Targeting Major Advances in Treatment of CNS Disorders

May 2019

TICKER SYMBOL OTCQB:RLMD
Forward Looking Statements

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Because actual results are affected by these and other potential risks, contingencies and uncertainties, the Company cautions investors that actual results may differ materially from those expressed or implied in any forward-looking statement. It is not possible to predict or identify all such risks, contingencies and uncertainties. The Company identifies some of these factors in its Securities and Exchange Commission (“SEC”) filings on Forms 10-K, 10-Q and 8-K, and investors are advised to consult the Company’s filings for a more complete listing of risk factors, contingencies and uncertainties effecting the Company and its business and financial performance.

The Company assumes no obligation to update forward-looking statements as circumstances change. Investors are advised to consult further disclosures that the Company makes or has made on related subjects in the Company’s Form 10-K, 10-Q and 8-K reports.
## Corporate Overview

Relmada is focused on advancing dextromethadone (REL-1017) as a rapid-acting oral treatment for depression and other CNS disorders.

| Compelling Lead Product Candidate: REL-1017 | Currently in Phase 2a trial for treatment of Major Depressive Disorder (MDD)  
Significant potential in multiple additional indications, including Rett Syndrome |
|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| Additional Valuable Pipeline Assets for Partnering | REL-1015 Levocap ER – Phase 3-ready abuse deterrent formulation of highly-potent opioid  
REL-1028 BuTab - oral formulation of modified release buprenorphine for chronic pain  
REL-1021 MepiGel - Novel topical version of local anesthetic mepivacaine for treatment of painful peripheral neuropathies |
| Corporate Summary | Cash of $2.4M at 12/31/18  
Shares Outstanding – ~30.3 million  
Public since 2014; Headquartered in NYC  
Lean and efficient operations – 3 full time employees and strong network of Scientific Advisors |
Highly-compelling lead product opportunity w/ REL-1017

Phase 2a MDD trial ongoing; data expected H1 ‘19
Strong rapid efficacy signal in depression established in three independent animal models
Strong IP position around REL-1017 with protection to the mid-2030s

REL-1017 has potential in multiple underserved markets

~32M Americans suffered from MDD in 2017
Rett Syndrome is an orphan disease affecting ~15k patients with no currently approved treatment

Management team and scientific advisors have considerable CNS expertise

Johnson & Johnson, Eli Lilly, Pfizer, Shire, Harvard, Yale, Cornell

Multiple key catalysts expected over next 12-18 months

MDD Phase 2a data
Rett Syndrome animal proof-of-concept data
NASDAQ listing
## Management Team and Key Scientific Advisors

### Management

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sergio Traversa</td>
<td>PharmD, MBA, Chief Executive Officer and Interim Chief Financial Officer</td>
</tr>
<tr>
<td>Ottavio Vitolo</td>
<td>Senior Vice President, Head of R&amp;D and Chief Medical Officer</td>
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### Advisors

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
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</thead>
<tbody>
<tr>
<td>Maurizio Fava</td>
<td>Scientific Advisor</td>
</tr>
<tr>
<td>Charles Inturrisi</td>
<td>Scientific Advisor</td>
</tr>
<tr>
<td>Paolo Manfredi</td>
<td>Scientific Advisor</td>
</tr>
<tr>
<td>Michael Bell</td>
<td>Financial Advisor</td>
</tr>
</tbody>
</table>
# Development Timeline REL-1017

## Indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q1 Q2 Q3 Q4</td>
<td>Q1 Q2 Q3 Q4</td>
</tr>
<tr>
<td>Major Depressive Disorder</td>
<td></td>
<td>REL-1017 ongoing Phase 2a</td>
</tr>
<tr>
<td>Restless Leg Syndrome*</td>
<td></td>
<td>Preclinical Formulation Phase 2 IND preparation</td>
</tr>
<tr>
<td>Rett Syndrome*</td>
<td></td>
<td>Preclinical proof of concept-IND enabling studies</td>
</tr>
</tbody>
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* Depends on preclinical results, FDA feedback and available capital resources.
Dextromethadone (REL-1017)
as a Treatment for Major Depressive Disorder
An Effective Treatment for Treatment-Resistant Depression (TRD) Remains a High Unmet Need

