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Overview

We apply innovative science to known molecules to develop life-saving medicines
## Multi-billion Dollar Potential in Psychiatry: NRX-101

### Psychiatry
NRX-101
Bipolar depression with suicidality
Breakthrough Therapy designation* & SPA

- “Composition of matter” patented NMDA-targeted antidepressant – (oral, non-addictive)
- NRX-101 Phase 2 Trial - bipolar depression with sub-acute suicidal ideation & behavior (SSIB) initiated 2Q 2022
  - Data readout expected 4Q 2022/1Q 2023
- NRX-101 SPA Phase 2b/3 Registration Trial in Bipolar Depression in Patients with acute suicidal ideation & behavior (ASIB) expected 2H 2022 with commercial supply
  - Data readout expected 2H 2023

* Treatment of Severe Bipolar Depression in Patients with Acute Suicidal Ideation & Behavior (ASIB) after initial stabilization with ketamine or other effective therapy

### Respiratory
ZYESAMI® (aviptadil)
Critical COVID-19 (ARDS)
Fast Track

- Intravenous Critical COVID-19 ARDS
  - Completed P2b/3 trial, re-submitted for EUA Feb 2022
  - NIH study stopped enrollment due to futility
- Evaluating potential in other acute and chronic lung disorders

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### Notes
- NRX-101 Phase 2 Trial - bipolar depression with sub-acute suicidal ideation & behavior (SSIB) initiated 2Q 2022
- NRX-101 SPA Phase 2b/3 Registration Trial in Bipolar Depression in Patients with acute suicidal ideation & behavior (ASIB) expected 2H 2022 with commercial supply
Leadership Team

Committed to rapid, cost efficient, and impactful drug development

Stephen Willard, JD – Chief Executive Officer and Director
30+ years of management of publicly traded biotechnology companies, with a strong background in law and finance. Served in CEO roles such as Cellphire Therapeutics, and Flamet Technologies, now Avadel Pharmaceuticals and has held leadership and director roles at the FDIC and on the board of E*Trade Financial. Mr. Willard currently serves on the National Science Board as a presidential appointee and has practiced law in New York, London, and Washington, D.C.

Randy Guggenheimer, MBA – Chief Business Officer
25 years in Life Science Investment Banking. Senior positions at Lehman Brothers, Dresdner. Kleinwort Wasserstein. Significant experience in life sciences financings, M&A

Seth Van Voorhees, PhD, MBA – Chief Financial Officer
30+ years of finance and accounting experience, including serving as CFO of PDS Biotechnology, Research Frontiers and American Pacific. Investment banking experience supporting chemical/pharmaceutical clients

Randy Guggenheimer, MBA – Chief Business Officer
25 years in Life Science Investment Banking. Senior positions at Lehman Brothers, Dresdner. Kleinwort Wasserstein. Significant experience in life sciences financings, M&A

Robert Besthof, MIM – Head of Operations and Chief Commercial Officer

Rick Panicucci, PhD – CMC and Technical Operations Advisor
25 years manufacturing leadership. Head of CCP, Novartis. VP of Manufacturing, WuXi Apptec

Michael Kunz, General Counsel & Corporate Secretary
30+ years legal and fiduciary leadership in biopharma, energy and project finance. Previous roles include general counsel positions at Rolls-Royce Power Ventures, Ltd. (London), Burmeister & Wain Scandinavian Contractors (BWSC-Denmark) and 10 years private practice with Dewey Ballantine.

Molly Cogan – Senior Director, Global Communications & Government Affairs
20+ years international public affairs and senior communications leadership in healthcare, population health, digital health tech, and private equity
## Experienced Board of Directors

