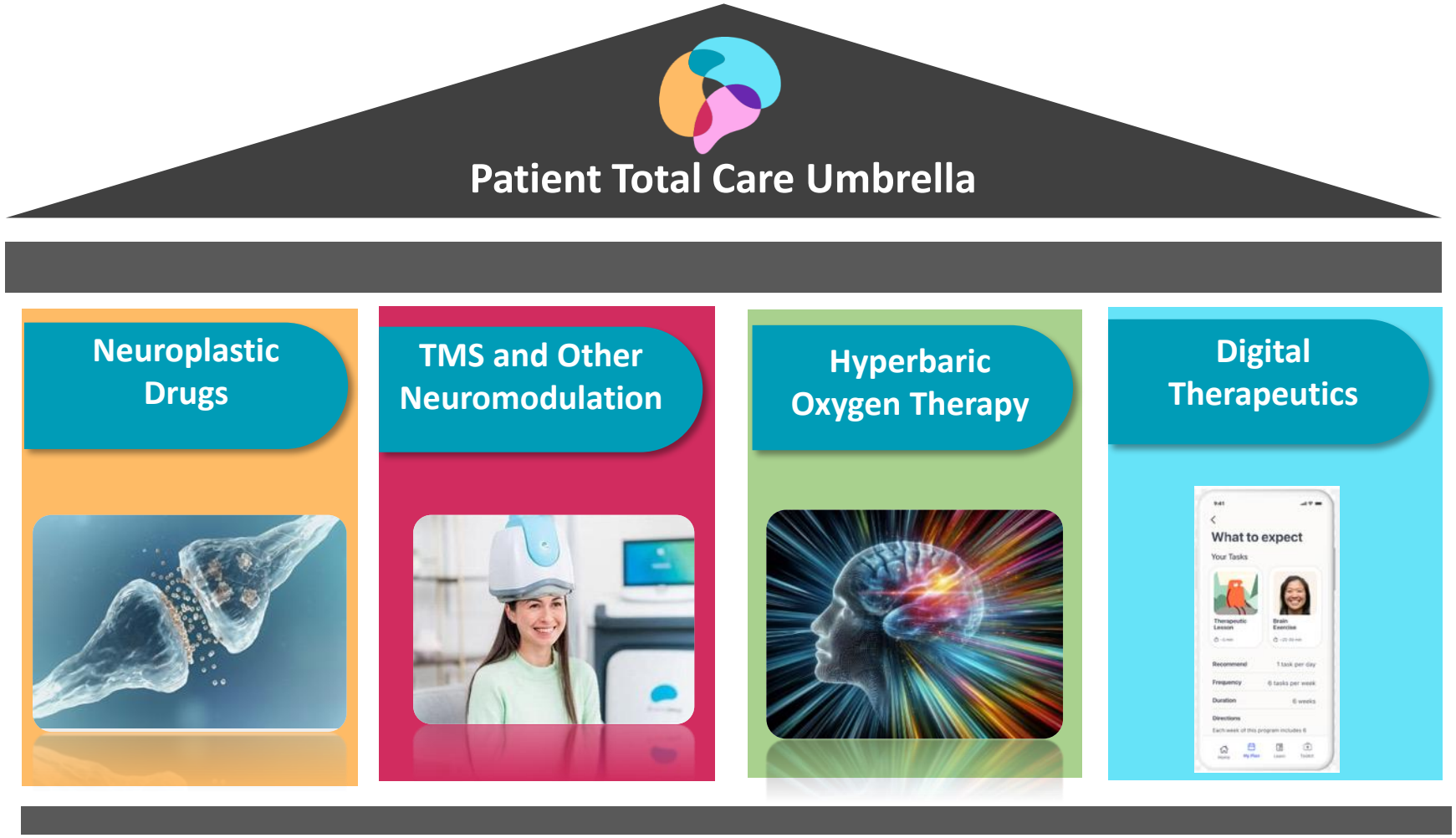
- *Stewart Dolin was a successful and well-liked partner at Reed Smith in Chicago. He developed an episode of depression and was treated with Paxil. That night, his family noticed that he could not stop tapping his feet at dinner and could not sit still.*
- *In the early afternoon on July 15, 2010, Stewart Dolin walked to a Chicago Transit Authority station shortly after a business lunch with a colleague. A woman at the station noticed that Mr. Dolin was pacing and appeared to be agitated as he looked in the direction of an approaching train that was not yet in sight. When the moving train appeared, the woman watched Mr. Dolin leap in front of the train*.