3. Estimated based on %30 TRD prevalence
Expanding Focus on NMDA’s Role in Treatment of Depression

Johnson & Johnson is reinventing the party drug ketamine to treat depression.
Dextromethadone is an NMDAR antagonist with Significant Potential Advantages in the Treatment of Depression

**Novel Mechanism of Action**

Dextromethadone and other NMDA antagonists represent new approach to treating depression with MOA markedly different from currently approved drugs (SSRIs, SNRIs, TCAs, MAOIs, etc.)

**Rapid Onset**

Potential for faster onset of antidepressant activity – after 24 hours.

Currently approved products can take 2-4 weeks to show AD activity.

**D-methadone can address a high unmet need in MDD**

~65% MDD patients do not respond to first antidepressant treatment.

~30% MDD patients do not respond to up to 4 different antidepressant treatments

Potentially equal or superior efficacy with better safety profile than ketamine

D-Methadone Could Set a New Standard in Risk/Benefit for NMDAR Antagonists

- NMDAR antagonist ketamine is clinically effective, but with side-effects that limit clinical use.¹

- Dextromethadone is a non-competitive antagonist that antagonizes signaling only when the NMDA receptor is activated.

- Presents opportunity for equivalent or superior efficacy with reduced risk of off-target events.


³ Pharmaceuticals 2013, 6(2), 251-268; NMDA Receptor Modulators in the Treatment of Drug Addiction. SE Tomek, et al.
Strong Evidence of Efficacy in Three Depression Animal Models

Improved performance on the rat forced swim test 24 hours after d-methadone treatment

Forced Swim Test

* = p<0.05 compared to placebo group
Strong Evidence of Efficacy in Three Depression Animal Models

Improved performance on the rat FUST and the NSFT 24 hours after d-methadone treatment

Female Urine Smell Test

Novelty Suppressed Feeding Test

* = p<0.05 compared to placebo group - Dr. Ron Duman’s laboratory - Yale Medical School
D-Methadone Prevents the Behavioral Effects Induced by Chronic Unpredictable Stress (CUS) a Model of Depression and Antidepressant Response

D-methadone induces a rapid and sustained response not seen with traditional antidepressants
D-Methadone Increases Synaptic Protein Expression in the Rat Medial Prefrontal Cortex (mPFC)

Increased expression of synaptic proteins suggests d-methadone neurotrophic effect

Dr. Ron Duman’s Laboratory - Yale Medical School
### Phase 1 SAD and MAD Study Showed Favorable Safety and Tolerability Profile

<table>
<thead>
<tr>
<th>Single Ascending Dose (SAD) Study Design</th>
<th>Multiple Ascending Dose (MAD) Study Design</th>
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<tbody>
<tr>
<td><strong>Parallel group, double-blind, placebo controlled</strong></td>
<td><strong>Parallel group, double-blind, placebo controlled</strong></td>
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<tr>
<td><strong>Objectives</strong></td>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td>• Establish PK, PD and safety of single dose administration</td>
<td>• Establish PK, PD and safety of once daily, 10 day administration</td>
</tr>
<tr>
<td><strong>Treatment Administration</strong></td>
<td><strong>Treatment Administration</strong></td>
</tr>
<tr>
<td>• Cohorts 5, 20, 60, 100, 150, 200 mg</td>
<td>• Cohorts 25, 50, 75 mg</td>
</tr>
<tr>
<td>• N = 42</td>
<td>• N = 24</td>
</tr>
<tr>
<td><strong>Study Conclusions</strong></td>
<td><strong>Study Conclusions</strong></td>
</tr>
<tr>
<td>• MTD = 150 mg (single dose)</td>
<td>• Doses up to 75mg per day well tolerated</td>
</tr>
<tr>
<td>• PK demonstrated linear proportionality of $C_{\text{max}}$ and $AUC_{0-\text{inf}}$ vs. dose</td>
<td>• Dose proportionality was demonstrated for the single-dose parameters $C_{\text{max}}$ and $AUC_{\text{tau}}$ on Day 1 and for the steady state parameters $C_{\text{max}}$, $AUC_{\text{tau}}$, and $C_{\text{ss}}$ on Day 10</td>
</tr>
<tr>
<td>• No clinically significant opioid effects of dextromethadone up to 150 mg</td>
<td></td>
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D-methadone Significantly Increased BDNF Plasma Levels Compared to Placebo in MAD Study

