Safe Harbor Statement

To the extent that statements contained in this press release are not descriptions of historical facts regarding Marinus, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Words such as “may”, “will”, “expect”, “anticipate”, “estimate”, “intend”, “believe”, and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Examples of forward-looking statements contained in this press release include, among others, statements regarding our interpretation of preclinical studies, development plans for our product candidate, including the development of dose forms, the clinical trial testing schedule and milestones, the ability to complete enrollment in our clinical trials, interpretation of scientific basis for ganaxolone use, timing for availability and release of data, the safety, potential efficacy and therapeutic potential of our product candidate and our expectation regarding the sufficiency of our working capital. Forward-looking statements in this release involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in the conduct of future clinical trials, the timing of the clinical trials, enrollment in clinical trials, availability of data from ongoing clinical trials, expectations for regulatory approvals, the attainment of clinical trial results that will be supportive of regulatory approvals, and other matters, including the development of formulations of ganaxolone, and the availability or potential availability of alternative products or treatments for conditions targeted by the company that could affect the availability or commercial potential of our drug candidates. Marinus undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see Marinus’ 10-K dated March 12, 2019 and other filings by the company with the U.S. Securities and Exchange Commission. You may access these documents for free by visiting EDGAR on the SEC web site at www.sec.gov.
Strategic Overview

**Ganaxolone**: a positive allosteric GABA<sub>A</sub> modulator with a well-defined MOA to treat patients suffering from epilepsy and neuropsychiatric disorders.

**Clinical development** includes late stage orphan diseases and large market opportunities with few or no treatment options.

**Multiple dose formulations** IV and oral – to meet the needs of adult and pediatric patients in acute and chronic care settings.

**Extensive safety record** in more than 1,600 subjects both pediatric and adult, at therapeutically relevant dose levels for up to two years.
Ganaxolone (GNX) Targets Synaptic & Extrasynaptic GABA<sub>A</sub> Receptors

GNX is a synthetic analog of allopregnanolone

GNX is designed to modulate both synaptic and extrasynaptic GABA<sub>A</sub> receptors to calm over-excited neurons
## Ganaxolone Development Pipeline

<table>
<thead>
<tr>
<th>GANAXOLONE</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>MILESTONES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orphan Refractory Seizure Programs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDKL5 Deficiency Disorder</td>
<td></td>
<td></td>
<td></td>
<td>Data Mid 2020</td>
</tr>
<tr>
<td>PCDH19-Related Epilepsy</td>
<td></td>
<td></td>
<td></td>
<td>Data 2021</td>
</tr>
<tr>
<td>Refractory Status Epilepticus</td>
<td></td>
<td></td>
<td></td>
<td>Data Q3 2019</td>
</tr>
<tr>
<td>Depressive Disorders*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe PPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRD</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*Pending regulatory interactions and funding
Orphan Refractory Epilepsy Indications
Refractory Status Epilepticus (RSE)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Brain trauma, tumor, stroke, infection, among others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Seizure lasting &gt;5 minutes or several seizures within 5 minutes with no recovery between seizures</td>
</tr>
<tr>
<td>Prevalence</td>
<td>~45,000 patients fail 1st line treatment (US)¹, ² Orphan Drug indication</td>
</tr>
<tr>
<td>Treatments</td>
<td>Few treatments available \nBenzodiazepines (1st line) \nPhenytoin/Fosphenytoin, valproic acid, levetiracetam, lacosamide (2nd line)</td>
</tr>
<tr>
<td>Mechanistic Rationale</td>
<td>Synaptic receptors internalized and unavailable with prolonged seizures - need to modulate extrasynaptic receptors \nProof of mechanism seen with allopregnanolone in P2 study</td>
</tr>
</tbody>
</table>

²LexisNexis PxDx Medical Claims data 2015
Care Continuum: Vision for Treating Patients with SE

