ReSynapse Therapeutics

Novel Multi-Target Drugs for Treatment-Resistant Depression

via precision computational drug design

Oct 2025 | Non-Confidential

The Need: Current Treatments Fall Short in Addressing Depression & Anxiety

137M people with depression and anxiety, 4-6 week onset times, and severe side effects

57M

suffer from **Depression** [1][2]

80M

suffer from **Anxiety Disorders** [3][4][5]

20%-30%

Are **treatment-resistant** [6][7][8]

$130B

Annual US economic burden

$15.7B

Global antidepressant market (7% CAGR)

US, EU & Japan (2023-2024)

ReSynapse Tx

Our Solution: A New Class of Multi-Target Drugs

Standard of Care

- **SSRI, SNRI, TCA**
  (Inhibition of serotonin transporters)
- **“Shotgun" Polypharmacology**
  (multi-receptor without selectivity)
  - Slow onset
  - Severe side effects
  - High failure rate
  - Treatment resistance

Psychedelics

Non-selective activation of various brain receptors

- Variable efficacy
- Risky & hallucinogenic
- Regulatory challenges

August 9, 2024

FDA Rejects Lykos’ MDMA-Assisted PTSD Therapy After Negative Adcomm

ReSynapse

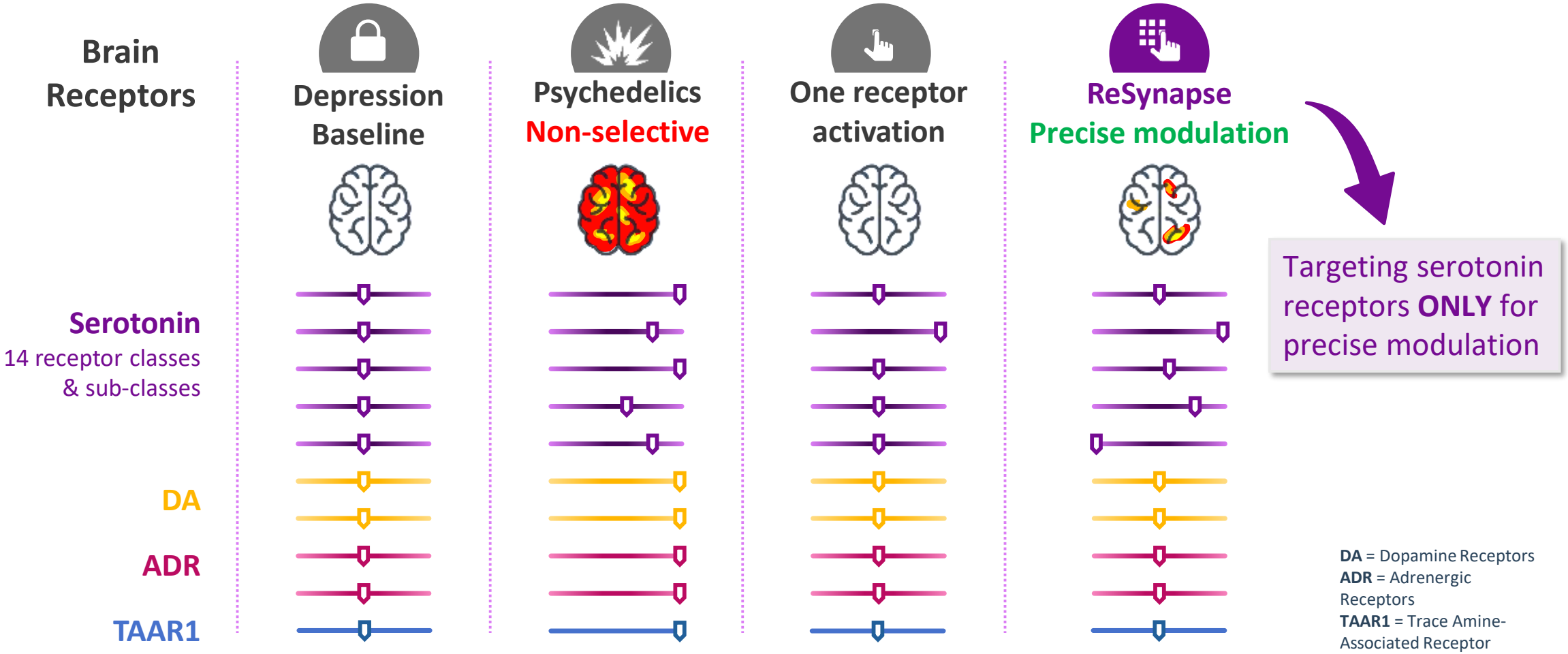
Single molecules targeting multiple serotonin receptors precisely