In his memory, the family founded the MISSD foundation to explain akathisia to the public. www.missd.co contains illustrative material

Hope Therapeutics

Four Ways to Treat Suicidal Depression

it's time to change the paradigm and do what works

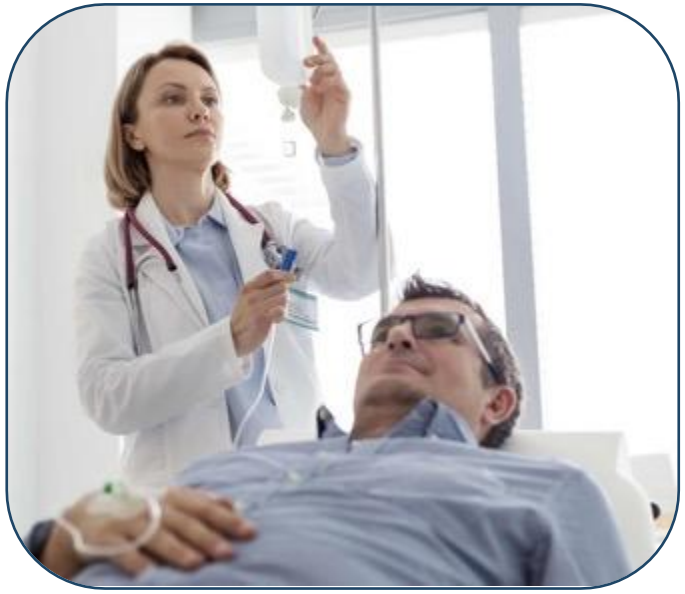


No FDA-Approved Medication for Suicidal Ideation

Only FDA-approved therapy is Electro-Convulsive Therapy (ECT)

Nasal S Ketamine approved for TRD, but not shown to decrease suicide

IV Ketamine is used off-label



Ketamine Binds to the NMDA Receptor to treat Depression and Suicidality
Developing NRX-100 (IV Racemic Ketamine) as an FDA-approved treatment

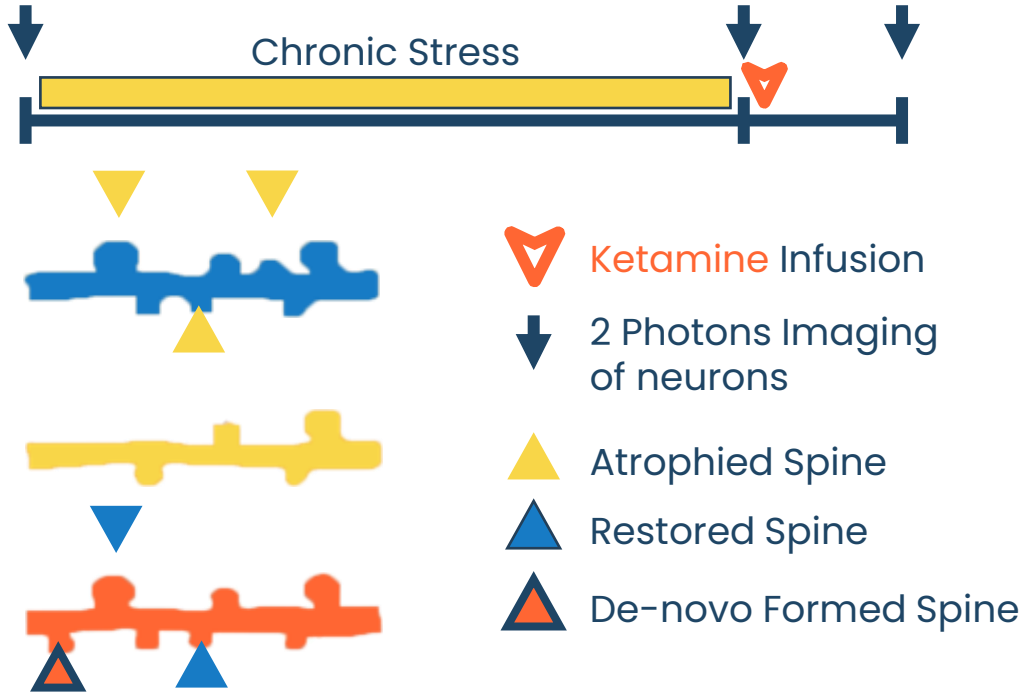
Ketamine is the first prototype Neuroplastic Drug