- **1st line**
  - Benzodiazepine Administered

- **2nd line**
  - IV AED’s

- **3rd line**
  - Traditional Anesthetics

- **4th line**
  - IV Ketamine and others

**40% death rate**
when progressing to 3rd line treatment
Rationale For Use of Ganaxolone in RSE

• GNX works on extrasynaptic GABA_\text{A} receptors, which are still functional after prolonged seizures with RSE

• Efficacy seen in benzodiazepine-resistant SE rat model

• Evidence of rapid effects on EEG after IV infusion (propofol-like effects) - PK/PD study in healthy volunteers

• Lower risk of respiratory depression (unlike propofol) - large therapeutic window in both animals and healthy volunteers

• Several IV formulations of AEDs but none approved in RSE
### Key Differences of Sage SRSE Trial vs. Marinus RSE Trial

<table>
<thead>
<tr>
<th></th>
<th>GNX</th>
<th>BRX</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Population</strong></td>
<td>More likely to respond than SRSE patients via engagement of the GABA receptor</td>
<td>SRSE: medically more difficult to treat than RSE; seizures less likely to respond than RSE patients</td>
</tr>
<tr>
<td><strong>Treatment Algorithm</strong></td>
<td>Failed one 2\textsuperscript{nd} line IV AED. Goal is to prevent proceeding to IV anesthetics</td>
<td>On IV anesthetics with goal to remove IV anesthetics</td>
</tr>
<tr>
<td><strong>Dose w/ targeted plasma level</strong></td>
<td>(~100\text{ng/mL})</td>
<td>(~50-100\text{ng/mL})</td>
</tr>
<tr>
<td><strong>Efficacy Objectives</strong></td>
<td>Block seizures and prevent progression of treatment</td>
<td>Prevent relapse to IV anesthetics</td>
</tr>
</tbody>
</table>
Phase 2 Open-Label Trial Design in RSE

Evaluate safety, tolerability, efficacy, and pharmacokinetics of GNX IV in RSE patients

**Trial Details**
- ~10-15 sites in US
- Up to 20 patients
- Open-label, PK group, dose-finding
- Top-line data expected Q3 2019

**Efficacy Objectives**
- Time to onset and # patients who do not require an IV anesthetic drug within the first 24 hours

---

Failed 1\textsuperscript{st} line benzodiazepines (not required)
Failed one 2\textsuperscript{nd} line IV AED

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**Screening**

**Treatment Period**
- Loading Dose
- Maintenance
- Taper
  - Bolus plus continuous infusion
  - Potential for 2-4 day infusion
  - 12 hour taper

**Follow up Period**
- Day After
- 3 Week FU
- 24hr in patient FU
- Weeks 2,3,4 FU

---

**RSE PATIENTS**
CDKL5 Deficiency Disorder (CDD) – Rare, Serious Epileptic Condition

<table>
<thead>
<tr>
<th>Cause</th>
<th>Mutation of the cyclin-dependent kinase-like 5 (CDKL5) gene, located on the X chromosome</th>
</tr>
</thead>
</table>
| Symptoms | Early-onset, treatment refractory seizures, & severe neuro-developmental delay  
Most can’t walk, talk or care for themselves  
Suffer from scoliosis, visual impairment, gastrointestinal difficulties & sleeping disorders |
| Prevalence | ~5-7K children US and EU5, predominantly affects females  
Genetic testing available  
Orphan Drug designation |
| Treatments | No approved treatments |
| Mechanistic Rationale | Potential GABA_A dysfunction |
### CDD - Phase 2 Trial Design

**Trial Details**
- 2 sites in US; 1 site in Italy
- 6 females, 1 male – ages 2-16
- Confirmed CDKL5 mutation, stable background treatment, >4 seizures per 28-day period in baseline

**Baseline Characteristics**
- Median number seizures - 343 (range 101 to 584)
- Median number seizure-free days - 4 (range 0 to 9)

**Endpoints**
- Primary: % change in seizure frequency per 28 days relative to baseline
- Secondary: % increase in seizure free days from baseline, safety and tolerability, CGI

