## AXSOME THERAPEUTICS

March 2017

#### 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 forwardlooking statements include risks and uncertainties, including, but not limited to, 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 and completion of the trials, interim analyses and receipt of interim results; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration or other regulatory authority approval of, or other action with respect to, our product candidates; the Company's ability to obtain additional capital necessary to fund its operations; the Company's ability to generate revenues in the future; 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; the enforceability of the Company's license agreements; the acceptance by the market of the Company's product candidates, if approved; and other factors, including general economic conditions and regulatory developments, not within the Company's control. These factors could cause actual results and developments to be materially different from those expressed in or implied by such statements. Forward-looking statements are not guarantees of future performance, and actual results may differ materially from those projected. The forward-looking statements are made only as of the date of this presentation and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, these projections, assumptions and estimates are necessarily subject to a high degree of uncertainty and risk.

## Developing novel therapies for CNS disorders.

Axsome is addressing growing markets, where current treatment options are limited or inadequate, by leveraging well-characterized compounds to create novel therapeutics to meet unmet medical needs and improve the lives of patients.

#### Our Candidates and Pipeline

- Two differentiated Phase 3-stage assets targeting significant and growing markets:
  - AXS-05: novel therapeutic combination with multiple mechanisms for CNS disorders
  - AXS-02: oral, non-opioid, long-acting, potentially first-in-class therapeutic for chronic pain
- Results from all 3 ongoing Phase 3 trials expected over the next 12 months.
- Novel indications, positive proofs of concept.
- Patent protection to 2034.
- Worldwide rights.

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05	Treatment Resista	nt Depression: Fast T	rack Granted	Initiated
(DM + BUP)	Agitation in Alzheir	ner's Disease		
AXS-02	CRPS: U.S. & E.U. (	Orphan Designation; Fa	st Track Granted	Initiated
(disodium zoledronate	Knee OA with BML	s: SPA Received; Fast	Track Granted	Initiated
tetrahydrate)	CLBP with MCs			
AXS-06	Pain			

Abbreviations: BUP = Bupropion; DM = Dextromethorphan; CRPS = Complex Regional Pain Syndrome; OA = Osteoarthritis; BML = Bone Marrow Lesions; SPA = Special Protocol Assessment; CLBP = Chronic Low Back Pain; MC = Modic Changes.

# + AXS-05

## Dextromethorphan (DM) + Bupropion (BUP)

Novel therapy for CNS disorders:

- Treatment Resistant Depression (TRD)
- Agitation in Alzheimer's Disease (AD)



## **CNS Disorders:** Mechanisms of Action

#### Pharmacodynamic Synergy

Mechanism of Action	DM	BUP	AXS-05 DM+BUP
NMDA Receptor Antagonist	1		<b>\</b>
Sigma-1R Agonist	1		<b>✓</b>
Norepinephrine Reuptake Inhibitor	1	/	<b>✓</b>
Serotonin Reuptake Inhibitor	1		<b>✓</b>
Dopamine Reuptake Inhibitor		/	<b>✓</b>
Nicotinic ACh Receptor Antagonist		1	<b>✓</b>

DM = Dextromethorphan; BUP = Bupropion.

✓ Present

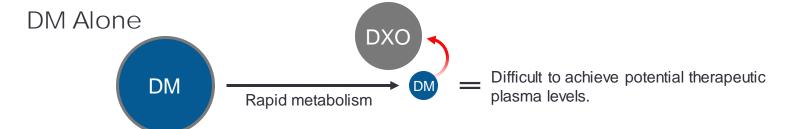
#### Mechanisms of Action and Relevant Indications

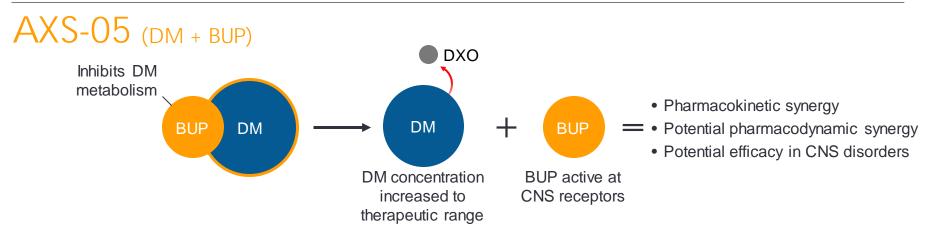
	Pha		odynamic ergy			var					ns¹	editor
Mechanism of Action	DM	BUP	AXS-05	P	OHO P	ntietal	the inte	1055) 1055)	or of	Pop	il Su	garage Related Agents <sup>2</sup>
NMDA Receptor Antagonist	1		<b>✓</b>									Ketamine     Memantine (Namenda®)
Sigma-1R Agonist	/		<b>✓</b>									<ul> <li>Fluvoxamine (Luvox®)</li> <li>Donepezil (Aricept®)</li> </ul>
Norepinephrine Reuptake Inhibitor	1	1	<b>✓</b>									<ul> <li>Duloxetine (Cymbalta®)</li> <li>Venlafaxine (Effexor®)</li> </ul>
Serotonin Reuptake Inhibitor	1		<b>✓</b>									<ul> <li>Escitalopram (Lexapro®)</li> <li>Fluoxetine (Prozac®)</li> <li>Sertraline (Zoloft®)</li> </ul>
Dopamine Reuptake Inhibitor		1	<b>✓</b>									Bupropion (Wellbutrin®)
Nicotinic ACh Receptor Antagonist		1	<b>✓</b>									• Bupropion (Wellbutrin®)
DM = Dextromethorphan; BUP = Bupropion.	<b>√</b> Pre	sent			Rel	evant	t					

<sup>1.</sup> Indications listed are associated with the mechanism of action and are not related to either DM or BUP, unless specifically noted.