Ketamine's effect on neuronal dendritic spines

High levels of NMDA activity are shown to cause atrophy of the "dendritic spines" that connect brain cells

Loss of dendritic spines is associated with depression-related behavior

NMDA blockade with ketamine is demonstrated to restore lost dendritic spines, while simultaneously reducing depression-related behavior



Chronic Stress

- Clustered Dendridic Spine Loss
- Ensemble Activity
- Depression-related Behavior

Ketamine

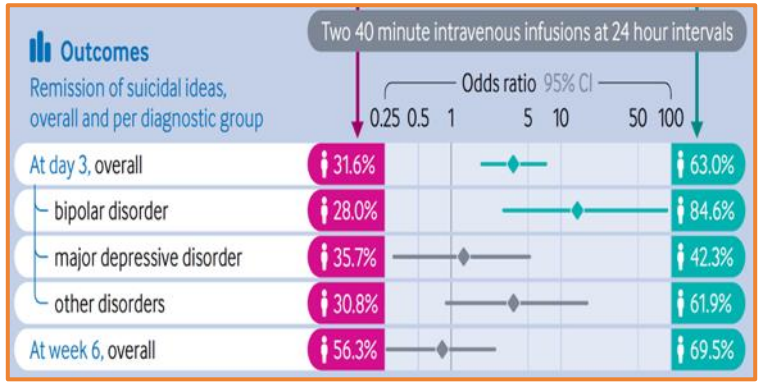
- Clustered Dendridic Spine Formation and Restores Spine Loss
- Ensemble Activity
- Depression-related Behavior

Moda-Sava RN, Murdock MH, Parekh, et.al. Sustained rescue of prefrontal circuit dysfunction by antidepressant-induced spine formation. Science 2019 April 12;364

Established Ketamine Efficacy Data

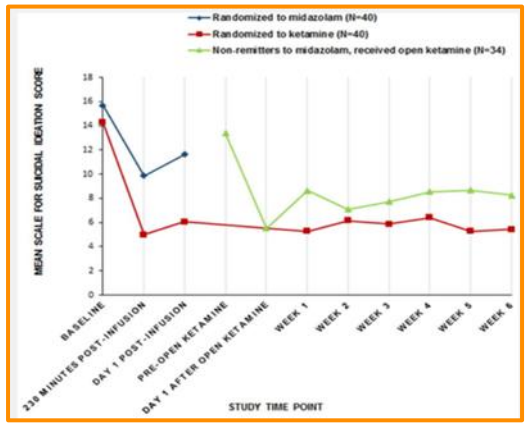
French Gov't Funded: Ketamine vs. Placebo

- 156 Patients, 7 Hospitals
- Admitted with acute suicidality
- Randomized to Ketamine vs. Placebo
- 84% remission on **Ketamine** vs. 28% on Placebo in bipolar depression subgroup
- Odds Ratio 4.6; P<.0001 on Primary Endpoint