**Baseline**
- 12 weeks

**Treatment**
- 26 weeks Ganaxolone
  - 600 mg 3x/day maximum

**Open-Label Phase**
- 52 weeks
  - 600 mg 3x/day maximum
**Efficacy & Safety in Phase 2 Trial in CDD**

44.4% Reduction in seizure frequency

- Patients experienced a median ‘minimally improved’ rating on CGI-I scale (Clinician rated) correlated with % change in seizure frequency
- GNX was generally safe and well-tolerated (no SAEs). No reports of somnolence or dizziness.
  - 2 of the 7 patients discontinued prior to completing treatment due to lack of efficacy

**Percent change in seizure frequency at day 28**

*excludes 6 days of data from one subject deemed unreliable by the PI and caregiver*

**Correlation between change in seizure frequency and CGI-I scale**

1: very much improved
2: much improved
3: minimally improved
4: no change
5: minimally worse
6: much worse
7: very much worse
Durable Responses Seen out to 18 Months in CDD Phase 2 Extension

- 4 of 7 subjects entered the extension period
- GNX demonstrated preliminary evidence of sustained, long-term (out to 18 months) efficacy in a small cohort of CDD patients
- Efficacy of existing AEDs and the ketogenic diet in patients with the CDKL5 mutation is low and the durability of effect is short¹

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**Patients Entering OLE**

<table>
<thead>
<tr>
<th>Subject</th>
<th>% Change in Seizure Frequency (per 28 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-100</td>
</tr>
<tr>
<td>2</td>
<td>-80</td>
</tr>
<tr>
<td>3</td>
<td>-60</td>
</tr>
<tr>
<td>4</td>
<td>-40</td>
</tr>
</tbody>
</table>

**54%**

Median change in seizure frequency at 6 months

---

**66%**

Median seizure frequency improved to 66% (as of 12/31)

---

Global Phase 3 Pivotal Study Design

Trial Details

~43 global sites; US, Europe & others

Ages 2-21, 16 major motor drop seizures/month; up to 4 concomitant AEDs

Endpoints

Primary Endpoint: % change in seizure frequency

Non-seizure secondary outcome measures: Behavioral/neuropsychiatric changes correlated with domains of attention & sleep
## PCDH19-Related Epilepsy – Rare, Serious Epileptic Condition

<table>
<thead>
<tr>
<th><strong>Cause</strong></th>
<th>Inherited mutation of protocadherin 19 (PCDH19) gene. Located on X chromosome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>Early-onset seizures, cognitive and sensory impairment, &amp; psychiatric and behavioral disorders. Seizures last from days to weeks; sensitive to fever</td>
</tr>
<tr>
<td><strong>Prevalence</strong></td>
<td>Affects ~10-12K children US and EU5&lt;br&gt;Predominantly females&lt;br&gt;Genetic testing becoming more readily available&lt;br&gt;Orphan Drug designation</td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td>No approved treatments. No previous clinical trials.</td>
</tr>
<tr>
<td><strong>Mechanistic Rationale</strong></td>
<td>Associated with low levels of allopregnanolone(^1) and potential GABA(_A) dysfunction</td>
</tr>
</tbody>
</table>

\(^1\)Gecez, et.al, Human Molecular Genetics, 2015
Significant Seizure Reduction in PCDH19 Phase 2 Trial in Patients with Low Allo Levels

- 25% decrease in median seizure frequency reported in Phase 2 \((n=11)\)
- Stratification of patients by baseline plasma Allo levels identifies a subpopulation with improved efficacy on GNX
- When comparing seizure frequency at 6 months to baseline:
  - The biomarker+ group (low Allo) significantly improved
  - The biomarker- group (high Allo) did not significantly deteriorate