<sup>2.</sup> Agents do not contain DM or BUP, unless specifically noted.

#### Novel Therapy for CNS Disorders





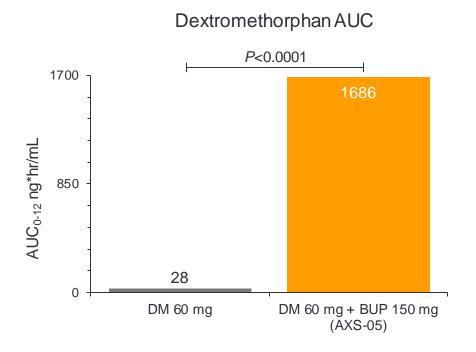
DM = Dextromethorphan; DXO = Dextrorphan; BUP = Bupropion.

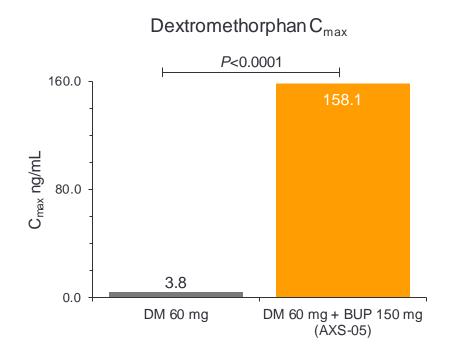
- Phase 1 trials with AXS-05 completed:
  - Significant increase in DM plasma levels.
- Phase 3 in TRD initiated.

#### **IP Overview**

• 17 issued patents – protection through 2034.

## **CNS Disorders:** PH 1 Results

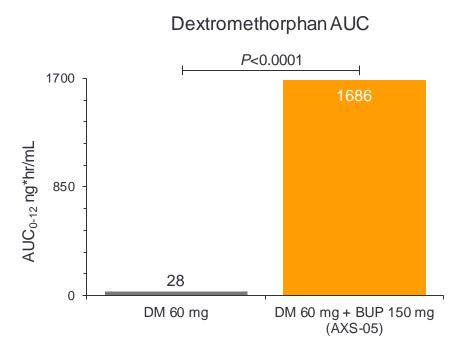




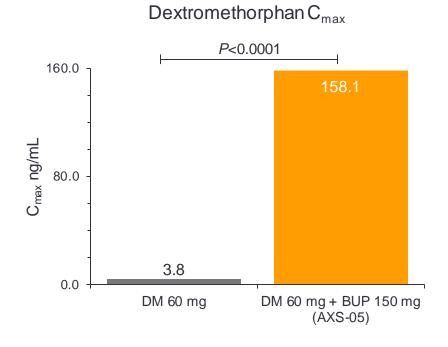
Axsome data on file. †DM, Dextromethorphan; BUP, Bupropion.



## **CNS Disorders:** PH 1 Results



Dose <sup>†</sup>	AUC <sub>0-12</sub> ng*hr/mL
DM 20 mg + Q 10 mg	525
DM 30 mg + Q 10 mg	883



Dose <sup>†</sup>	C <sub>max</sub> ng/mL		
DM 20 mg + Q 10 mg	53		
DM 30 mg + Q 10 mg	85		

Axsome data on file.

<sup>†</sup> Nuedexta® NDA 021879, FDA Clinical Pharmacology Review . DM, Dextromethorphan; Q, Quinidine; BUP, Bupropion.



#### TRD Overview

- Major Depressive Disorder (MDD) is a leading cause of disease burden in the US.<sup>4</sup>
- 63% and 44% of MDD patients have inadequate response to initial therapy and second line therapy, respectively.<sup>2</sup>
- Only 1 approved drug for TRD = unmet medical need.
- AXS-05 combines the MOA of 4 distinct anti-depressant drug classes into one novel oral therapeutic.
- DM antidepressant effects demonstrated preclinically and clinically.
- Phase 3 ongoing.

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05	Treatment Resista	nt Depression		Initiated

- 1. Marcus SC, Olfson M. Arch Gen Psychiatry 2010;67:1265-1273.
- 2. Rush AJ, et al. Am J Psychiatry 2006;163:1905-1917.
- 3. U.S. Census Bureau, Population April 1, 2010 to July 1, 2013.
- 4. Mathers CD, PLoS Med 2006; 3(11): e442.