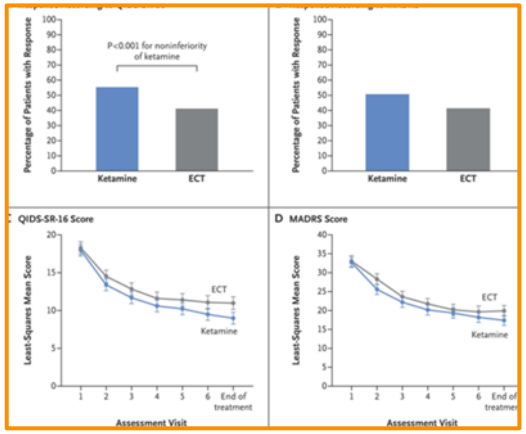
NIH Funded: Ketamine vs. Midazolam

- 96 pt. Randomization to Ketamine vs. midazolam
- Dramatic ketamine effect on suicidality and depression vs placebo (Odds Ratio 5.0; P<.001)
- Midazolam failures treated with open-label Ketamine and similar dramatic effect was seen with Ketamine as secondary treatment



PCORI Funded: Ketamine vs. ECT

- 400 pts. superiority favoring Ketamine P=.007 (superiority is post-hoc)
- Significant memory loss in ECT vs. none with Ketamine (-9.7 vs. -0.9; P<.0001)
- 6 month relapse ECT 56.3 vs. Ketamine 34.5 (P<.0001)



