Forward Looking Statements & Safe Harbor

Certain information contained in this presentation may include “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. We may, in some cases, use terms such as “predicts,” “believes,” “potential,” “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. In particular, the Company’s statements regarding trends and potential future results are examples of such forward-looking statements. The forward-looking statements include risks and uncertainties, including, but not limited to, the continued commercial success of our Sunosi® and Auvelity® products and the success of our efforts to obtain any additional indication(s) with respect to solriamfetol and/or AXS-05; the success, timing and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation, pace of enrollment and completion of the trials (including our ability to fully fund our disclosed clinical trials, which assumes no material changes to our currently projected revenues or expenses), futility analyses and receipt of interim results, which are not necessarily indicative of the final results of our ongoing clinical trials, and the number or type of studies or nature of results necessary to support the filing of a new drug application (“NDA”) for any of our current product candidates; our ability to fund additional clinical trials to continue the advancement of our product candidates; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration (“FDA”) or other regulatory authority approval of, or other action with respect to, our product candidates; whether issues identified by FDA in the complete response letter may impact the potential approvability of the Company’s NDA for AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment for the MOMENTUM clinical trial; the Company’s ability to successfully defend its intellectual property or obtain the necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company’s research and development programs and collaborations; the success of the Company’s license agreements; the acceptance by the market of the Company’s products and product candidates, if approved; the Company’s anticipated capital requirements, including the amount of capital required for the continued commercialization of Sunosi and Auvelity and for the Company’s commercial launch of its other product candidates, and the potential impact on the Company’s anticipated cash runway; unforeseen circumstances or other disruptions to normal business operations arising from or related to COVID-19; and other factors, including general economic conditions and regulatory developments, not within the Company’s control. The factors discussed herein could cause actual results and developments to be materially different from those expressed in or implied by such statements. The forward-looking statements are made only as of the date of this press release and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

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Rapidly Growing, CNS-Focused Biopharma

2 Marketed Products

8 New Target Indications

5 Late-stage Product Candidates

162 Million Potential Patients Targeted
# Leading CNS Portfolio

<table>
<thead>
<tr>
<th>Product</th>
<th>MOA</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA</th>
<th>Marketed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auvelity</td>
<td>NMDA receptor antagonist and sigma-1 receptor agonist, aminoketone CYP2D6 inhibitor</td>
<td>Major Depressive Disorder (MDD)</td>
<td></td>
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<tr>
<td>SUNOSI</td>
<td>Dual-acting dopamine and norepinephrine reuptake inhibitor (DNRI) and TAAR1 agonist</td>
<td>Excessive Daytime Sleepiness (EDS) Associated with Narcolepsy or Obstructive Sleep Apnea (OSA)</td>
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</tr>
<tr>
<td>AXS-05</td>
<td>NMDA receptor antagonist and sigma-1 receptor agonist, aminoketone CYP2D6 inhibitor</td>
<td>Alzheimer's Disease Agitation (ADA)</td>
<td></td>
<td>FDA Breakthrough Therapy Designation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AXS-07</td>
<td>MoSEIC™ COX-2 pref. inhibitor + 5-HT1B/1D agonist</td>
<td>Smoking Cessation</td>
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</tr>
<tr>
<td>AXS-12</td>
<td>Highly selective NE reuptake inhibitor</td>
<td>Migraine</td>
<td></td>
<td></td>
<td>FDA Orphan Drug Designation</td>
<td></td>
</tr>
<tr>
<td>AXS-14</td>
<td>Enantiomerically purified highly selective NE reuptake inhibitor</td>
<td>Narcolepsy</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>solriamfetol</td>
<td>Dual-acting dopamine and norepinephrine reuptake inhibitor (DNRI) and TAAR1 agonist</td>
<td>Attention Deficit Hyperactivity Disorder (ADHD)</td>
<td>Binge Eating Disorder (BED)</td>
<td>Shift Work Disorder (SWD)</td>
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<td></td>
</tr>
</tbody>
</table>

AXS-05, AXS-07, AXS-12, AXS-14, and solriamfetol for ADHD are not approved by the FDA, and their safety and effectiveness have not been established.