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>N=</th>
<th>Median % change in seizure rates</th>
<th>P-value (Wilcoxon)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomarker + (Allo-S &lt;2,500 pg mL(^{-1}))</td>
<td>7</td>
<td>-50%</td>
<td>P=0.02</td>
</tr>
<tr>
<td>Biomarker – (Allo-S &gt;2,500 pg mL(^{-1}))</td>
<td>4</td>
<td>84%</td>
<td>P=0.63</td>
</tr>
</tbody>
</table>
**Biomarker Stratified Phase 3 Pivotal Study in PCDH19**

**Trial Details**
- ~35 global sites; US, Europe & others
- Ages 1-17, 8 or more seizures in 8 weeks; failed 2 or more AEDs
- Data expected 2021

**Endpoint**
- Primary Endpoint: % change in seizure frequency

---

Primary efficacy analyses will be conducted using this cohort.

PCDH19 (all-subjects) n~ 70

- **Low Allo-S Biomarker +**
  - n = 50
  - R 1:1
  - Placebo
  - Ganaxolone
    - Up to 600 mg liquid suspension 3x/day

- **High Allo-S Biomarker -**
  - n~ 20
  - R 1:1
  - Placebo
  - Ganaxolone
    - Up to 600 mg liquid suspension 3x/day

---

Trial Details

~35 global sites; US, Europe & others

Ages 1-17, 8 or more seizures in 8 weeks; failed 2 or more AEDs

Data expected 2021

**Endpoint**

Primary Endpoint: % change in seizure frequency
Broad Potential for Biomarker Driven Strategy in Rare Genetic Epilepsies

PCDH19 Phase 2 data patient stratification resulted in identification of subpopulation of patients with improved GNX responses: low Allo-S patients

Based on the strength of these data, retrospective Allo-S biomarker analyses are being conducted to identify other rare genetic epilepsies which may benefit from biomarker stratification

Depending on results, additional biomarker trials for rare genetic epilepsies may be started
Allo-S as Potential Biomarker Across Various Genetic Epilepsies

Patients / subjects aged 1 - 14

Allo pregnanolone-sulfate (ng mL⁻¹)

Control  PCDH19  CDD  Undisclosed
Postpartum Depression
PPD Market Segmentation and Value

Total Annual U.S. PPD Prevalence*
~550K Patients (100%)

10% - 20% of moderate and severe PPD patients require hospitalization

*PPD prevalence estimated at ~13% of total 2018 live births of 4.1MM – RBC Analyst report 10/18/18
Systematic Evaluation of Ganaxolone Dosing Regimens for PPD

**Part 1**
48-hour IV + 12-hour taper

**Part 2**
6-hour IV + 900mg oral

- Early onset of action
- Good safety
- Attractive efficacy

**Low Dose**
Oral 675mg

**High Dose**
Oral 675mg/BID for 2 days then 1125 mg for 26 days
IV Ganaxolone: Competitive Profile for Onset of Action, Safety/Tolerability and Ease of Administration

PART 1
48 hour plus 12 hour taper IV provided rapid onset of action that was durable through one month after stopping treatment

Dose response observed

Multiple efficacy scales (clinician- and patient-rated) are consistent with HAM-D17 reduction

PART 2
6 hour IV followed by oral dosing provided rapid onset of action with clinically meaningful HAM-D17 reductions at 6 and 24 hours

Multiple efficacy scales (clinician- and patient-rated) are consistent with HAM-D17 reduction, particularly in Per Protocol Population

Least-squares (LS) mean reductions reported
Efficacy Results: HAM-D17 Mean Change from Baseline

HAM-D17 Mean Change from Baseline
ITT Population

HAM-D17 Mean Change from Baseline
Per Protocol Population

Least-squares (LS) mean reductions reported
Part 2 Efficacy Results: CGI-I Mean Change from Baseline

CGI-I Score
ITT Population

CGI-I Score
Per Protocol Population

Least-squares (LS) mean reductions reported
HAM-D17 Response and Remission Rates - ITT Population