- Fast onset
- Favorable safety profile
- Non-hallucinogenic
- Potential Improved efficacy for treatment-resistant cases

Our competitive differentiation:

- Validated receptor biology eliminates target risk +
- Proprietary computational methodologies enable systematic multi-target design impossible with standard tools +
- Science-first approach vs. empirical trial-and-error

A New Class: Serotonin Modulation by Targeting Multiple Serotonin Receptors



Our Distinct Innovation

Identified a precise combination & modulation of serotonin receptors

Defined a set of chemical requirements for one molecule targeting multiple serotonin receptors

Built computational methodologies for designing/identifying multi-target compounds

Aiming for faster onset, improved therapeutic effect, and minimum side effects

Our Validated Approach

Target Specificity

Complete hypothesis defined:

- 4 specific serotonin receptors identified for depression
- Agonist/antagonist profile for each
- Combination mechanistic rationale from 25+ studies
- Liability mitigation designed into target selection strategy

Details Disclosed under NDA

Computational Methodology

Proprietary methodologies refined over 15 years of pharmaceutical experience:

- Simultaneous multi-target design from first principles (not sequential)
- Selection criteria for molecules hitting multiple targets
- Various parameter optimization

Not available in commercial software

Validation Strategy

6-layer de-risking:

- Computational prediction
- In vitro multi-receptor binding
- Functional assays
- PK/PD & ADME
- In vivo efficacy (depression models)
- POC Mechanism confirmation

Each layer confirms before advancing

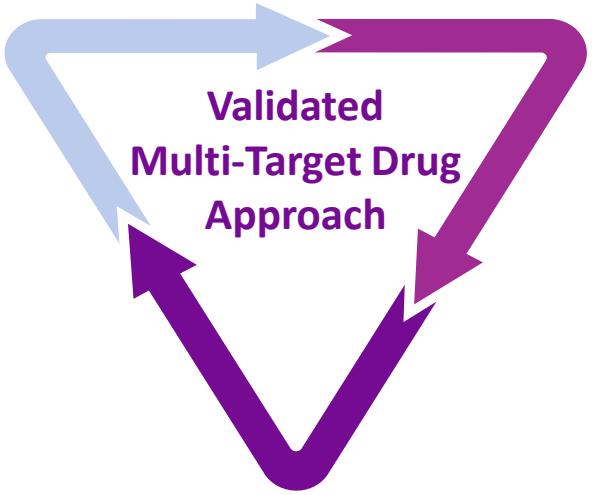
Drug Design, Not Target Discovery

We're using proprietary methods to design molecules hitting validated targets simultaneously

De-Risked Scientific Foundation:
Why Selective Multi-Target Drug Approach Works Now?

Each Target Has a Proven Antidepressant Role

- Individual serotonin receptor mechanisms established in literature
- ReSynapse target selection is based on proven MOA



Multi-Target Combination Delivers Superior Outcomes

- Preclinical evidence shows enhanced efficacy vs single targets
- Recent findings of serotonin receptor structure & function

Validated & Feasible

- FDA/EMA precedent: multi-target CNS drugs successfully approved
- Advances in computational chemistry drug design, and AI tools

Convergence of Validated Biology + Functional Data + Computational Power

Highly Skilled, Experienced, Dedicated Team

We know what it takes, and we are committed to achieving it.

Dorit Cohen Carmon, Ph.D.
Co-Founder | CEO

- Experienced CEO
- Expert in Neurobiology
- 10+ years of small molecule drug discovery & development
- Strategy building & value creation

Itai Bloch, Ph.D.
Co-Founder |CTO

- 15 years CADD, cheminformatics, and GPCR inhibitors.
- Integrates structural data using proprietary methodologies to optimize the discovery of new pharmaceutical compounds.