Abbreviations:
- CNS = Central Nervous System
- MOA = Mechanism of Action
- NMDA = N-Methyl-D-aspartate
- COX-2 = Cyclooxygenase-2
- 5-HT = 5-Hydroxytryptamine
- NE = Norepinephrine
- CYP2D6 = Cytochrome P450 Family 2 Subfamily D Member 6
- MoSEIC = Molecular Solubility Enhanced Inclusion Complex


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Marketed and Late-stage CNS Portfolio with Potential to Impact the Lives of >162M U.S. Patients

Abbreviations:
MDD = Major Depressive Disorder; OSA = Obstructive Sleep Apnea; AD = Alzheimer’s Disease; ADHD = Attention Deficit Hyperactivity Disorder; BED = binge eating disorder; SWD = shift work disorder
Potentially Marketed Indications by 2025

- AXS-12: Narcolepsy
- AXS-14: Fibromyalgia
- AXS-07: Migraine
- AXS-05: AD agitation

**AUVELITY®**
(dextromethorphan HBr and buproprion HCl)
extended-release tablets 45mg/105mg

**SUNOSI.**
(solriamfetol)
75, 150 mg tablets

Excessive daytime sleepiness
associated with narcolepsy or
obstructive sleep apnea

Major depressive disorder

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Marketed Products
Treating adult patients living with major depressive disorder

First and only oral rapid acting NMDA receptor antagonist for MDD\(^1\)-\(^2\)

New approach to treat MDD that is different from other oral antidepressants approved in more than 60 years\(^1\)-\(^3\)

Rapid symptom improvement starting at Week 1, sustained at Week 6 vs placebo\(^1\)

Rapid remission as early as Week 2, sustained and increased vs control through Week 6\(^4\)

Abbreviations: TRx = total prescriptions; NMDA = N-Methyl-D-aspartate; MDD = major depressive disorder


Source: Symphony METYS

© Axsome Therapeutics, Inc.
Improving wakefulness in adult patients with EDS associated with narcolepsy or OSA

First and only DNRI indicated for EDS associated with narcolepsy or OSA

First and only wakefulness promoting agent proven to improve wakefulness through 9 hours

90% of patients reported feeling better with Sunosi 150 mg

Quarterly nTRx Launch to Date

Source: Symphony METYS. nTRx normalizes number of pills in each Trx for 30-day period.

Abbreviations: nTRx = normalized total prescriptions; EDS = excessive daytime sleepiness; OSA = obstructive sleep apnea; DNRI = dopamine-norepinephrine reuptake inhibitor

Development Pipeline
AXS-05
(dextromethorphan-bupropion)

a new approach to treating multiple CNS conditions
Alzheimer’s Disease Agitation:
High Unmet Medical Need, Novel Approach

- Agitation is seen in up to 70% of Alzheimer’s disease patients\(^1,2\)
- Associated with accelerated cognitive decline, earlier nursing home placement, increased mortality risk\(^4,5\)
- High unmet medical need for safe and effective options
- AXS-05 pharmacology relevant to implicated disease pathways

14 million by 2060\(^3\)

6 million patients with AD in 2020\(^1\)

>70%

Suffer from agitation

Brain regions implicated in AD agitation\(^6\)

AXS-05 pharmacological actions\(^7,8\)


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Alzheimer’s Disease Agitation: Clinical Results and Program Status

- Primary endpoints met in two controlled trials:
  - ADVANCE-1 Phase 2/3, parallel group trial
  - ACCORD Phase 3, randomized withdrawal trial
- ADVANCE-2 Phase 3 trial ongoing, with expected completion by 1H 2024
- FDA Breakthrough Therapy Designation received

Abbreviations:
CMAI = Cohen Mansfield Agitation Inventory
Alzheimer’s Disease Agitation:
ADVANCE-2 Phase 3 Trial

A Phase 3 trial to assess efficacy and safety of AXS-05 as compared to placebo in the treatment of Alzheimer’s disease agitation.