### Drug development, health policy, biosecurity

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Experience and Highlights</th>
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</table>
| Patrick Flynn, MBA        | Chair, Audit & Compensation Committees | 30 years senior executive experience  
CEO Health Dialog – exit to BUPA International  
Bank of America (15 years), VP World Banking and Risk Management  
BS Finance, Wharton School, University of Pennsylvania |
| Sherry A. Glied, PhD      | Dean, NYU Wagner                      | Former Assistant Secretary for Health (ASPE)  
Health Economist, Mental Health Policy Expert |
| Aaron J. Gorovitz, JD     | General Counsel, AHG Group            | Former Director and President, Teva International Group  
Chairman, CH Health |
| Chaim Hurvitz             |                                      | 25 years in drug development  
Participated in 6 successful drug and device launches  
Blockbuster drugs at Merck, Allergan, Eyetech |
| Jonathan C. Javitt, MD, MPH| Co-Founder, Chief Scientist           | Presidential-commissioned White House health advisor  
Prof. Johns Hopkins University |
| Stephen Willard, JD       | Chief Executive Officer               | Former CEO Cellphire Therapeutics & Flamel Technologies  
Former Associate Director, FDIC  
Former Director, E*Trade Financial  
Practiced Law in New York, London and Washington, D.C |

Currently serving as a Presidential appointee  
National Science Board, 2018-2024
# NRx R&D Pipeline

<table>
<thead>
<tr>
<th>Indication</th>
<th>Compound</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Regulatory Interactions</th>
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<tbody>
<tr>
<td><strong>PSYCHIATRY</strong></td>
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<td>Bipolar Depression with Suicidal Ideation and Behavior</td>
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<td>Severe Bipolar Depression in patients with ASIB</td>
<td>NRX-100 / NRX-101™</td>
<td>Breakthrough Therapy Designation, SPA, Biomarker Letter of Support</td>
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<td>Bipolar Depression in patients with SSIB</td>
<td>NRX-101™</td>
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<td><strong>RESPIRATORY/COVID-19</strong></td>
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<td>Critical COVID-19 / Acute Respiratory Failure</td>
<td>Intravenous ZYESAMI* (Aviptadil)</td>
<td>Fast Track</td>
<td>EUA Declined – for post-hoc subgroup</td>
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<td>Critical COVID-19 / Acute Respiratory Failure – NIH</td>
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<td><strong>ARDS</strong></td>
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<td>Acute Respiratory Distress Syndrome</td>
<td>VIP</td>
<td>Investigator Initiated Study</td>
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<td>Data and rights held by The Research Foundation for the State University of New York; NRx has a license</td>
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*ZYESAMI* is a registered trademark of Zydus National Pharmaceutical Co., Ltd., India.
NRX-101

The first oral, non-addictive medicine in development to treat Bipolar Depression in Patients with ASIB* and SSIB**

*ASIB - requiring hospitalization
**SSIB – not requiring hospitalization
Why target Suicidal Bipolar Depression?

Suicide kills ~50,000 Americans annually* - suicide is particularly high in bipolar disorder

If you know two people with bipolar depression, one will attempt suicide
If you know five people with bipolar depression, one will succeed

*Centers for Disease Control – all suicides
### The Emerging Science of Depression and Suicidality

#### Depression and Suicidality – though overlapping is not the same

<table>
<thead>
<tr>
<th>Depression with Suicidality</th>
<th>Implications for Bipolar Depression with Suicidality</th>
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<tbody>
<tr>
<td>• Antidepressants (5HT2a / SSRIs) can increase suicidality – suicidality routinely an exclusion in depression studies</td>
<td>• Highest suicidality of depressive disorders ~ 50% attempt suicide</td>
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<td>• NMDA antagonists (ketamine) can stabilize depression and suicidality –</td>
<td>• Available drugs improve depression but can increase suicidality</td>
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<tr>
<td>• Suicidality improvement not strictly a function of improvements in depression</td>
<td>• Drug abuse and overdose of great concern – addictive agents may require REMS</td>
</tr>
<tr>
<td>• Ketamine can create hallucinations, may be highly addictive, requires supervised administration</td>
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</table>

### Development of Depression drugs has mostly avoided addressing Suicidality

- Antidepressants (5HT2a / SSRIs) can increase suicidality – suicidality routinely an exclusion in depression studies
- NMDA antagonists (ketamine) can stabilize depression and suicidality –
  - Suicidality improvement not strictly a function of improvements in depression
  - Ketamine can create hallucinations, may be highly addictive, requires supervised administration

**Sources:**
Selected Unmet Needs for New Antidepressants

**EFFICACY**
- Higher % responders
- Faster Onset

**SAFETY/ TOLERABILITY**
- Decrease or no increase in Suicidality
- Lower Side Effects

Sources:
- Greden, J., Journal of Clinical Psychiatry, 2002;63 (suppl 2)
Though numerous drugs have been approved for MDD and Bipolar Depression, faster, more robust response, and reduction of suicidality remain the unmet need.