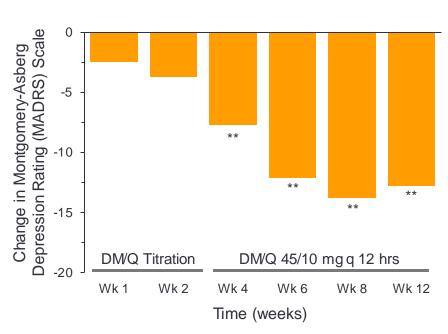




## **CNS Disorders:**TRD Clinical Rationale

• DM and metabolic inhibitor reduce depressive symptoms in TRD and in AD.

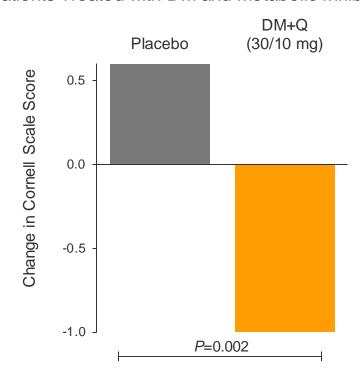
Symptom Reduction in TRD Patients
Treated with DM and Metabolic Inhibitor<sup>1</sup>



- Failed 2 to 10 prior treatments
- 45% of patients had ≥ 50% reduction in MADRS

- 1. Murrough, et al., ACNP 2016.
- 2. Cummings J, et al. JAMA. 2015;314:1242-1254.

Depressive Symptom Reduction in AD Agitation Patients Treated with DM and Metabolic Inhibitor<sup>2</sup>



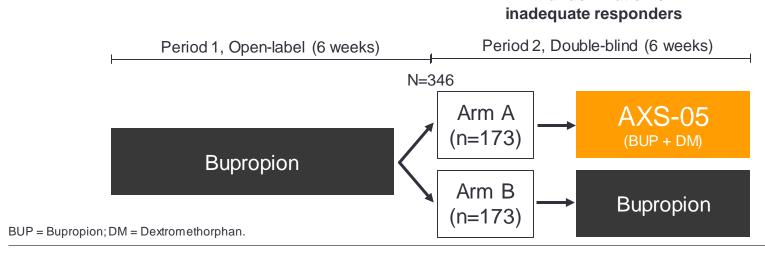
<sup>\*\*</sup> P<0.01 versus baseline

## CNS Disorders: TRD Phase 3 Design



A Phase 3 trial to assess the efficacy and safety of AXS-05 in the treatment of TRD.

1:1 randomization of



- **Primary Endpoint:** Change in depression score from randomization to end of study, measured using the Montgomery-Asberg Depression Rating Scale (MADRS).
- Key Inclusion Criteria:
  - Male or female 18-65 years old
  - History of inadequate response to 1 or 2 adequate antidepressant treatments

#### Agitation in AD Overview

- Agitation and aggression seen in approximately 45% of AD patients during 5-year period.<sup>3</sup>
- Characterized by emotional distress, aggressive behaviors, disruptive irritability, disinhibition, and caregiver burden.<sup>4</sup>
- Associated with<sup>4,5</sup>:
  - Accelerated cognitive decline
  - Earlier nursing home placement
  - Increased mortality
- No approved medication = unmet medical need.
- Proof of concept: DM plus metabolic inhibitor reduced agitation in AD patients.
- FDA clearance received for IND for Phase 2/3 trial.

Product Candidate	Preclinical Preclinical	Phase 1	Phase 2	Phase 3
AXS-05	Agitation in Alzheir	ner's Disease		

<sup>1.</sup> Ryu, SH, et al. Am J Geriatr Psychiatry. 2005;13:976-983.



<sup>2.</sup> Hebert, LE, et al. Neurology. 2013;80:1778-1783.

<sup>3.</sup> Steinberg M, et al. Int J Geriatr Psychiatry. 2008;2:170-177.

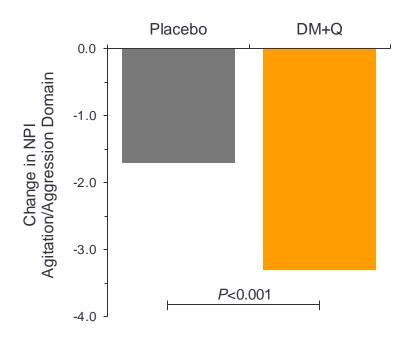
<sup>4.</sup> Antonsdottir IM, et al. Expert Opin Pharmacother. 2015;11:1649-1656.

<sup>5.</sup> Rabins PV et al. Alzheimers Dement. 2013; 9:204-207.

#### Agitation in AD Clinical Rationale

- Randomized, double-blind, placebocontrolled, two-stage trial.
  - Placebo (n=125), 30 mg DM + 10 mg quinidine (Q) (n=93), for stage 1.
- DM+Q treatment reduced agitation/ aggression in AD by 46% vs. 24% for placebo (P<0.001)—primary endpoint.</li>
- Statistically significant improvement in multiple secondary endpoints.
- DM plasma levels achieved with AXS-05 in target therapeutic range.
- Potential for additional contribution from bupropion component of AXS-05.

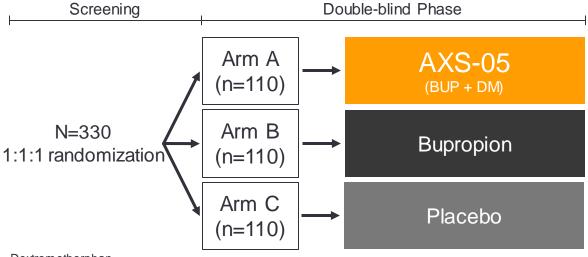
Change in Agitation/Aggression Scores in AD with DM and Metabolic Inhibitor Quinidine (Q)



Cummings J, et al. *JAMA*. 2015;314:1242-1254.