> 20,000 patients of Confirmatory Real World Data

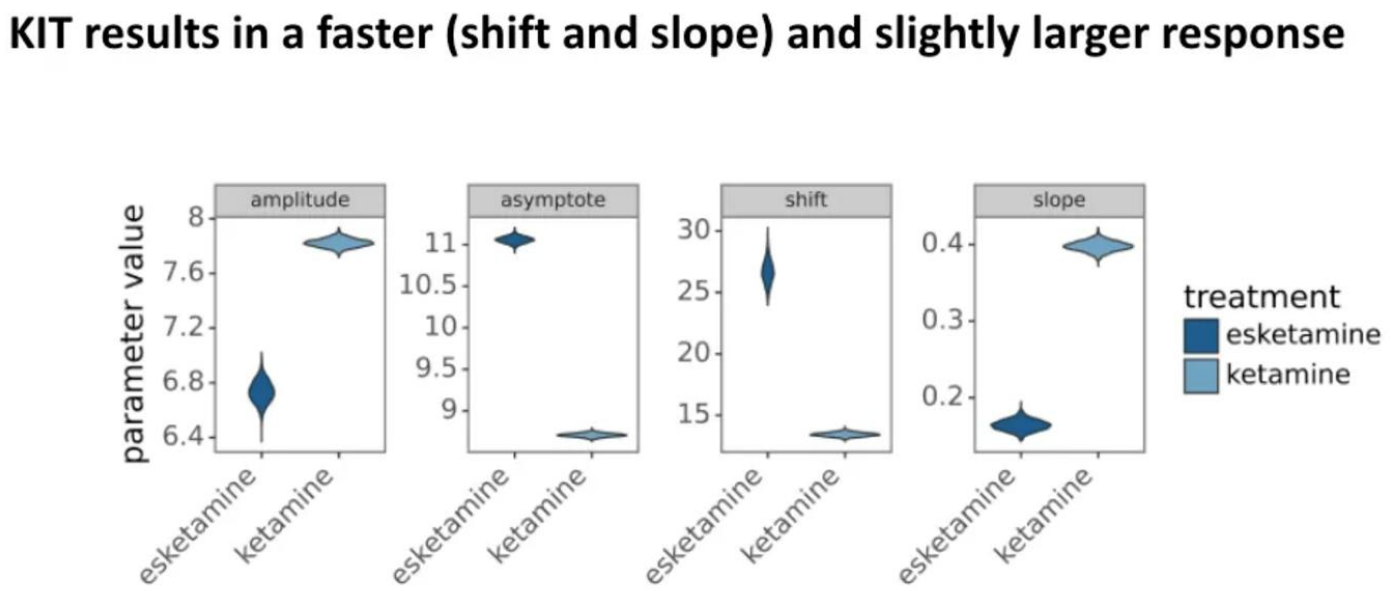


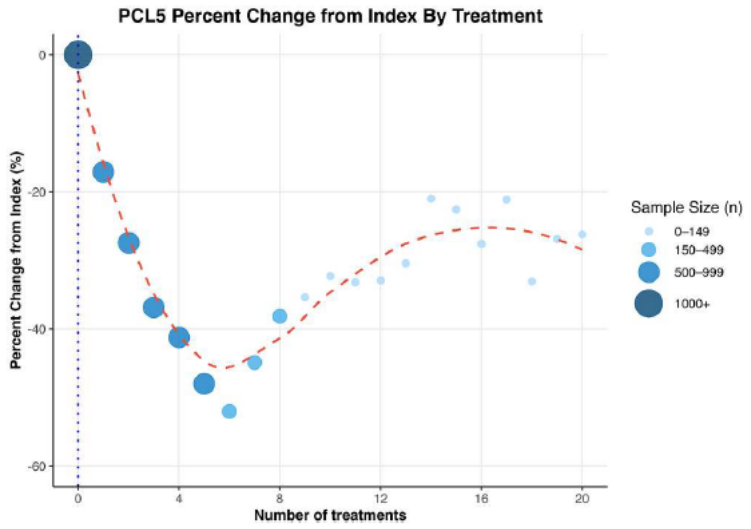
Figure: Estimated amplitude, asymptote (plateau), shift (time until the response kicks in) and slope (speed at which the response develops once it is initiated) of intravenous ketamine (KIT) vs. nasal S-ketamine in real world experience (source: Osmind, Inc.)

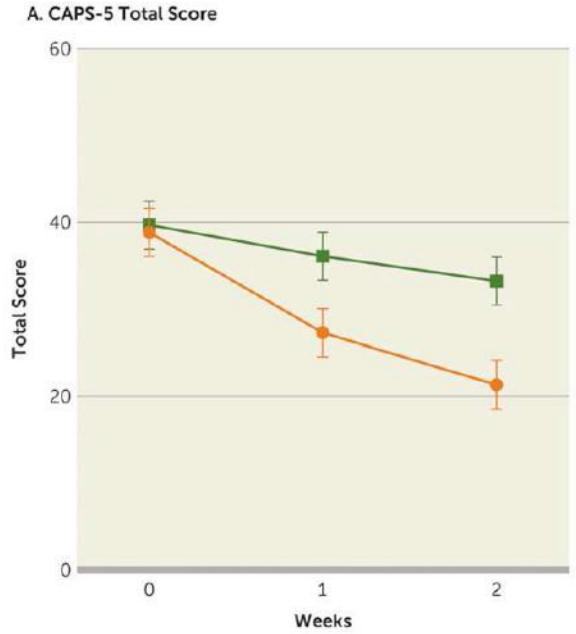
Data presented by Osmind, Inc., from medical records of more than 20,000 patients treated with IV Ketamine or nasal S-ketamine (ASCP June 2024)

https://www.osmind.org/blog/esketamine-and-iv-ketamine-for-major-depression

New Evidence on Ketamine in PTSD

Some drugs treat symptoms of depression in PTSD. No approved drug treats the symptoms of PTSD itself





Osmind, Inc. Real World Data in 8,000+ patients confirms earlier clinical trial data (N=30) demonstrating effect of IV ketamine in reducing PTSD symptoms independent of effect on depression

McInnes, et al. Psychiatry Research 2025: online August 2025

Transcranial Magnetic Stimulation (TMS)