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Average Plasma BDNF ng/ml (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-treatment</td>
</tr>
<tr>
<td>d-Methadone</td>
<td>0.84 (0.60)</td>
</tr>
<tr>
<td>Placebo</td>
<td>0.81 (0.38)</td>
</tr>
</tbody>
</table>
REL-1017-202 – Phase 2a Study Will Determine Safety and Tolerability, PK and Efficacy in Treatment Resistant Depression

- RDPC study of 7-day dosing at 25 mg and 50 mg QD as adjunctive therapy in MDD subjects who did not respond to antidepressants
- 11 US sites
- Dose selection based on effect measured in pre-clinical studies
- ~60 subjects randomized to three arms:
  - placebo, 25 mg/day, 50 mg/day
- **Primary Endpoints**
  - safety and tolerability
- **Secondary Endpoints**
  - efficacy (MADRS, SDQ, CGI)
  - pharmacokinetic profile
## Potential Competitive Advantages of Dextromethadone

### Safety and Tolerability, Oral Dosing, Outpatient Administration

<table>
<thead>
<tr>
<th>Compound (Company)</th>
<th>Mechanism of Action</th>
<th>Delivery</th>
<th>Current Clinical Stage</th>
<th>Dosing Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextromethadone (Relmada)</td>
<td>Non-competitive NMDA channel blocker</td>
<td>Oral</td>
<td>Phase II</td>
<td>Once Daily</td>
</tr>
<tr>
<td>Esketamine (Janssen/J&amp;J)</td>
<td>Multimodal (NMDA+others)</td>
<td>Nasal (administered in clinic)</td>
<td>Approved and launched</td>
<td>Biweekly</td>
</tr>
<tr>
<td>AXS-05 DM 45 mg + BUP 105 mg (Axsome)</td>
<td>Multimodal (NMDA+others)</td>
<td>Oral</td>
<td>Phase III</td>
<td>Twice daily</td>
</tr>
<tr>
<td>GLYX-13 (Allergan)</td>
<td>Modulation of glycine site of NMDA</td>
<td>IV (modified peptide)</td>
<td>Failed in Phase III</td>
<td>Weekly</td>
</tr>
<tr>
<td>AV-101, L-4-chlorokyurenine (VistaGen)</td>
<td>Modulation of glycine site of NMDA</td>
<td>Oral (prodrug)</td>
<td>Phase II (failed first Phase II)</td>
<td>Once Daily</td>
</tr>
</tbody>
</table>
Corporate Information
Upcoming Milestones

- **H1 2019**: NASDAQ listing
- **Q2/Q3 2019**: Phase 2 TRD data
- **2019**: Rett Syndrome proof-of-concept animal data
- **H1 2020**: Phase 2 enabling IND in Rett Syndrome filed
Financial Overview

**Cash & Equivalents**
(as of 12/31/18)  
$2.4 million

**Common Shares Outstanding**
(as of 2/28/19)  
~30.3 million

**52-Week Stock Price Range**
$0.61 to $1.94
Highly-compelling lead product opportunity w/ REL-1017

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