#### Agitation in AD Phase 2/3 Design

A Phase 2/3 trial to assess the efficacy and safety of AXS-05 in the treatment of Agitation in AD.



BUP = Bupropion; DM = Dextromethorphan.

- Primary Endpoint: Cohen-Mansfield Agitation Inventory (CMAI)
- Key Inclusion Criteria:
  - Diagnosis of probable Alzheimer's disease
  - Clinically significant agitation

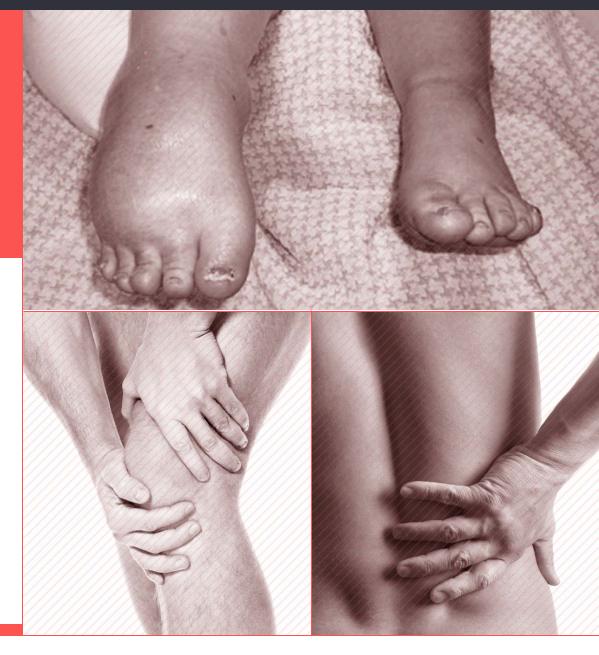
# AXS-02

### Disodium Zoledronate Tetrahydrate

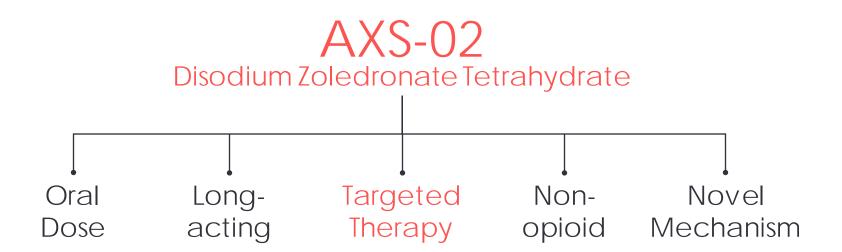
Novel therapy for chronic pain:

- Complex Regional Pain Syndrome (CRPS)
- Knee Osteoarthritis (OA) with Bone Marrow Lesions (BMLs)
- Chronic Low Back Pain (CLBP)
   with Modic Changes (MCs)

CRPS image source: Voet C, et al. F1000Reseach. 2014;3:97.



## Chronic Pain: Differentiated Therapy

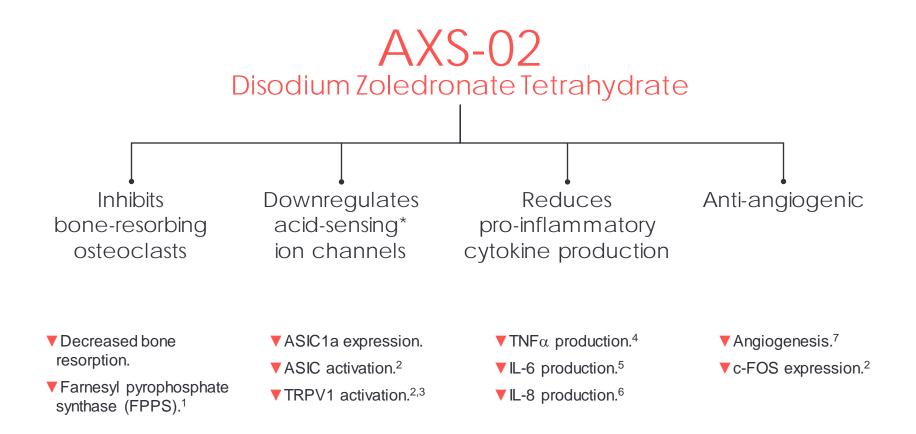


#### **IP Overview**

- 37 issued patents\* protection through 2034.
- Drug delivery, pharmacokinetic, composition of matter, and method of use claims.
- U.S. Orphan Drug Designation (7 years exclusivity).
- E.U. Orphan Medicinal Product Designation (10 years exclusivity, 12 years with PIP).

<sup>\*</sup>Claims\_cover AXS-02 and related substances and disease indications.

#### Chronic Pain: Therapy via Multiple Mechanisms of Action



<sup>\*</sup> Acid is a well known cause of pain.