Creates a potent neuroplastic effect in the brain

TMS repairs
Brain Pathways
by causing Neuroplasticity

An FDA-cleared treatment. TMS alone achieves remission in ~50% of patients

Not all TMS is Created Alike

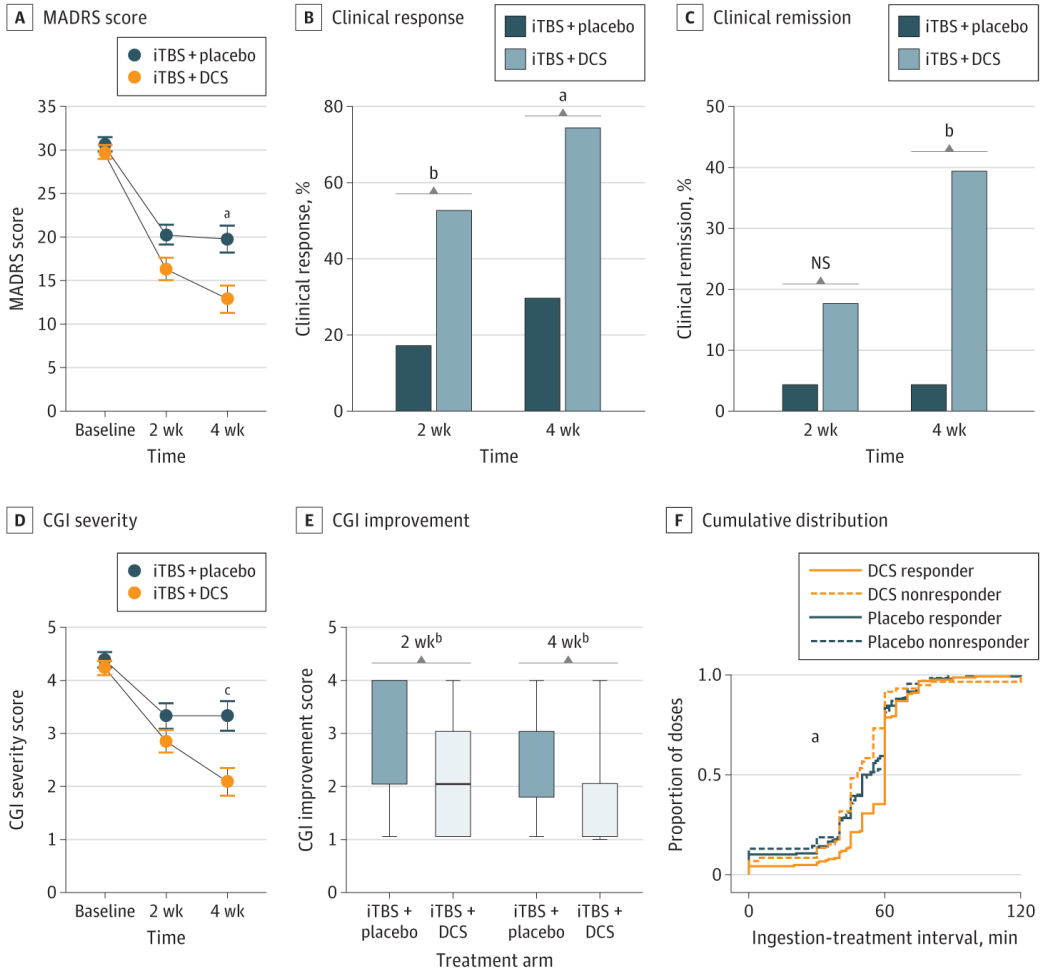
Most TMS works for depression because it's a broad target in the brain

When you can aim TMS with the benefit of MRI and neuronavigation software, you can treat:

- PTSD
- Anxiety
- OCD
- TBI
- Autism
- Parkinsons
- Cognitive Dysfunction

TMS with Cycloserine gives over 80% response

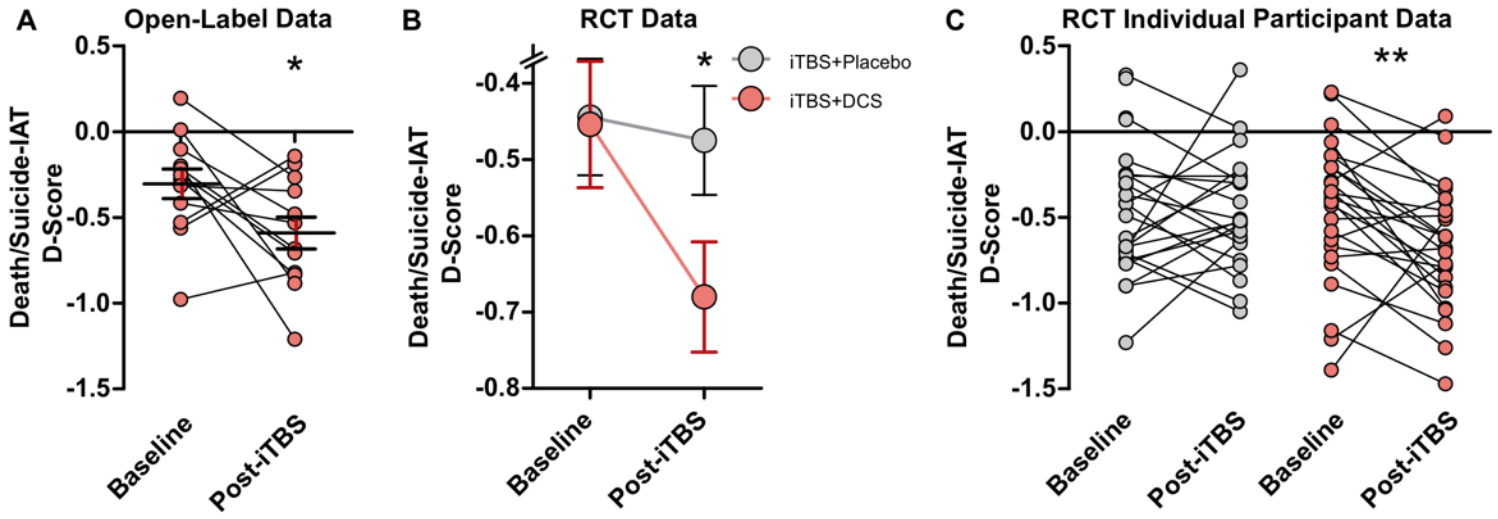
- Adding a neuroplastic drug to TMS is like fertilizing the field before you plant the seed
- **This initial trial is now confirmed at Harvard McClean, University of Toronto and multiple other sites**
- Significant reduction in mean MADRS at 4 weeks with DCS (P<.01)
- > 2-fold better response (P<.001) and 8-fold increase in remission from depression (P<.01) at 4 weeks with DCS adjunctive therapy compared to placebo



Cole, et. al. JAMA Psychiatry 2022:79(12):1153-1161

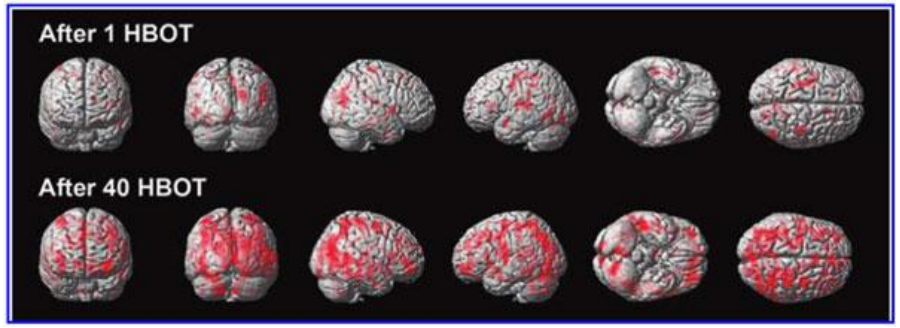
Reduction in Suicidality associated with DCS + TMS

- TMS + DCS is superior to placebo in association with Theta-burst Transcranial Magnetic Stimulation in reducing suicidality on the IAT scale (P<.05)
- MADRS item 10 (suicidality) also showed statistically-significant reduction (P<.001)