**HAM-D17 Response Rates**

<table>
<thead>
<tr>
<th>Time</th>
<th>Ganaxolone (%)</th>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 hours</td>
<td>6%</td>
<td>38%</td>
</tr>
<tr>
<td>14 days</td>
<td>50%</td>
<td>46%</td>
</tr>
<tr>
<td>28 days</td>
<td>57%</td>
<td>47%</td>
</tr>
</tbody>
</table>

**Response: HAM-D17 decrease > 50%**

<table>
<thead>
<tr>
<th>Time</th>
<th>n = 17</th>
<th>n = 16</th>
<th>n = 16</th>
<th>n = 13</th>
<th>n = 14</th>
<th>n = 15</th>
</tr>
</thead>
</table>


**HAM-D17 Remission Rates**

<table>
<thead>
<tr>
<th>Time</th>
<th>Ganaxolone (%)</th>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 hours</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>14 days</td>
<td>25%</td>
<td>23%</td>
</tr>
<tr>
<td>28 days</td>
<td>43%</td>
<td>27%</td>
</tr>
</tbody>
</table>

**Remission: HAM-D17 > 7 points**

<table>
<thead>
<tr>
<th>Time</th>
<th>n = 17</th>
<th>n = 16</th>
<th>n = 16</th>
<th>n = 13</th>
<th>n = 14</th>
<th>n = 15</th>
</tr>
</thead>
</table>
Amaryllis – Oral Dosing Shows Encouraging Efficacy in High Dose Cohort

Baseline HAM-D17 scores: low dose - 25.5, high dose - 25.4

<table>
<thead>
<tr>
<th>Day</th>
<th>Low dose (675mg)</th>
<th>High dose (1125mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 2</td>
<td>0.8</td>
<td>2.7</td>
</tr>
<tr>
<td>Day 15</td>
<td>9.8</td>
<td>9.3</td>
</tr>
<tr>
<td>Day 29</td>
<td>12.2</td>
<td>14.5</td>
</tr>
</tbody>
</table>

n = 25

n = 43
Favorable Safety Profile Across Regimens

01 Ganaxolone appeared safe and well-tolerated

02 Most common reported AEs were dizziness and sedation

03 No SAEs, no discontinuations due to a TRAE

04 Consistent with prior studies, no reports of syncope or loss of consciousness
Multiple Milestones

**2019 – Q2**
- Initiated enrollment in Violet Study

**2019 – Q3**
- Ganaxolone IV to oral data from part 2 of Magnolia Study
- Ganaxolone oral data from Amaryllis Study
- Ganaxolone IV data from Phase 2 in RSE

**2019 - 2H**
- Announce next program in pediatric epilepsy
- Announce next steps in depression
- Announce next steps in RSE
<table>
<thead>
<tr>
<th>Patent Portfolio: Multiple Layers Of Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orphan Drug protection (SE, CDD, PCDH19)</td>
</tr>
<tr>
<td>IV formulations and methods of use applications filed</td>
</tr>
<tr>
<td>IV formulations containing exclusively in-licensed proprietary captisol product</td>
</tr>
<tr>
<td>Nanoparticle formulation patents issued in the US (e.g., # 7,858,609, #8,022,054), Australia, Canada, China, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, &amp; South Korea - patent life 2026 plus patent term restoration</td>
</tr>
<tr>
<td>Synthesis patents issued in US, Australia, China, Europe, Japan, Mexico &amp; New Zealand</td>
</tr>
<tr>
<td>NCE market exclusivity</td>
</tr>
</tbody>
</table>
Ganaxolone’s Potential to Offer Continuity of Care

**Status Epilepticus, Pediatric Seizure Disorders, Postpartum Depression**

- Attractive orphan indications & large market indications
- Significant unmet medical need – no or few treatment options
- Targeted patient populations – understood dysfunctional GABA system
- IV to convenient oral – continuity of treatment from hospital to outpatient transition

**New MOA, Differentiated, Convenient Dosing, Targeted CNS Therapy**
Thank You