<sup>1.</sup> Green JR, Rogers MJ. Drug Dev Res. 2002;55:210-24.

<sup>2.</sup> Nagae M, et al. Bone. 2006;39:1107-15.

<sup>3.</sup> Abe Y. et al. J Bone Miner Metab. 2015:33:125–134.

<sup>4.</sup> Wolf AM, et al. Haematologica. 2006;91:1165-71.

<sup>5.</sup> Derenne S, et al. Bone Miner Res. 1999;14:2048-56.

<sup>6.</sup> Stathopoulos GT, et al. Am J Respir Crit Care Med. 2008;178:50-9.

<sup>7.</sup> Misso G. et al. Cancer Biol Ther. 2012:13:1491-500.

#### Chronic Pain: Lead Indications and Market Potential

#### Complex Regional Pain Syndrome (CRPS)

- Localized bone resorption. 1,2
- Increased pro-inflammatory cytokines.<sup>3</sup>

## 80,000 new cases per year in the U.S.4

- 1. Capello ZJ, et al. J Hand Surg Am. 2012;37:288-296.
- 2. Krämer HH, et al. Pain. 2014;155:889-895.
- 3. Parkitny L, et al. Neurology. 2013;80:106-117.
- 4. Moseley GL, et al. J Pain. 2014;15:16-23.
- 5. Driban JB. et al. Arthritis Res Ther. 2013:15:R112.
- 6. Hunter DJ. et al. Arthritis Res Ther. 2009:11:R11.
- 7. Kazakia GJ, et al. Osteoarthritis Cartilage. 2013;21:94-101.
- 8. Zhang Y, et al. Eur Spine J. 2008;17:1289-1299.

Knee Osteoarthritis (OA) with Bone Marrow Lesions (BMLs)

- BMLs are associated with pain in knee OA.<sup>5</sup>
- BMLs: Increased bone turnover; Decreased bone mineral density.<sup>6,7</sup>

7 M patients in the U.S.<sup>11-14,16</sup>

Chronic Low Back Pain (CLBP) with Modic Changes (MCs)

- MCs are associated with low back pain.<sup>8</sup>
- MCs: Increased bone turnover, pro-inflammatory cytokines, vascular density.<sup>9,10</sup>

1.6 M patients in the U.S.<sup>11,12,15,16</sup>

- 9. Järvinen J, et al. *Spine: ISSLS Society Meeting Abstracts*. Oct. 2011(vol suppl, abstract GP127).
- 10. Rahme R, Moussa R. Am J Neuroradiol. 2008;29:838-42.
- 11. Law rence RC, et al. Arthritis Rheum. 2008;58:26-35.
- 12. Zhang Y, Jordan. JM Clin Geriatr Med. 2010;26:355-69.
- 13. Tanamas SK, et al. Rheumatology. 2010;49:2413-19.
- 14. Guermazi A, et al. BMJ. 2012;345:e5339.
- 15. Jensen OK, et al. Spine J. Feb. 14, 2014;pii:S1529-9430(14)00214-9.
- 16. U.S. Census Bureau, Population April 1, 2010 to July 1, 2013.

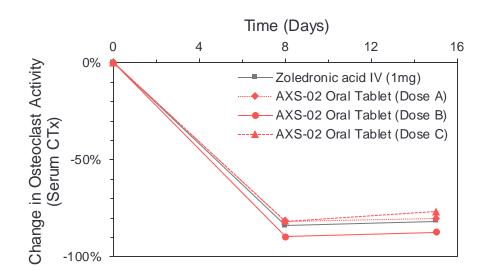
#### Phase 1 Results and Oral Preference

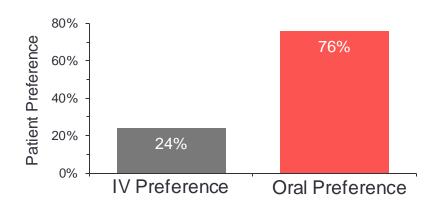
#### **Phase 1 Summary**

- Oral administration of AXS-02 resulted in rapid absorption of zoledronic acid.
- Significant plasma levels attained.
- Robust pharmacodynamics (PD) effects.
- PD relevant to targeted pain indications.
- AXS-02 was well tolerated.

#### Patient-stated Preference for Oral vs IV1,2

- Assessed in 6,097 patients treated 3 years with oral or IV bisphosphonates:
  - Oral: clodronate or ibandronate, daily
  - IV: zoledronic acid, monthly, then every 6 months
- Oral preference at randomization and therapy completion: 76%, 73% respectively.
- Potential safety advantage.





- 1. Gralow, et al. J Clin Oncol. 33, 2015 (suppl; abstr 503).
- 2. Gralow, et al. *J Clin Oncol*. 32.5, 2014 (suppl; abstr 558).

#### **CRPS** Overview

- Severe, continuous, disabling pain in a limb:
  - Sensation described as burning, stabbing, grinding, throbbing
- Localized bone resorption,<sup>1,2</sup> increased pro-inflammatory cytokines.<sup>3</sup>
- Common pain meds (e.g., NSAIDs, opioids, gabapentin) are considered ineffective.<sup>4</sup>
- No approved drug = high unmet need.
- Phase 3 ongoing.
- Issued U.S. patents: protection into 2034 uses of oral zoledronic acid for CRPS.