- **Primary Endpoint:** Efficacy of AXS-05 compared to placebo on the change from baseline in CMAI total score
- **Key Inclusion Criteria:**
  - Male or female 65-90 years old
  - Diagnosis of probable AD and of clinically significant agitation resulting from probable AD
- **Target Enrollment:** 350
- **Topline Data:** 1H 2024
Smoking Cessation

Fast Facts

• Smoking is single largest cause of preventable death in the U.S.\(^1\)

• 70% of smokers want to quit\(^2\)

• Only 3-5% who attempt to quit without assistance are successful for 6-12 months\(^2\)

AXS-05 Key Updates

• AXS-05 represents a potentially new mechanism of action for smoking cessation

• Positive FDA Pre-IND meeting guidance received from the FDA – can proceed to pivotal Phase 2/3 trial

• Planned trial initiation in 4Q 2023 or 1Q 2024

Abbreviations: NMDA = N-methyl D-aspartate
AXS-07
(MoSEIC™ meloxicam-rizatriptan)

a multi-mechanistic approach to treating migraine
Migraine: Significant Need for More Efficacious Treatments

- Unmet need for improved efficacy in migraine: disability on par with dementia, quadriplegia, active psychosis\(^1,2\):
  - >70% not fully satisfied with current treatment
  - ~80% would try a new therapy

- $78 billion direct and indirect costs in the U.S. each year\(^3\)
- Mechanisms of AXS-07 address multiple disordered physiological processes observed during migraine attacks

Migraine: Clinical Results and Program Status

• Rapid and sustained efficacy as compared to placebo and active comparator rizatriptan, in three positive Phase 3 trials:
  • MOMENTUM trial, in patients with history of inadequate response, vs. placebo and rizatriptan
  • INTERCEPT trial, in early treatment, vs. placebo
  • MOVEMENT trial, long-term open-label treatment, up to 12 months
• Class 2 NDA resubmission anticipated in the first half of 2024

INTERCEPT Study: Headache Pain Freedom
AXS-12
(reboxetine)

a potentially new treatment option for narcolepsy
Narcolepsy

- Narcolepsy is a debilitating disorder characterized by excessive daytime sleepiness and cataplexy, with limited treatment options

1. 185,000 patients in the U.S. 70% suffer from cataplexy

- Loss of excitatory hypocretin/orexin neurons in the brain lead to dysregulation of norepinephrine resulting\(^1\):
  - Loss of muscle tone while awake (cataplexy)
  - Decreased wakefulness during the day (EDS)
- AXS-12 (reboxetine) improves regulation of norepinephrine signaling in narcolepsy

Narcolepsy:
Clinical Results and Program Status

• Positive Phase 2 results with AXS-12
  • Significant reduction in cataplexy attacks
  • Significant improvement in excessive daytime sleepiness
  • Significant improvement in cognitive function
• SYMPHONY Phase 3 trial ongoing, with expected completion in 4Q 2023
Narcolepsy:
SYMPHONY Phase 3 Trial

A Phase 3 trial to assess efficacy and safety of AXS-12 as compared to placebo in the treatment of cataplexy in narcolepsy.

- **Primary Endpoint:** Change in the frequency of cataplexy attacks
- **Key Inclusion Criteria:**
  - Male or female 15-75 years old
  - Primary diagnosis of narcolepsy with cataplexy
- **Trial Completion:** expected in 4Q 2023
AXS-14 (esreboxetine) a potentially new treatment option for fibromyalgia
**Fibromyalgia**

- Debilitating, chronic, CNS disorder characterized by widespread pain, fatigue, disturbed sleep, depression, and cognitive impairment; ~90% affected are women

- Limited treatment options with only 3 approved agents: variable efficacy, and do not address all symptoms

- AXS-14 (esreboxetine) increases descending norepinephrine inhibition of pain signaling

---

1. Decision Resources Group 2019
Fibromyalgia:
Clinical Data and Program Status

• Positive Phase 3 and Phase 2 efficacy results with AXS-14 in fibromyalgia:
  • Significant reduction in pain and improvement in function
• NDA submission planned for fourth quarter of 2023 or first quarter 2024

### Phase 3 Efficacy Data

**Pain Reduction**
- Placebo: -1.11
- Esreboxetine 4 mg/day: -1.76
- Esreboxetine 8 mg/day: -1.85
- Esreboxetine 10 mg/day: -1.55

**Improvement in Function**
- Placebo: -6.41
- Esreboxetine 4 mg/day: -12.63
- Esreboxetine 8 mg/day: -13.42
- Esreboxetine 10 mg/day: -11.73