Prof. Alexandre Varnek
Scientific Advisor

Principal Investigator - University of Strasbourg & ICReDD (Japan)

- World leader in AI -based drug design of small molecules
- Skolnik prize 2024 winner for Chemoinformatics, QSAR.

Ramin-Bio
PROTEKT Therapeutics
WEIZMANN INSTITUTE OF SCIENCE
MIGAL Galilee Research Institute
EPIX Pharmaceuticals
Uni Stra
wpi ICReDD Hokkaido University Institute for Chemical Reaction Design and Discovery

ReSynapse Tx

Current Status of R&D Process

Reduces risks of preclinical development

ReSynapse has Identified a Specific Combination

First indication: Treatment-Resistant Depression

Done

A combination of 4 serotonin receptors for targeting

Multiple Serotonin Receptor Drug Design

- Multiple receptor modeling
- Rational science-based multi-target drug design
- **Various drug candidates identified**

We are here

IP Patent filing

Within 4 months

Experimental Validation

- Compound synthesis
- In vitro and in-vivo POC
- Rapid feedback loop

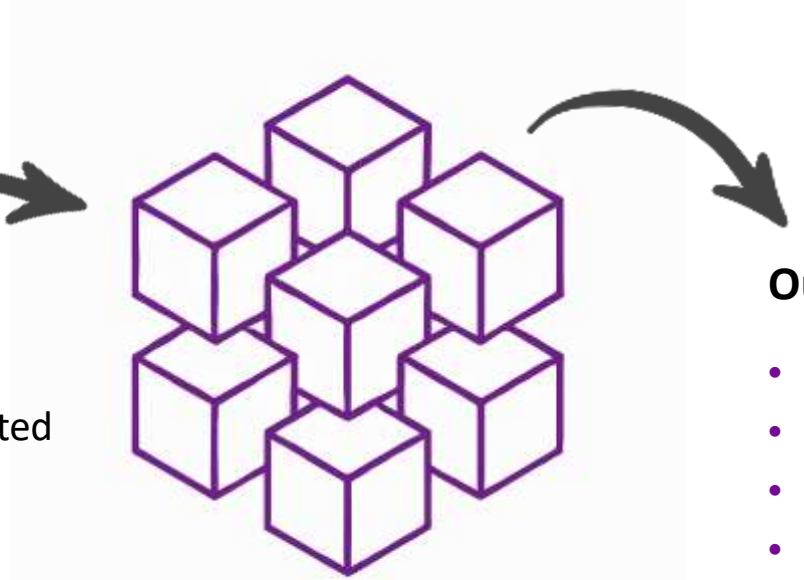
POC validation

Within an additional 6-8 months

Our Computational Serotonin Platform: Systematic Multi-Target Drug Design at Scale

Key Inputs (Big Data)

- 39 systematically analyzed 5-HT receptor structures across 4 validated receptors
- Millions of Ligands
- Patents & Scientific Publications
- Experimental data Indications



Computational Chemistry Engine

Proprietary methodologies refined through 15 years' experience

- Multi-Target Modeling
- Receptor–Ligand Binding Precision
- Massive Compound Virtual Screening Capability
- AI-Driven Safety + BBB penetration Prediction
- Accelerated Lead Optimization

Outputs

- Optimized Multi-Target Drug Candidates
- Mode-of-Action per Indication
- De-risked Early-Stage Pipeline
- Faster Time to IND / Lower Attrition

5-Year Development Roadmap

Strategy: Milestone-Based Funding and Preclinical Pharma Deals

Year 1-2

- Computational modeling, drug design , IP filing
- POC: In vitro and in-vivo validation
- Lead candidates' optimization

Year 3-4

- Preclinical Candidate Selection
- IND-enabling studies
- File IND for lead candidate

Year 5

- **FIH Phase 1 clinical trial**

Value Creation Roadmap

24-Month Development Plan Milestones-Based Step:

- **Step 1: Months 1-15**
  - POC Experimental validation
  - IP filing (NCE) & Computational expansion
- **Step 2: Months 16-24**
  - Lead(s) optimization
  - In vivo efficacy studies
  - Computational expansion