Orphan Disease

80,000 new cases per year in the U.S.5

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-02	CRPS: U.S. & E.U. (	Orphan Designation; Fa	st Track Granted	Initiated

<sup>\*</sup> Goebel A, Complex regional pain syndrome in adult. *Rheumatology (Oxford)*. 2011;50(10):1739-1750, by permission of Oxford University Press.

<sup>\*\*</sup> Sampath S, et al. Indian J Nucl Med.2013; Jan-Mar; 28(1):11–16.

<sup>1.</sup> Capello ZJ, et al. J Hand Surg Am. 2012;37:288-296.

Krämer HH, et al. Pain. 2014;155:889–895.

<sup>3.</sup> Parkitny L, et al. Neurology. 2013;80:106-117.

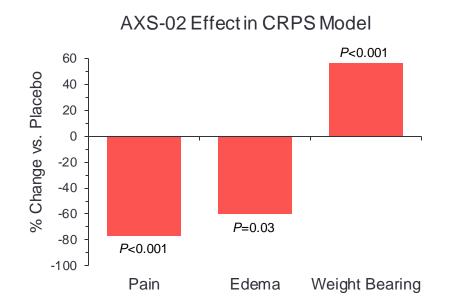
<sup>4.</sup> Bruehl S. Anesthesiology. 2010;113:713-725.

Moseley GL, et al. J Pain. 2014;15:16-23.

#### **CRPS** Preclinical and Clinical Rationale

#### Preclinical:

- Well validated CRPS model replicates: Inciting trauma, clinical presentation, natural history, and pathologic changes.
- Oral administration of AXS-02: Significant pain and edema reduction; improved weight bearing.



#### Clinical:

- Clinical Trials: 5 randomized, double-blind, placebo-controlled trials, with 4 different bisphosphonates.<sup>1-5</sup>
- Pain reduction: Mean 54% reduction in VAS pain scores (range 33% to 66%) during double-blind phases.
- Statistical significance: *p*<0.0001, *p*=0.001, *p*<0.01, *p*<0.05, *p*=0.048.
- Potency of bisphosphonates: 1/1000 to 1/20 potency of AXS-02.6

<sup>1.</sup> Adami S, et al. Ann Rheum Dis. 1997;56:201-204.

<sup>2.</sup> Varenna M, et al. J Rheumatol. 2000;27:1477-1483.

Robinson JN, et al. Pain Med. 2004;5:276-280.

<sup>4.</sup> Manicourt DH, et al. Arthritis Rheum. 2004;50:3690-3697.

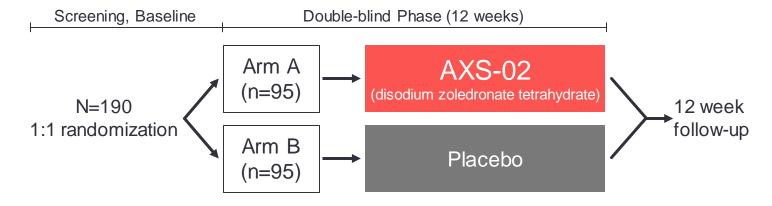
<sup>5.</sup> Varenna M, et al. Rheumatology (Oxford). 2013;52:534-542.

<sup>6.</sup> Green JR, Rogers MJ. Drug Dev Res. 2002;55:210-224.

#### Chronic Pain: CRPS Phase 3 Design



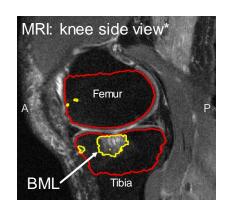
A Phase 3 trial to assess the efficacy and safety of AXS-02 in the treatment of pain associated with CRPS type 1.



- **Primary Endpoint:** Change in pain intensity from baseline to week 12, measured using the 0-10 Numerical Rating Scale (NRS).
- Key Inclusion Criteria:
  - Male or female ≥18 years old, recently diagnosed with CRPS type 1
  - Average NRS pain intensity score of ≥5
- Dosage: Once per week for six weeks; no drug for last six weeks.
- Interim analysis: When half of patients have completed double-blind phase.

#### Knee OA with BMLs Overview

- Bone marrow lesions (BMLs) on MRI are associated with pain in knee osteoarthritis (OA).<sup>1</sup>
- BMLs are regions of increased bone turnover, and reduced mineral density.<sup>2,3</sup>
- Zoledronic acid inhibits bone resorption and increases mineral density.
- Phase 2 results: Zoledronic acid reduced pain and BML size in patients with knee osteoarthritis.
- Phase 3 being conducted under Special Protocol Assessment (SPA).
- Issued U.S. patents: protection into 2034 uses of zoledronic acid for knee pain.





Product Candidate	Preclinical Preclinical	Phase 1	Phase 2	Phase 3
AXS-02	Knee OA with BML	s: SPA Received; Fast	Track Granted	Initiated

<sup>\*</sup> MRI showing BML in medial tibia from Driban, et al. Arthritis Res Ther. 2013;15:R112.

<sup>1.</sup> Driban JB. et al. Arthritis Res Ther. 2013:15:R112.