Scale: 0 = no pain; 10 = worst pain
Baseline Scores: Placebo 6.5, 4 mg 6.4, 8 mg 6.5, 10 mg 6.5
Baseline Scores: Placebo 55, 4 mg 54, 8 mg 55, 10 mg 56

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Solriamfetol

a potentially differentiated option for the treatment of CNS disorders
Attention Deficit Hyperactivity Disorder

- ADHD is a serious disorder characterized by inattention, hyperactivity or impulsivity

17.4 million
in the U.S. with ADHD

11.4 million
adults¹

6 million
youth²

- Associated with significant impairment in social, academic, and occupational functioning or development

- Solriamfetol targets neurotransmitter pathways in the brain implicated in ADHD³

Neurotransmitter Pathways Implicated in ADHD¹

Attention Deficit Hyperactivity Disorder:
FOCUS Phase 3 Trial

A Phase 3 trial to assess efficacy and safety of solriamfetol as compared to placebo in the treatment of ADHD.

- **Primary Endpoint:** Change in the Adult ADHD Investigator Symptom Report Scale (AISRS)
- **Key Inclusion Criteria:**
  - Adults, aged 18 to 55 inclusive.
  - Primary diagnosis of ADHD (inattentive, hyperactive, or combined subtype) using DSM-5 criteria and confirmed via the clinician administered ACDS
- **Target Enrollment:** 450
- **Topline Data:** 2H 2024
CNS portfolio with potential to generate total U.S. peak sales of up to $11.5B

<table>
<thead>
<tr>
<th>Program</th>
<th>Launch Year</th>
<th>Est. Peak U.S. Sales</th>
<th>Key Highlights</th>
</tr>
</thead>
</table>
| **MDD**          | 2022        | $1- $3B              | • Rapid and substantial efficacy, as early as week 1¹  
• First oral antidepressant with a new MOA in 60 years⁴⁻⁴ |
| **EDS associated with OSA and narcolepsy** | 2022        | $300 - $500M         | • First and only wakefulness promoting agent to improve wakefulness through 9 hours⁵  
• First FDA approved dual-acting DNRI to treat EDS in OSA or narcolepsy                      |
| **AXS-05**       | 2025 est.   | $1.5 - $3B           | • Rapid and substantial effect, as early as Week 2, with no associated cognitive impairment or sedation                                    |
| **AXS-05**       | TBD         | $0.5 - $1B           | • Represents a potentially new mechanism of action for smoking cessation  
• Planned Phase 2/3 trial initiation in 4Q 2023 or 1Q 2024                                         |
| **AXS-07**       | 2024 est.   | $0.5 - $1B           | • Rapid and consistent relief with reduced symptom recurrence                                                                                |
| **AXS-12**       | 2025 est.   | $0.5 - $1B           | • Improved cataplexy, EDS, and cognitive function                                                                                             |
| **AXS-14**       | 2025 est.   | $0.5 - $1B           | • Reduced pain with improved function with effect on fatigue                                                                                  |
| **Migraine**     | TBD         | $1B                  | • Phase 3 trial ongoing; topline data expected in 2H 2024                                                                                   |
| **Fibromyalgia** | TBD         | $1B                  |                                                                                                                                             |


Auvelity and Sunosi refs are on Slides 8 and 9, respectively.
## Strong Intellectual Property and Barriers to Entry

<table>
<thead>
<tr>
<th>Product</th>
<th>Intellectual Property and Barriers to Entry</th>
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</thead>
</table>
| Auvelity® | - Protected by a robust patent estate extending out to at least 2043; Multiple pending  
- Proprietary drug product formulation |
| Sunosi™ | - Protected by a robust patent estate extending out to at least 2040 / allowed claims out to 2042; Multiple pending  
- Proprietary drug substance and drug product formulation |
| AXS-05 | - >120 Issued U.S. Patents and >70 Issued O-U.S. Patents  
Claims extending to at least 2034-43; Multiple pending  
- Proprietary drug product formulation |
| AXS-07 | - >85 Issued U.S. Patents and >103 Issued O-U.S. Patents  
Claims extending to at least 2038; Multiple pending  
- Proprietary MoSEIC™ formulation and drug product formulation |
| AXS-12 | - Orphan Drug Designation  
- 6 issued patents; Claims extending to at least 2040; Multiple pending  
- Proprietary drug substance and drug product formulation |
| AXS-14 | - Pending U.S. patents  
- Proprietary drug substance and drug product formulation |
Financial Snapshot