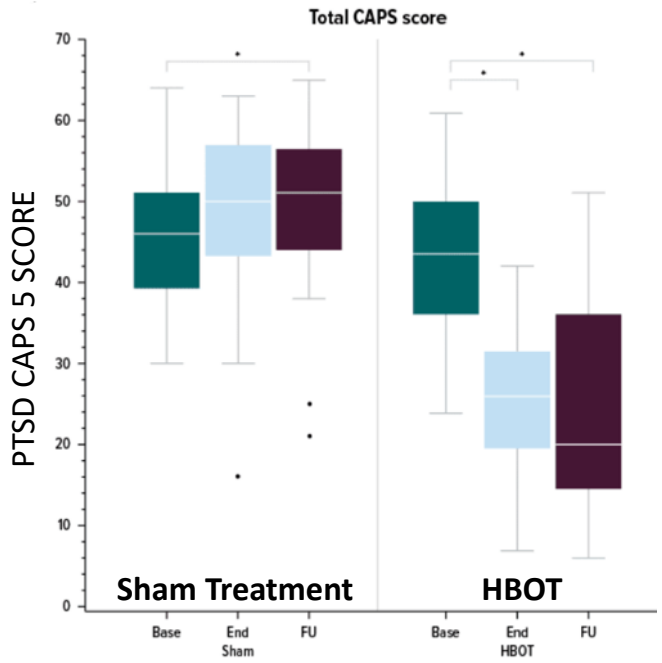


Sohn, et. al. Psychological Medicine, 55, e13, 1–8

Hyperbaric Oxygen Therapy (HBOT) increases brain oxygenation, stimulates Neuroplasticity and may reactivate brain stem cells



40% reduction in CAPS 5 (P<.001)



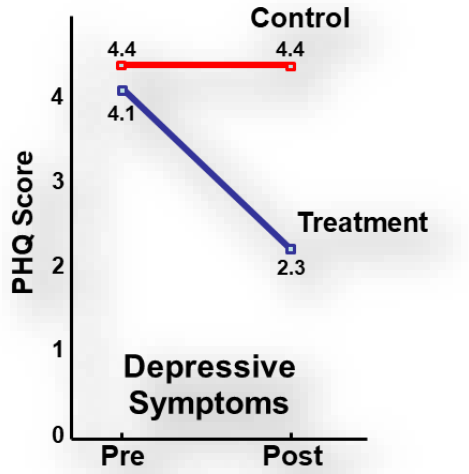
The Israel Defense Forces (IDF) has implemented HBOT Therapy for PTSD and there is pending legislation in the US

DIGITAL THERAPEUTICS:

Gamifying our way to a cure

- Transcendental meditation works by synchronizing breathing and heart rate, causing autonomic coherence
- It's hard to teach and practice meditation
- It's easy to build a video game that you win by synchronizing breathing and heart rate
- Proven by DARPA in Riverine Warriors and First Responders
- Initial research targeted combat stress. Subsequent data demonstrated reduced depression in First Responders

Digital Therapeutics were developed in the military and shown to reduce stress and depression



HOPE Therapeutics

The First National Network to Integrate Care for Depression and PTSD

Now Part of the VA Community Cares Program

The first network providing neuroplastic Pharmaceutical Therapy, TMS, Hyperbaric Therapy, and Digital Therapeutics, for suicidal depression, PTSD, anxiety, OCD and more.

Our Mission

To offer state of the art neuroplastic therapy to render suicidal depression and PTSD a curable disease with overnight results, offering HOPE to patients and families without stigma.

HOPE's Value Proposition

"Give Us a Week and We Will Give You Back your Self."

HOPE Therapeutics: Cost Effectiveness of Care

- Drastic improvement over four decades in the outcomes and survivability of care for common cancers, heart disease, and other lethal conditions with no improvement in survival of suicidal depression
- For the first time, we are changing the survival outlook for suicidal depression and PTSD
- Our integrated care for this lethal condition costs considerably less than commonly reimbursed care for other potentially lethal conditions

Condition	Cost per treatment episode
Suicidal Depression (HOPE Therapy)	< $10,000
Cardiac Disease	~$35,000
Breast Cancer	~$35,000
Prostate Cancer	~$35,000
Brain Tumor	$150,000+

Suicidal depression and PTSD predominantly affect younger people with more years of productive life that can be saved

Thank You

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