<sup>2.</sup> Hunter DJ. et al. Arthritis Res Ther. 2009:11:R11.

<sup>3.</sup> Kazakia GJ, et al. Osteoarthritis Cartilage. 2013;21:94-101.

<sup>4.</sup> Law rence RC. et al. Arthritis Rheum. 2008:58:26-35.

<sup>5.</sup> Zhang Y, Jordan. JM Clin Geriatr Med. 2010;26:355-69.

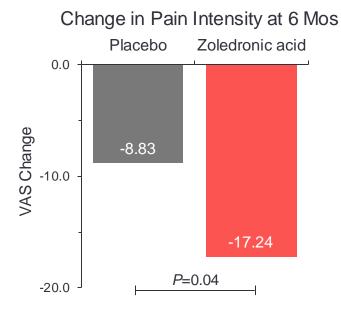
<sup>6.</sup> Tanamas SK, et al. Rheumatology. 2010;49:2413-19.

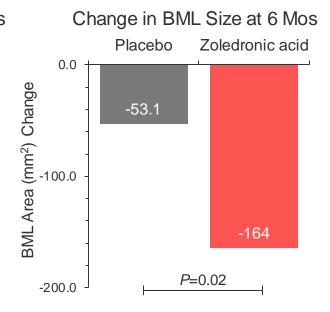
<sup>7.</sup> Guermazi A, et al. BMJ. 2012;345:e5339.

<sup>8.</sup> Jensen OK, et al. Spine J. Feb. 14, 2014;pii:S1529-9430(14)00214-9.

<sup>9.</sup> U.S. Census Bureau, Population April 1, 2010 to July 1, 2013.

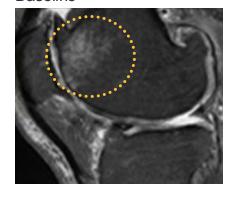
#### Knee OA with BMLs Phase 2 Results



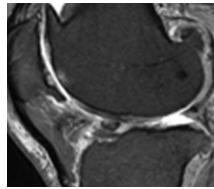


BML at Baseline and Post Zoledronic Acid Treatment

Baseline



6 Months Post Treatment



- Randomized, double-blind, placebo-controlled trial (N=59):
  - Placebo (n=28), zoledronic acid IV (n=31)
- Primary endpoints:
  - Pain intensity measured using 100-mm VAS
  - BML size on MRI

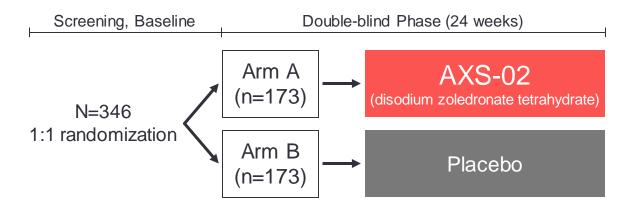
Laslett LL, et al. *Ann Rheum Dis.* 2012;71:1322-8. MRI images courtesy of Prof. Graeme Jones.

#### Knee OA with BMLs Phase 3 Design



A Phase 3 trial to assess the efficacy and safety of AXS-02 in the treatment of pain of knee OA associated with BMLs.

Special Protocol Assessment (SPA) received



- **Primary Endpoint:** Change in pain intensity from baseline to week 24, measured using the 0-10 Numerical Rating Scale (NRS).
- Key Inclusion Criteria:
  - Male at least 50 years of age or postmenopausal female, with knee OA and BMLs
  - Moderate or worse knee pain
- Dosage: Once per week for six weeks; no drug for remainder of double-blind phase.
- Interim analysis to be performed on the first approximately 60 subjects enrolled.

#### **CLBP** with MCs Overview

- Modic changes (MCs) type 1 (M1) on MRI are associated with chronic low back pain (CLBP).<sup>1</sup>
- Increased bone turnover on bone scan is seen in M1 lesions.<sup>2</sup>
- Increased pro-inflammatory cytokines, and vascular density seen in M1 lesions.<sup>3</sup>
- Zoledronic acid reduces bone turnover, suppresses the production of inflammatory mediators, and is anti-angiogenic.
- Phase 2 results: Zoledronic acid reduced pain in patients with CLBP
- FDA clearance received for IND for Phase 3 trial initiation contingent upon resources.
- Issued U.S. patents: protection into 2034 uses of oral zoledronic acid for low back pain.



1.6 M patients in the US 4-7

Product Candidate	   Preclinical	Phase 1	Phase 2	Phase 3
AXS-02	CLBP with MCs			

<sup>\*</sup> MRI showing modic type 1 lesions from Luoma K, et al. European Congress of Radiology (ECR). 2014; Poster B-0458.

<sup>1.</sup> Zhang Y, et al. Eur Spine J. 2008;17:1289-1299.

Järvinen J, et al. Spine: ISSLS Society Meeting Abstracts. Oct. 2011; Volume Suppl, Abstract GP127.

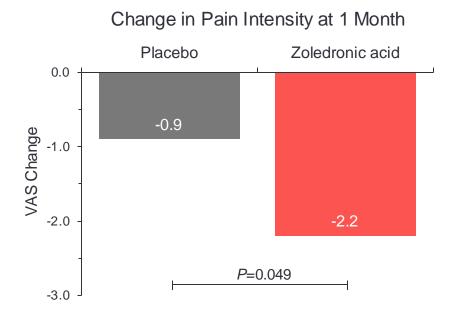
<sup>3.</sup> Rahme R, Moussa R. Am J Neuroradiol. 2008;29:838-42.