Compelling Market Opportunity & Pharma Interest

Massive Unmet Need

$15.7B
Global antidepressant market growing 7% CAGR

$1.9B
Treatment-resistant depression segment

- **First Indication**: Treatment-resistant depression (2.8M Americans, 11M Europeans)

Strong Pharma Deal Market

J&J / Intra-Cellular **$14.6B**
Phase 2 Depression (Jan 2025) | Acquisition

AbbVie/ Cerevel **$8.7B**
Phase 2 Schizophrenia (Aug 2024) | Acquisition

Boehringer/ Kinoxis **$273M**
Preclinical Depression (May 2023) | Partnership

Computational Scalability: Upon validation, same systematic approach can be applied to anxiety, PTSD, using validated disorder-specific receptor combinations → Multiple Therapeutic Programs.

Investment Highlights: Why ReSynapse Now

Market demand

Addressing significant unmet needs in mental health treatment

An experienced team with a proven track record

Neurobiology, drug discovery & development, and IP creation

Innovative Technology

Selective multi-target serotonin modulators for mood disorders

Systematic computational multi-target drug design

De-Risked Science

Validated receptor biology, FDA precedents, and designing compounds with optimal therapeutic effects

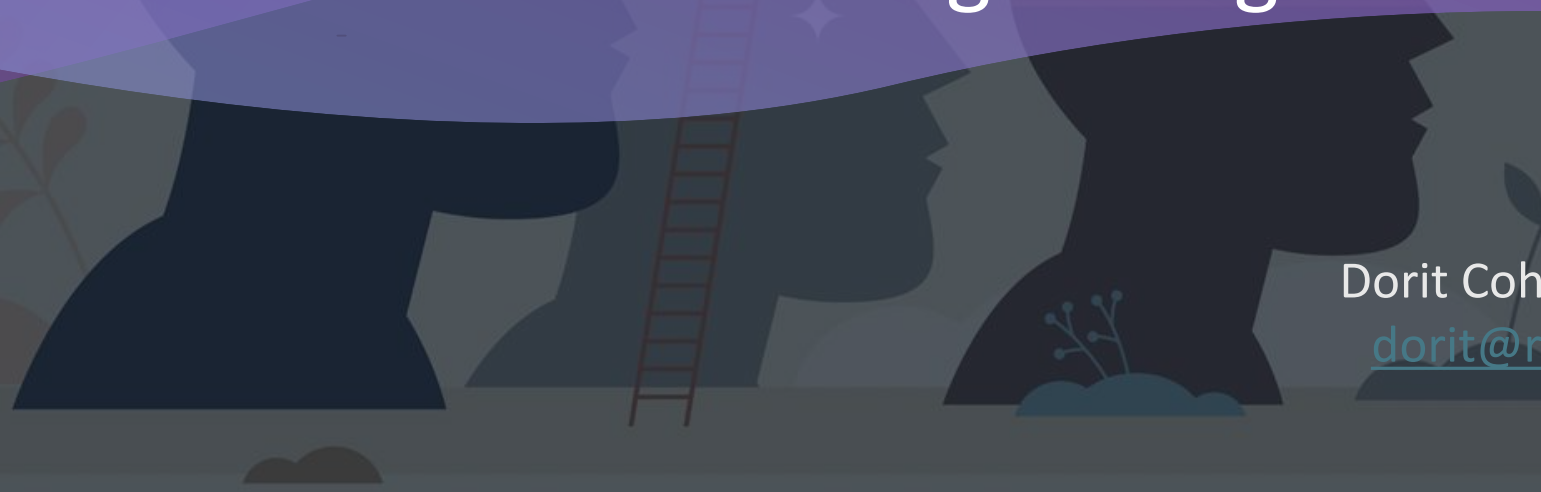
Pipeline Scalability

Upon POC validation, pipeline expansion for various mood & anxiety disorders through disorder-specific receptor combinations

ReSynapse Therapeutics

Thank You

Transforming Neuropsychiatry Through
Selective Multi-Target Drugs



Contact:
Dorit Cohen Carmon, Ph.D.
dorit@resynapse-tx.com