### Drugs for Major Depressive Disorder (MDD) & Treatment Resistant Depression (TRD)

123 and counting

- **Axsome**
- **AXS-05**
- **REL-1017**

### Drugs for Bipolar Depression

- All antipsychotics

### Warning

- Increased risk of Suicide

### Drugs for Depression with Suicidality

### No Suicidality

### Sub-acute Suicidality

### Acute Suicidal Ideation & Behavior

### Initial NRX-101 Target

### Potential Expansion
NRX-101 Market Opportunity in Bipolar Depression with Suicidality

Patients in Clinics and outpatient being treated for Bipolar Depression with Suicidality

Sources:
- U.S. Census Bureau.
- HCUP Analysis June/July 2017
- https://www.nami.org/mhstats
The NRx Discovery
Simultaneous Blockade of NMDA and 5-HT$_{2A}$

D-Cycloserine acts as an NMDA antagonist above certain dosages
Studies have shown that DCS + 5HT2a increases the antidepressant response and reduces suicidality
Phase 2 Study showed effect of D-Cycloserine in Depression / Suicidality

If Phase 2 results are replicated in Phase 3, this will meet criteria for FDA approval

- Primary endpoint is mean MADRS score over 42 days
- A clinically and statistically significant difference ($p=0.03$) was seen on the mixed model through day 42. The mean 7.7 point difference on MADRS is similar to or larger than that seen with Esketamine
- 40% relapse in control group, no relapse in NRX-101 group
- Patients who would otherwise have been in the hospital for 1 week plus were discharged after 1-2 days
Studies of DCS with 5HT2a / SSRIs

A series of smaller studies have shown an improved antidepressant and anti-suicidal effect of DCS when added to 5HT2a / SSRIs

**Heresco-Levy et. al.**

26 patients – randomized, placebo controlled

**Kantrowitz et. al.**

Treatment Resistant Bipolar Depression after single iv. Ketamine
8 patients – open label

**Chen et. al.**

Treatment Resistant MDD + Bipolar Depression after two iv. Ketamine
32 patients total – placebo controlled

**Javitt D. et. al ACNP 2018**

Bipolar Depression with ASIB after single i.v. ketamine. NRX-101 vs lurasidone (randomized)

4. Javitt D. et.al: Poster presentation ACNP 2018
NRX-101 Clinical Trial Program

**Phase 2 Study**

Bipolar Depression in Patients with Sub-Acute Suicidal Ideation & Behavior (SSIB)

- 70 Patients
- 2 x BID
- MADRS ≥ 30
- C-SSRS 3 or 4
- NRX-101 1:1
- Lurasidone
- Outpatient
- Recruitment ongoing

**Phase 2b/3 Program**

Stabilization Study & SPA Study

Bipolar Depression in Patients with Acute Suicidal Ideation and Behavior (ASIB)

- 144 Patients
- One infusion
- NRX-100 (Ketamine) 3:1
- Placebo
- MADRS ≥ 30
- C-SSRS 4 or 5
- Inpatient
- Stabilization
- SPA Study - Outpatient
- Starting 2H 2022

Dosages used are not commercially available
Established IP Position: 30+ issued patents

NRx has Composition of Matter Patent Protection

- Composition of matter patent for NRX-101 until 2033
- Pharmaceutical composition for treatment of depression and associated suicidality with D-cycloserine (DCS)/ Lurasidone
- Five patent families, 60+ filed applications, 30+ issued patents in US/EU/CN/JP/KO/AU
- Creates opportunity for platform across range of combinations
- Combinations involving dextromethorphan, d-methadone, and S-ketamine are identified in the spec of US 10,583,138

Allowed Claims

1. A pharmaceutical composition for treatment of depression and associated suicidality comprising: an NMDAR-antagonist effective amount of D-cycloserine; and an effective amount of an atypical antipsychotic that is a combined dopamine D2/S-HT2A receptor antagonist, wherein the NMDAR-antagonist effective amount of D-cycloserine is sufficient to produce a sustained blood plasma concentration in excess of 25 microgram/mL but lower than 125 microgram/mL; and wherein the atypical antipsychotic is lurasidone, and wherein the effective amount of the lurasidone is between 20 mg-200 mg per day.