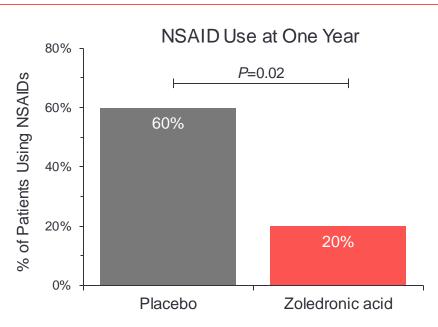
<sup>4.</sup> Law rence RC. et al. Arthritis Rheum. 2008:58:26-35.

<sup>5.</sup> Zhang Y, Jordan. JM Clin Geriatr Med. 2010;26:355–69.

Jensen OK, et al. Spine J. Feb. 14, 2014;pii:S1529-9430(14)00214-9.7. U.S. Census Bureau, Population April 1, 2010 to July 1, 2013.

#### **CLBP** with MCs Phase 2 Results

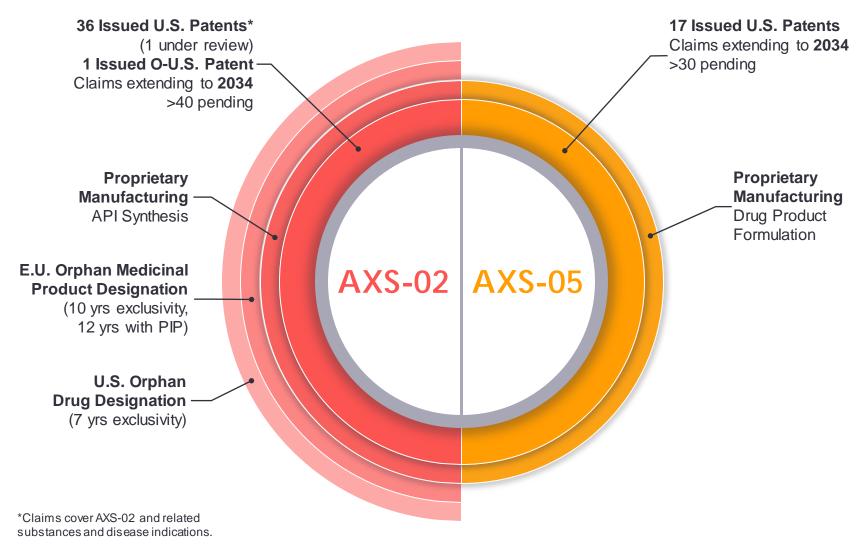




- Randomized, double-blind, placebo-controlled trial (N=40):
  - Placebo (n=20), zoledronic acid IV (n=20)
- Primary endpoint: Pain intensity measured using 10-cm VAS.

Axsome data on file.

#### **Barriers to Entry**



#### **Our Team**

#### Management

Herriot Tabuteau, MD Founder & CEO



Connie Ames, CPA VP, Finance

Mark Jacobson, MA VP, Operations













#### **Board of Directors**

Wellcome

Roger Jeffs, PhD
Former President, Co-CEO, Director
United Therapeutics Corp.
Prior positions at Amgen, and Burroughs

Mark Saad
Former CFO
Bird Rock Bio, Inc.
Former COO of the Global Healthcare
Group at UBS

Mark Coleman, MD
Medical Director
National Spine and Pain Centers
Diplomat of the American Board of
Anesthesiology

Herriot Tabuteau, MD Chairman

#### **Key Financial Information**

\$36.6 Million
\$10.0 Million
19,158,417
2,109,746

• **Financial guidance**: Cash anticipated to fund operating requirements through the first quarter of 2018.

<sup>2.</sup> Consists of 1,772,050 options and 337,696 warrants.



<sup>1.</sup> Excludes debt discount of \$0.3 million.

#### **Anticipated Near-Term Clinical Milestones**

Product Candidate	Indication	1H 2017	2H 2017	1H 2018
AXS-05	TRD	√ Fast Track designation		• STRIDE-1 top-line results (1Q)
(DM + BUP)	AD Agitation	✓ Ph 2/3 IND FDA clearance		
		• Ph 2/3 trial start (2Q)		
	CRPS		CREATE-1 interim efficacy analysis readout (4Q)	
AXS-02 (disodium zoledronate tetrahydrate)	Knee OA		COAST-1 interim analysis readout (3Q)	
.c.anyanato)	CLBP	✓ Ph 3 IND FDA clearance		

Abbreviations: AD = Alzheimer's Disease; BUP = Bupropion; CLBP = Chronic Low Back Pain; CRPS = Complex Regional Pain Syndrome; DM = Dextromethorphan; OA = Osteoarthritis; TRD = Treatment Resistant Depression.



<sup>✓</sup> Accomplished milestone.

<sup>•</sup> Upcoming milestone.

## AXSOME THERAPEUTICS

#### Thank you.

For more information, please contact

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