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<thead>
<tr>
<th><strong>Cash Balance:</strong></th>
<th>$ 437.1 M</th>
</tr>
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<tbody>
<tr>
<td>(as of June 30, 2023)</td>
<td></td>
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<table>
<thead>
<tr>
<th><strong>Debt (Face Value):</strong></th>
<th>$ 180 M</th>
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<tr>
<td>(as of June 30, 2023)</td>
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<table>
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<tr>
<th><strong>Market Cap:</strong></th>
<th>$ 3.4 B</th>
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<td>(as of August 4, 2023)</td>
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<tr>
<th><strong>Shares Outstanding:</strong></th>
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<td>(as of June 30, 2023)</td>
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<thead>
<tr>
<th><strong>Options, RSUs, and Warrants Outstanding</strong>¹:</th>
<th>8.8 M</th>
</tr>
</thead>
</table>

¹ Consists of 7.93 M options, 0.78 M RSUs, and 0.080 M warrants

Runway to reach cash flow positivity, based on the current operating plan

Pro forma cash balance - $468.8 M
# Leadership Team

## Management

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herriot Tabuteau, MD</td>
<td>Founder &amp; CEO</td>
</tr>
<tr>
<td>Nick Pizzie, CPA, MBA</td>
<td>Chief Financial Officer</td>
</tr>
<tr>
<td>Mark Jacobson, MA</td>
<td>Chief Operating Officer</td>
</tr>
<tr>
<td>Hunter Murdock, JD</td>
<td>General Counsel</td>
</tr>
<tr>
<td>Lori Englebert, MBA</td>
<td>EVP, Commercial &amp; Business Dev.</td>
</tr>
</tbody>
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## Board of Directors

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roger Jeffs, PhD</td>
<td>CEO</td>
</tr>
<tr>
<td></td>
<td>Liquidia Corporation</td>
</tr>
<tr>
<td></td>
<td>Former President, Co-CEO, Director United Therapeutics Corp.</td>
</tr>
<tr>
<td></td>
<td>Prior positions at Amgen and Burroughs Wellcome</td>
</tr>
<tr>
<td>Mark Saad</td>
<td>Former CFO</td>
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<tr>
<td></td>
<td>Bird Rock Bio, Inc.</td>
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<tr>
<td></td>
<td>Former COO of the Global Healthcare Group at UBS</td>
</tr>
<tr>
<td>Mark Coleman, MD</td>
<td>Director of Clinical Services</td>
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<td></td>
<td>National Spine and Pain Centers</td>
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<tr>
<td></td>
<td>Diplomat of the American Board of Anesthesiology</td>
</tr>
<tr>
<td>Herriot Tabuteau, MD</td>
<td>Chairman</td>
</tr>
</tbody>
</table>

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Anticipated Upcoming Clinical and Regulatory Milestones

Regulatory and Commercial

**AXS-07**  
Migraine NDA, planned resubmission – 1H 2024

**AXS-14**  
Fibromyalgia NDA, planned submission – 4Q 2023 or 1Q 2024

Clinical Trial Readouts

**AXS-12**  
SYMPHONY Phase 3 trial in narcolepsy, completion – 4Q 2023

**AXS-05**  
ADVANCE-2 Phase 3 trial in Alzheimer’s disease agitation, completion – 1H 2024

**solriamfetol**  
FOCUS Phase 3 trial in adult ADHD, completion – 2H 2024

Clinical Trial Initiations

**AXS-05**  
Phase 2/3 trial in smoking cessation, initiation – 4Q 2023 or 1Q 2024

**solriamfetol**  
Phase 3 trial in binge eating disorder – 4Q 2023

**solriamfetol**  
Phase 3 trial in shift work disorder – 1Q 2024
Rapidly Growing, CNS-Focused Biopharma

- 2 Marketed Products
- 8 New Target Indications
- 162 Million Potential Patients Targeted
- 5 Late-stage Product Candidates
thank you

for more information, please contact:

mark jacobson
chief operating officer
212-332-3243
mjacobson@axsome.com
www.axsome.com