2. The pharmaceutical composition of claim 1, wherein the NMDAR-antagonist effective amount of D-cycloserine is in excess of 500 mg/day and less than 1000 mg.

3. The pharmaceutical composition of claim 1 wherein the NMDAR antagonist effective amount of D-cycloserine is in excess of 10 mg/kg/day and, is less than 25 mg/kg/d.

4. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is formulated for sustained release.

5. The pharmaceutical composition of claim 1, further comprising an enteric coating.

6. The pharmaceutical composition of claim 1, wherein the NMDAR-antagonist effective amount of D-cycloserine is provided as a prodrug.
NRX-101 offers a differentiated profile for Suicidal Bipolar Depression with an FDA agreed upon path to NDA

Phase 3 with FDA Breakthrough Therapy designation

NMDA – A Validated Mechanism
- Depression & Suicidality
- Esketamine, NRX-101 Phase 2, etc.

Addresses High Unmet Need
- Treats depression and suicidality (bipolar space)
- Oral, not addictive (not scheduled), avoids hallucinations
- Outpatient

Composition of Matter Patent
- NRx has a composition of matter patent for NRX-101 and an array of NMDA+5HT2A compounds,
- Five patent families, 60+ applications, 30+ issued patents

FDA Agreed Upon Regulatory Path
- Special Protocol Agreement, Breakthrough Therapy designation: Treatment of Severe Bipolar Depression in Patients with ASIB after initial stabilization with ketamine or other effective therapy

Efficient Clinical Development Path to NDA
- Seeking to replicate P2 study
- NRX-100 (144 pts.) NRX-101 (~80 pts.) pivotal study (severely depressed and acutely suicidal) to start 2H22
- Path to NDA filing in 2023

Exploring expansion in earlier population
- NRX-101 Phase 2 trial (Bipolar Depression in sub-acute suicidality) initiated 2Q 2022
NRX-101 could be a potential Paradigm Shift in the Treatment of High Unmet Psychiatric Conditions – especially those with Suicidality

Bipolar Depression with Suicidality:
• ASIB: Rapid stabilization with ketamine and discharge after 1-2 days with oral, non-addictive drug
• SSIB: Periodic use when suicidality present

PTSD with and without Suicidality:
• ~9M (3.6%) of US adult population had PTSD in the last year, of which 1/3 had severe PTSD
• Up to 10% may attempt suicide / have suicidality
• Only 2 drugs indicated for PTSD, limited efficacy and carry warning for increased risk of suicide

Sources:
National Institute of Mental Health
Wilcox, H. et. al, Posttraumatic Stress Disorder and Suicide Attempts in a Community Sample of Urban American Young Adults Arch Gen Psychiatry. 2009
We apply innovative science to known molecules to develop life-saving medicines
Financial Position

NRXP

Publicly traded on NASDAQ following SPAC merger completed in May 2021

NRx Cash Position:
$24.5 million as of 6/30/2022

Total Shares Outstanding:
~67 million shares as of 8/1/2022

Data readouts expected in the next 9-18 months
Revenue potential in 2024
Demonstrated ability to execute

Revenue potential in 2024

Demosntrated ability to execute
Bipolar Depression with ASIB & SSIB - Areas of Very High Unmet Need

Opportunity to expand to PTSD and beyond

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<th>Psychiatry – NRX-101</th>
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<td>✓ Breakthrough Therapy designation &amp; SPA for Bipolar Depression with ASIB</td>
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<td>✓ Oral &amp; non-addictive NMDA</td>
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<tr>
<td>✓ Composition of matter patent &amp; other exclusivity elements</td>
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<td>✓ Fewer than 150 patients in registrational program</td>
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<td>✓ Opportunity to expand to larger non-acute population</td>
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<tr>
<td>✓ Opportunity to expand to Bipolar Depression with SSIB, PTSD, etc.</td>
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<tr>
<td>Bipolar Depression with Suicidality:</td>
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<tr>
<td>$2B</td>
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<tr>
<td>PTSD</td>
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<td>$5B</td>
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